RECEPTIVITY TO BARIATRIC SURGERY IN QUALIFIED PATIENTS

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Abstract

Although bariatric surgery has been demonstrated to be the most effective weight loss intervention, there are low levels of interest among qualified individuals. The aim of this thesis was to examine the factors related to interest in bariatric surgery. Patients of the Wharton Weight Management Clinic who qualified for bariatric surgery were asked to complete an elective questionnaire. Of the 371 patients, 23% were interested in bariatric surgery. Participants who were interested in bariatric surgery had greater weight loss expectations from surgery, higher BMI, stronger social support and receptivity to surgery, but had less financial concerns and success in previous weight loss attempts ($P<0.05$). Even though all patients overestimated the weight loss effect of bariatric surgery, there is still a low interest in surgery and this may be related to social and financial factors, and the notion that bariatric surgery should only be done after other efforts have failed.

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1.0 General Introduction

The increasing prevalence of obesity is a critical public health issue as obesity is associated with increased risk of multiple comorbidities, increased mortality risk, and higher healthcare costs[1–3]. Current treatment guidelines recommend weight loss for all obese individuals[2]. While both lifestyle and pharmacological interventions have been reported to be associated with the 5-10% body weight loss that is recommended for attaining health benefits[4–6], individual expectations for weight loss generally far exceed this[7]. In fact, individuals report desired weight loss of 38%[7], which even exceeds the expected 15-25% weight loss seen with bariatric surgery[8,9]. In fact, unlike lifestyle and pharmacological interventions, bariatric surgery is the only obesity intervention that is effective long-term for weight loss and lowers mortality risk[8,10,11]. However, very few individuals who are qualified for bariatric surgery are interested in the procedure[12]. It is currently unclear why there is such low receptivity to bariatric surgery.

The objective of this thesis was to identify factors that are associated with interest in bariatric surgery in qualified individuals. It is unclear from previous studies if there are differences in the motivating factors behind those who are interested versus those not interested in bariatric surgery.

2.0 Review of Related Literature

Introduction

Obesity and obesity related comorbidities are a growing public health concern. However, traditional methods of weight loss through lifestyle interventions including diet and physical activity have been shown to be ineffective when considering follow ups greater than 1 year[4,5]. Curioni et al. report that nearly half of participants experience weight regain within 1 year after intervention[13]. Furthermore, a study examining the National Weight Control Registry reports that only 20% of participants are successful at maintaining a weight loss greater than or equal to 10% of initial body weight for longer than 1 year[14]. This is troubling as weight cycling, or repeated weight loss followed by weight regain, may have detrimental effects on body composition[15,16], as well as increased risk for metabolic syndrome[17,18]. Limited success has also been demonstrated with pharmacotherapy with modest weight loss when compared to placebo (8.8% vs 5.8% of body weight loss)[6]. Additionally, Padwal et al. report that pharmacotherapy interventions have high attrition rates (33%-48%) and efficacy of less than 5% of body weight loss when compared to placebo[19]. Bariatric surgery, comparatively, has been shown to be a much more effective intervention for weight loss, diabetes management, dyslipidemia, and reducing mortality risk[8,10,11,20].

Bariatric Surgery Interventions

Bariatric surgery involves the surgical reconfiguration of the digestive system to reduce the effectiveness of nutrient absorption or restrict total gastric volume to induce weight loss[21–23].

The two most common forms of bariatric surgery currently are Roux-en-Y gastric bypass (RYGB) and adjustable gastric banding (AGB)[24]. RYGB is currently the only surgery that is covered by all Canadian provincial health insurance plans[23], while the Ontario Health Insurance Plan (OHIP) also covers vertical sleeve gastrectomy[22]. The Ontario Health Technology Advisory Committee recommends that bariatric surgery should be considered for individuals who have been unsuccessful at weight loss with nonsurgical interventions with at least a BMI of 40 kg/m^2 or a BMI of 35 kg/m^2 or greater with comorbidities[22].

Bariatric Surgery Outcomes

The effectiveness of bariatric surgery for weight loss and long-term weight maintenance has been long studied[8,20]. The Swedish Obese Subjects Study reports that the bariatric surgery group had a greater reduction in body weight as compared to the non-surgery control group at 2 years (-23.4% vs 0.1%, $p < 0.001$) and 10 years (-16.1% vs 1.6%, $p < 0.001$) follow-up[8]. Furthermore, while primarily considered a weight loss intervention, bariatric surgery has more recently also been shown to be associated with improvements of several obesity related comorbidities[8,25]. Individuals who underwent bariatric surgery had superior rates of remission from type 2 diabetes, hypertriglyceridemia, low HDL, and hypertension when compared to a non-surgery control group[8,25]. This effect on obesity related comorbidities is thought to be due to a variety of consequences of bariatric surgery including reduced caloric intake, reduced nutrient absorption, reduced body fat percentage, modified gut hormone signaling, and changes in gut microbiome[11,26–28]. In comparison to more traditional interventions, Mingrone et al. report that bariatric surgery is a more effective intervention for both weight loss and glycemic control than a

combined lifestyle and drug intervention[10]. Furthermore, undergoing bariatric surgery reduces the risk of mortality in severely obese individuals with an 82% reduction in mortality risk for patients who underwent surgery when compared to a non-surgery control group[29,30]. Comparing patients who underwent surgery to a non-surgery control group, mortality due to diabetes, heart disease, and cancer is reduced by 92%, 56%, and 60% respectively[30]. When considering the effect on weight loss, obesity related comorbidities, and mortality, bariatric surgery is the most effective intervention that is currently available.

Bariatric Surgery Complications, Side Effects, and Impressions

As with any surgical procedure, there are possible complications. Common adverse events include vomiting, dumping syndrome, dehydration, gallstone formation, and vitamin B12 and iron deficiency[31,32]. Furthermore, in a study of 4776 patients undergoing bariatric surgery, 0.3% of patients died within 30 days of surgery, while 4.1% of patients had a severe adverse outcome including deep vein thrombosis, venous thromboembolism, re-intervention, or failure to be discharged within 30 days after surgery[33]. However, bariatric surgery is still a relatively safe intervention. Comparatively, knee and hip replacement surgery has a higher risk of 30 day mortality after surgery at 1%[34]. Despite the relative safety of bariatric surgery, many individuals qualified for bariatric surgery still have negative impressions about the efficacy and safety of this intervention[12].

Thus, although bariatric surgery is possibly the most effective intervention for weight loss, obesity related comorbidities, and reduction in mortality risk, there are still very low levels of interest in the procedure. In a study of 77 severely obese patients, 57% were not interested in

bariatric surgery with 45% of patients citing risk of death and complications as a reason they were opposed to surgery[12]. However, it remains unclear what the major motivating factors were for those who were interested in surgery, and how this might differ from those not interested. Furthermore, participants in this study were hospitalized or visiting clinics for reasons not related to bariatric surgery and it is unclear if existing health conditions influenced the responses in this study. On the other hand, the Brantly et al. report that the top reasons for considering surgery were listed as health concerns (52%) and obesity related comorbidities (28%)[35]. Very few participants listed physical fitness (5%), appearance (4%), or insurance coverage (4%) as a motivating factor[35]. However, this study only examined participants who were already approved and proceeding with surgery and it remains unclear how the motivating factors for those who were not interested in a surgical intervention differed.

Motivating Factors Driving Receptivity to Bariatric Surgery in Qualified Individuals

The belief that weight loss is achievable without surgery and fear of other complications from surgery may be preventing patients from considering bariatric surgery. However, non-surgical weight loss interventions have been shown to be largely ineffective. As weight gain and weight cycling have been demonstrated to be associated with increased health risk, it may be important to consider surgical interventions for improved weight loss, weight maintenance, and prevention of obesity related comorbidities.

Thus, the objective of this thesis study was to identify factors that are associated with receptivity to bariatric surgery in qualified individuals. Our current study seeks to expand on previous research by examining the motivating factors behind those who are interested as well as those not interested in bariatric surgery. The findings from this study will have important clinical implications for patients and health care providers by providing insight on the factors that may be driving receptivity to bariatric surgery and where additional resources may be required.

3.0 Manuscript

Receptivity to Bariatric Surgery in Qualified Patients

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Abstract

Objectives: Bariatric surgery has been shown to be an effective intervention for weight loss and diabetes management. Despite this, many patients qualified for bariatric surgery are not interested in undergoing the procedure. The objective of this study is to determine the factors associated with interest in bariatric surgery among those who qualify for the procedure.

Methods: Participants selected for this study were patients of the Wharton Medical Clinic (WMC) who qualified for bariatric surgery. Participants were asked to complete an elective research questionnaire between February 2013 and April 2014.

Results: A total of 371 patients (72% female) completed the questionnaire. Only 87 (23%) participants were interested in bariatric surgery. Individuals interested in bariatric surgery had a higher BMI than those not interested (48.0 versus 46.2 kg/m^2, p=0.03). Individuals interested in bariatric surgery believed that they would lose more weight with surgery than those not interested (51 versus 44 kg, p=0.0069). Those who scored highly on past weight loss success or financial concerns were less likely to be interested in bariatric surgery, whereas those who scored highly on receptivity to surgery and positive social support regarding surgery were more likely to be interested in bariatric surgery.

Conclusion: Although respondents overestimated the effect of bariatric surgery on weight loss, most were still not interested in bariatric surgery. Individuals who scored highly on statements regarding receptivity to surgery or positive social support regarding surgery were more likely to be interested in bariatric surgery

3.1 Introduction

In Canada, the rate of overweight and obesity in the adult population are 59% and 23% respectively[2]. Obesity has been demonstrated to be associated with a variety of conditions and comorbidities including stroke, dyslipidemia, type 2 diabetes, hypertension, osteoarthritis and increased mortality risk[1,2] as well as higher healthcare expenditure[3].

As a modest weight loss of 5-10% body weight is demonstrated to improve fasting plasma glucose, HbA1c, CVD risk, and other obesity related comorbidities[36], Canadian guidelines recommend weight loss for overweight or obese adults[2]. However, traditional methods of weight loss through lifestyle interventions including diet and physical activity have been shown to be ineffective when considering follow up lengths of greater than 1 year[4,5]. Limited weight loss success has also been reported with pharmacotherapy with or without lifestyle interventions[6]. Bariatric surgery, comparatively, has been shown to be a much more effective intervention for weight loss, diabetes management, dyslipidemia, and reducing mortality risk[8,10,11]. However, many individuals qualified for bariatric surgery have negative impressions about the efficacy and safety of surgical weight loss interventions[12].

As such, this study aims to identify the factors associated with receptivity to bariatric surgery in qualified individuals. This study seeks to expand on previous research by examining the motivating factors behind those who are interested as well as those not interested in bariatric surgery.

3.2 Methods

The Wharton Medical Clinic (WMC) is a referral based weight and diabetes management clinic. All patients are referred by a family or specialist physician to participate in the weight management program. The program is covered by the Ontario Health Insurance Plan (OHIP) and all services including physician visits, nutritional consultation, exercise prescription, cardiorespiratory fitness testing, blood work, and educational sessions are provided with no additional charge to patients. The multidisciplinary team includes physicians, nutritionists, and bariatric educators. The program focus is on educating overweight and obese individuals on weight management and healthy lifestyle through lifestyle modification. Bariatric surgery is not performed at WMC; however WMC physicians provide consultations on bariatric surgery for qualified patients and physicians are able to make referrals if a patient is interested. Visits to the clinic continue leading up to the surgery as well as post-surgery for additional support. All participants freely gave their full informed written consent for the use of their questionnaire data and medical data for research purposes. Access to this medical data was facilitated by collaboration between York University and the WMC. The study protocols were reviewed and approved by York University's Ethics Review Board.

Participants selected for this study were qualified for bariatric surgery with a BMI of 40 kg/m^2 or greater or a BMI of 35 kg/m^2 or greater and obesity related comorbidities such as diabetes, high blood pressure, or an elevated lipid profile. Participants were recruited from clinic locations within Ontario, including Burlington, Hamilton, Stoney Creek, Toronto, and Etobicoke. These patients completed a 2 page questionnaire evaluating receptivity to bariatric surgery following a bariatric surgery educational consultation administered by a WMC physician.

Questionnaires were completed on a rolling basis starting February 2013. Participants with missing BMI (n=29) were excluded from this analysis.

Data was analyzed using SAS 9.4. Differences between groups were assessed using t-tests and chi-square test for continuous and categorical variables respectively. Survey responses regarding receptivity to bariatric surgery based on rating scale (1 = strongly disagree, 5 = strongly agree) were categorized into four groups: past weight loss success, receptivity to surgery, positive social support for surgery, and financial concerns regarding surgery. Where necessary, scores were inverted to match category direction. Once categorized, scores were summated and standardized to a scale of 5. Poisson regression was used to determine the relative risk between interest in bariatric surgery and the four thematic categories. This analysis was adjusted for BMI, age, and sex.

3.3 Results

Table 1 presents the respondent characteristics of the sample (N=371). Only 87 (23%) participants were interested in bariatric surgery. Participants had a mean age of 48.0 ± 11.4 years, weight of 136.4 ± 25.7 kg, and BMI of 48.4 ± 6.8 kg/m^2. The prevalence of type 2 diabetes was 11%. The sample is predominately white (79%), and female (72%). There were no significant differences in sex, ethnicity, age or prevalence of type 2 diabetes between those interested and not interested in bariatric surgery (P>0.05). Individuals interested in bariatric surgery had a higher BMI than those not interested (48.0 versus 46.2 kg/m^2, P=0.03). Additionally, individuals interested in bariatric surgery believed that they would lose more weight with surgery than those not interested (51 versus 44 kg, p=0.0069 or 37% versus 33% of body weight, p=0.01).

The top cited reasons for not being interested in bariatric surgery (**Table 2**) are fear of other complications from surgery (51.1%), that they did not need surgery to lose weight (32.0%), and fear of dying (24.6). Among those not interested in bariatric surgery, only 7.7% of respondents stated that they did not believe that bariatric surgery would work. The top cited reasons for being interested in bariatric surgery (table 2) are health benefits (94.3%), greater weight loss (89.7%), and improved mobility (85.1%).

The mean scores for Likert scale questions regarding bariatric surgery are listed under the 4 thematic categories and presented in table 3. After adjusting for BMI, sex, and age, those who scored high in past weight loss success (RR = 0.71 (0.57-0.87)) and financial concerns regarding surgery (RR = 0.49 (0.40-0.60)) were less likely to be interested in bariatric surgery while those

who scored high in receptivity to surgery (RR = 1.90 (1.56-2.31)) or positive social support (RR = 1.86 (1.51-2.29)) were more likely to be interested in bariatric surgery (**Table 3**).

3.4 Discussion

To our knowledge this is the first study to demonstrate factors associated with interest for bariatric surgery in qualified patients within a publically funded clinic. Individuals who were interested in bariatric surgery had a higher BMI than those not interested. Although both groups overestimated the weight loss that should be expected from bariatric surgery, individuals who were interested in bariatric surgery thought that they would lose even more weight with this intervention. Those who scored highly on statements regarding past weight loss success or financial concerns regarding surgery were less likely to be interested in bariatric surgery while those who scored highly on statements regarding receptivity to surgery or positive social support regarding surgery were more likely to be interested in bariatric surgery.

Although bariatric surgery has been demonstrated to be an effective method of weight loss and intervention for many obesity related comorbidities[8,10,11], there is still a resistance to surgery in many patients[12]. In a study examining 77 morbidly obese patients attending a clinic for routine outpatient appointments or hospitalization for other reasons, Afonso et al. report that 57% were not interested in bariatric surgery[12], while our study found even more extreme results, with 77% of qualified participants not interested in bariatric surgery. As the participants in the current study are participating in a weight management clinic, it is surprising that there is less receptivity to bariatric surgery in our sample. However, as health benefits was the number one reason respondents were interested in bariatric surgery, it is possible that the higher level of interest is due to the greater prevalence of health issues in the Afonso study. Interestingly, although bariatric surgery has been demonstrated to be an effective treatment for remission of type 2 diabetes[10,37], there was no difference in prevalence of type 2 diabetes between those who

were interested and those who were not interested in bariatric surgery. This may suggest that although participants are aware of the weight loss benefits, perhaps they are not fully aware of the value of bariatric surgery as an intervention for diabetes and other obesity-related health conditions.

All participants at the clinic underwent personalized physician consultation for bariatric surgery, and specialized individual and group weight management education sessions at the clinic. It appears that those who were not interested in bariatric surgery are not driven by a lack of belief in effectiveness of surgery as only 7.7% of these individuals stated that they did not believe that bariatric surgery would work. However, individuals who were interested in bariatric surgery believed that they would lose more weight than those not interested. In fact, both groups had unrealistically high weight loss expectations (37% vs 33% of body weight respectively) as compared to the 16-23% weight loss typically observed with bariatric surgery[8]. However, these bariatric surgery weight loss expectations are in line with the weight loss expectations for any general weight loss intervention, with patients reporting an expected weight loss of 38% of body weight and a disappointing weight loss as 24% of body weight[38]. In fact, even the disappointing weight loss is at the high end of what is generally expected with bariatric surgery[8,10,11] and is much higher than the 5-10% body weight loss recommended for health benefits[2,36]. Thus, it appears that it is not a perceived lack of effectiveness in bariatric surgery as a weight loss intervention that is driving the high level of disinterest in the procedure.

Participants who scored highly in past weight loss success were less likely to be interested in bariatric surgery. Previous studies report that the majority of qualified patients are not interested in surgical interventions to manage their weight[12]. This was also reflected in the current study with approximately a third of participants who were not interested in bariatric

surgery stating that they did not need surgery to lose weight. However, this must be taken in context, as the majority of patients of the Wharton Medical Clinic were likely unsuccessful at weight loss in previous non-surgical attempts as previous studies generally report low levels of successful weight loss maintenance (5-21% success rate)[39,40]. This reflects a large disparity between what should be realistically expected from both surgical and non-surgical weight loss interventions and what patients believe is achievable through these interventions[7]. This may suggest that greater emphasis must be placed on educating patients on realistic weight management intervention expectations.

All participants agreed that surgery would cause both a drastic change in eating habits and lifestyle. However, those who agreed more strongly with statements in this category were more likely to be interested in bariatric surgery. Previous studies suggest that these lifestyle changes can be difficult to maintain, and even with bariatric surgery, the majority of patients report noncompliance with at least one behavioural recommendation post surgery[41]. Furthermore, fear of other complications due to surgery, which included lifestyle changes, was the top reason cited by respondents not interested in bariatric surgery. However, despite possible complications, bariatric surgery is a relatively safe procedure. In a study of 4776 patients undergoing bariatric surgery, 0.3% of patients died within 30 days of surgery, while 4.1% of patients had a severe adverse outcome including deep vein thrombosis, venous thromboembolism, re-intervention, or failure to be discharged within 30 days after surgery[33]. Comparatively, the 30 day mortality risk for hip or knee replacement is higher at approximately 1%[34]. On the other hand, patients who underwent bariatric surgery had a 89% reduction in relative risk of death (0.68% vs 6.17%) over a 5 year follow up[42]. Although it is realistic to have

concerns regarding any surgical procedure, it is possible that greater emphasis should be placed on the relative safety and overall health benefits of this intervention.

A hesitance to consider bariatric surgery has been demonstrated in a previous study, with the majority of respondents holding negative impressions of bariatric surgery[43]. To our knowledge, this is the first study demonstrating that positive social support is related with interest in bariatric surgery itself. Previous studies report a non-significant trend towards increased weight loss in bariatric surgery patients with positive social support [44,45]. Thus, strong positive social support may be important for both bariatric surgery interest and success. This is unsurprising as the majority of participants agreed strongly that surgery would be a last resort. It is possible that considering bariatric surgery for these participants is internally viewed as a failure at previous interventions and positive social support helps ameliorate these concerns.

The Heads Up study reports that insurance coverage did not appear to be a driving factor for patients' interest in bariatric surgery[35]. However, the authors cautioned that these patients were all offered coverage by their insurance for bariatric surgery and thus were perhaps not generalizable to all individuals. Our study furthers these results in that the participants who more strongly agreed with both the statements "I would get surgery if the costs were covered" and "I would pay for surgery myself" were more likely to not be interested in bariatric surgery. However, in those not interested in bariatric surgery, cost was one of the top 5 reasons cited as a barrier to this intervention. It is possible that there are extraneous costs to the actual surgery itself, such as taking time off work, additional childcare costs, or the cost of lifestyle adjustments that are factoring into these individuals receptivity to surgery or that it is still unclear to these individuals the coverage available for surgery even after being told during the physician

consultation. Future studies should be directed at a deeper analysis of financial motivations behind receptivity to bariatric surgery.

Several strengths and limitations of the present study warrant mention. The majority of the sample was white and female, and thus may not be generalizable to the general population. This sample does allow for an examination of receptivity to bariatric surgery without the influence of the cost of surgery itself as all participants were eligible to have this intervention covered by OHIP. Furthermore, this analysis was performed with a larger sample size than previous studies. All individuals in our sample actively participate in the weight management clinic and all received specialized individual and group weight management education through physicians and other members of a multidisciplinary healthcare team. Thus, misconceptions regarding bariatric surgery are likely to be even greater among the general population.

The driving motivations behind receptivity to bariatric surgery are complex and multi-faceted. However, our study suggests that several key issues require greater education regarding weight management goals and surgical interventions. Although those interested in bariatric surgery had a higher BMI than those not interested, both groups still have unrealistic expectations regarding bariatric surgery as a weight loss intervention. It appears that weight loss expectations are not a major driving factor of interest in bariatric surgery, as there are still very low levels of interest in bariatric surgery. Furthermore, greater educational emphasis should be placed on the relative safety of bariatric surgery as well as the effectiveness of bariatric surgery as an intervention for type 2 diabetes.

Table 1 – Respondent characteristics in 371 patients who qualify for bariatric surgery

N = 371, %	**Interested in bariatric surgery**	**Not interested in bariatric surgery**
	87 (23)	**284 (77)**
Female, %	**67** (77)	**200** (70)
White, %	**63** (72)	**236** (83)
Age, years	**47.5** (11.2)	**48.2** (11.5)
Type 2 Diabetes, %	**14** (16)	**26** (9)
BMI, kg/m^2	**48.0** (8.2)	**46.2** (6.6) *

Age and BMI are presented as mean (SD)

* Significantly different from Interested in bariatric surgery ($P<0.05$)

Table 2 – Reasons respondents cited for being interested or not interested in bariatric surgery

Interested in bariatric surgery (n=87)		**Not Interested in bariatric surgery (n=284)**	
Health benefits, %	**82** (94.3)	**Fear of other complications from surgery,** %	**145** (51.1)
Greater weight loss, %	**78** (89.7)	**Don't need surgery to lose weight,** %	**91** (32.0)
Improve mobility, %	**74** (85.1)	**Fear of dying,** %	**70** (24.6)
Aesthetics appearance, %	**44** (50.6)	**Fear of surgery in general,** %	**68** (23.9)
Diabetes management, %	**26** (29.9)	**Cost,** %	**58** (20.4)
		Pain, %	**39** (13.7)
		Don't believe it will work, %	**22** (7.7)
		Fear of judgment, %	**9** (3.2)
		Religious or cultural reasons, %	**2** (0.7)

Table 3 – Mean scores for responses to questions regarding receptivity to bariatric surgery

	Interested	Not interested	Relative risk (95%CI)
Past weight loss success	**2.3 (0.6)**	**2.5 (0.6)***	**0.71 (0.57-0.87)**
Dieting has helped me manage my weight in the past	2.7 (1.2)	3.3 (1.2)*	0.74 (0.63-0.87)
Exercise has helped me manage my weight in the past	3.1 (1.1)	3.6 (1.2)*	0.77 (0.66-0.90)
Weight loss medication has helped me manage my weight in the past	2.0 (1.1)	1.9 (1.2)	1.07 (0.92-1.25)
Diets are easy to stick to	1.9 (0.9)	2.2 (1.0)	0.81 (0.66-1.00)
Exercise is easy to stick to	2.2 (1.0)	2.5 (1.1)	0.83 (0.69-0.99)
I have lost weight in the past but cannot keep it off (i)	1.7 (1.2)	2.2 (1.1)*	Not estimatable
Receptivity to surgery	**2.7 (0.5)**	**2.1 (0.6)***	**1.90 (1.56-2.31)**
Surgery will help maintain my current weight	2.7 (1.5)	2.3 (1.1)*	1.80 (1.63-1.99)
Surgery would be a last resort (i)	2.8 (1.3)	1.5 (1.1)*	1.79 (1.64-1.96)
Surgery will cause a drastic change in my eating habits (i)	1.8 (1.0)	2.2 (1.3)*	0.79 (0.65-0.96)
Surgery will cause a drastic change in my lifestyle (i)	1.8 (1.1)	2.3 (1.3)*	0.74 (0.61-0.90)
I believe surgery will be effective in helping me reach my goal weight	4.5 (0.8)	2.7 (1.3)*	2.85 (2.21-3.68)
Positive social support regarding surgery	**3.5 (1.2)**	**2.7 (0.9)***	**1.86 (1.51-2.29)**
My family approves of surgery	3.8 (1.3)	2.5 (1.2)*	1.75 (1.48-2.08)
My partner approves of surgery	3.9 (1.3)	2.4 (1.2)*	1.85 (1.53-2.22)
My friends approve of surgery	3.7 (1.2)	2.6 (1.1)*	1.76 (1.49-2.07)
People will judge me if I get bariatric surgery (i)	2.3 (1.2)	2.3 (1.3)	1.02 (0.87-1.19)
Financial concerns regarding surgery	**1.8 (0.7)**	**2.6 (0.8)***	**0.49 (0.40-0.60)**
I would get surgery if the costs were covered (i)	1.5 (1.0)	3.6 (1.4)*	0.40 (0.31-0.52)
I would pay for surgery myself	2.2 (1.2)	1.6 (1.0)*	1.36 (1.20-1.56)

Data are presented as mean (SD) and as relative risk (95% confidence interval) adjusted for BMI, sex, and age. Scores are on a scale of 1 (strongly disagree) to 5 (strongly agree). (i) Signifies inverted score for category score calculation (i.e. 1 = strongly agree and 5 = strongly disagree.

* Significantly different from Interested in bariatric surgery ($P<0.05$)

4.0 General Discussion

Obesity and obesity related comorbidities are a major public health issue and the increasing prevalence of obesity is associated with dramatically increased health care expenditures[46]. In Canada, the prevalence of individuals with type 2 diabetes is expected to increase from 1.4 million to 2.4 million from 2000 to 2016[47]. Unchecked, this will place enormous strain upon the public health system, increasing healthcare costs for individuals with diabetes from $4.66 billion to $8.16 billion Canadian dollars. Similarly, the total economic cost of diabetes in the United States has risen 41% from 2007 to 2012 ($174 billion to $245 billion US dollars)[48]. Zhuo et al. report that a community based lifestyle intervention program for preventing type 2 diabetes could possible prevent 885 000 cases of type 2 diabetes and save $5.7 billion in the United States[49]. Additional consideration should be directed at examining the economic savings of a bariatric surgery based intervention program targeting both prevention and treatment of obesity and type 2 diabetes to supplement these lifestyle management programs.

Bariatric surgery has proven to be the most effective weight loss intervention for weight loss, reduction in obesity related comorbidities, and mortality risk for severely obese individuals with obesity-related comorbidities[8,10,11,20]. Our study demonstrates that although bariatric surgery may be the best intervention, there are very low levels of interest among qualified individuals. Furthermore, it is not lack of confidence in the actual outcomes of bariatric surgery as participants overwhelmingly believe that bariatric surgery can help with drastic weight loss. Thus, future studies should be directed at what can possibly shift receptivity to bariatric surgery in not only qualified patients, but also how to also improve receptivity and support within the patients social network, as we demonstrated that positive social support was important to those considering bariatric surgery.

However, receptivity to bariatric surgery may not be the only barrier preventing wider implementation of this intervention. Even with the low levels of interest in bariatric surgery reported in our study, there are still wait times of greater than 5 years for bariatric surgery in Canada[50]. This is the longest waiting time for any surgical procedure and Christou et al. report that 12 patients, all with obesity related comorbidities, died at the McGill University Health Centre while awaiting bariatric surgery[50]. Greater funding to increase the availability of bariatric surgery would improve the health, reduce mortality risk, and possibly reduce the economic burden of obesity and the related comorbidities for these patients.

Although additional funding for obesity interventions may help ameliorate the increasing prevalence of obesity and the financial burden on healthcare costs, obesity is a complex issue and it is unlikely that any single intervention will provide a complete and systematic answer[51]. Further attention must be placed on preventative measures targeting early childhood education and the built environment. Previous studies demonstrate that obese children are more likely to become obese adults[52] and as such, it is possible that preventative interventions should be targeted at early childhood lifestyle and dietary education. Several studies have demonstrated limited success with early childhood education targeting reduction in obesity[53,54], but it is still unclear if these benefits are carried forward long term into adulthood. It will be critical to further study the long term impact of these early childhood obesity interventions.

However, there are additional environmental factors that may be driving the increased prevalence of obesity external to individual lifestyle behaviours. Several studies have examined the issue of current "obesogenic" environments[55,56]. This refers to the current built environment that contributes to increasing obesity rates through a variety of pathways. Sedentary time and low walkability are associated with an increased prevalence of obesity[55,57], and many

communities are designed in such a way that promotes sedentary behavior[58]. Communities are designed for ease of transportation via car as opposed to walkability[58]. Further, the increase of screen time is also associated with increased prevalence of obesity[59]. This sedentary screen time has become pervasive in all aspects of life, with increasing availability of mobile screens and computers in addition to traditional television time[60]. Hill et al. suggest that small changes amounting to 100 kilocalories per day could help prevent weight gain in the general population and that this could be achieved fairly simply via an additional 15-20 minutes walking or 4-5% reduction in total daily energy intake[61]. Additionally, it is important to note that there are possible health benefits to improving or maintaining high levels of cardiorespiratory fitness independent of weight loss (Appendix C). With an issue as complex as obesity, multiple approaches will be required, including both prevention and intervention. In light of these environmental factors, bariatric surgery, or any intervention for obesity after the fact, is only addressing the symptoms of this multifaceted issue and not the source.

Thus, although bariatric surgery is currently the best intervention for weight loss and reduction in obesity related comorbidities, it should not be viewed as an all-encompassing answer to the obesity issue. Surgical intervention is one tool that can be applied in conjunction with wider societal tools that include early childhood education and changes to the built environment to prevent obesity. Only by addressing the multiple aspects of obesity can we reverse the increasing prevalence of obesity that is affecting the health, quality of life, and sustainability of the public healthcare system of Canadians.

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Appendix A: Bariatric Surgery Questionnaire Consent Form

YORK
UNIVERSITÉ
UNIVERSITY

INFORMED CONSENT FOR DATA RELEASE

Study Title: York University Research Study - Wharton Weight Management Clinic

Researcher: Jennifer L. Kuk, PhD, Associate Professor

PURPOSE OF THE RESEARCH

The following brief is intended to provide you with the details you should be aware of prior to your consent as a participant in this study. Please read the following information carefully and feel free to ask any questions that you may have. The study is a study conducted by York University (Dr. Jennifer Kuk). The purpose of the study is to investigate how novel obesity markers, weight perception and weight discrimination are related to weight management or other questions related to our understanding of obesity and health research. For this study, you will be asked to complete a questionnaire and this data will be linked with your medical records at the Wharton Medical Clinic.

RISKS AND BENEFITS - There are no risks or benefits of participating.

CONFIDENTIALITY

All information obtained during the course of this study is strictly confidential and your anonymity will be protected at all times. Your identity will not be revealed in any description or publication, and confidentiality will be provided to the fullest extent possible by law. By signing this consent form, you do not waive your legal rights nor release the investigator(s) and sponsors from their legal and professional responsibilities. Your paper data will be securely stored at the Wharton Medical Clinic and then be transferred to York University, and only research staff will have access to this information. Your data will then be entered electronically on a secure password protected computer/hard-drive after which your paper data will be shredded. Your electronic data will be archived for 10 years after the study results are published. After this time, the researchers will decide if information should be destroyed, made anonymous, or kept for further research.

VOLUNTARY CONSENT

This research has been reviewed by the Human Participants Review Committee, York University's Ethics Review Board and conforms to the standards of the Canadian Tri-Council Research Ethics guidelines. I have been given an opportunity to ask any questions concerning the procedures. All of my questions regarding the research project have been satisfactorily answered. I understand that my results are considered confidential and will never be released in a form that is traceable to me, with the exception of my physician or me. I understand that I am free to deny consent at any time, have all collected data destroyed if requested, and that refusal to participate will not jeopardize the current or future relationship or care given at The Wharton Medical Clinic and Weight Management Centre, York University or any other group associated with this project.

Should I have any questions about the study, I know that I can contact any of the following: Dr. Jennifer Kuk (416-736-2100 x20080), or the Sr. Manager & Policy Advisor for the Office of Research Ethics, 5th Floor, York Re. My signature below means that I freely agreed to participate in this study.

Date	Volunteer's Signature	Volunteer Name

Witness' Signature

Appendix B: Bariatric Surgery Questionnaire

Bariatric Surgery Questionnaire

Patient ID | | | | | | | |

Are you interested in bariatric surgery? ○ Yes ○ No ○ Not Sure

If yes,
Why are you interested? (Check all that apply)

- ○ Greater weight loss
- ○ Health benefits
- ○ Improve mobility
- ○ Aesthetics (appearance)
- ○ Diabetes management
- ○ Other

Specify, if other _____

If no,
Why are you not interested in bariatric surgery? (Check all that apply)

- ○ Fear of dying
- ○ Fear of surgery in general
- ○ Don't need surgery to lose weight
- ○ Fear of judgement
- ○ Fear of other complications from surgery. (stroke, vomiting, change in lifestyle)
- ○ Religious or cultural reasons
- ○ Don't believe it will work
- ○ Pain
- ○ Cost
- ○ Other

Specify, if other _____

Everyone please answer all of the following.

How strongly do you agree or disagree with the following statements?

	1 = strongly disagree				5 = strongly agree
Dieting has helped me manage my weight in the past	○ 1	○ 2	○ 3	○ 4	○ 5
Exercise has helped me manage my weight in the past	○ 1	○ 2	○ 3	○ 4	○ 5
Weight loss medication has helped me manage my weight in the past	○ 1	○ 2	○ 3	○ 4	○ 5
Diets are easy to stick to	○ 1	○ 2	○ 3	○ 4	○ 5
Exercise is easy to stick to	○ 1	○ 2	○ 3	○ 4	○ 5

	1 = strongly disagree			5 = strongly agree	
Surgery will help maintain my current weight	○ 1	○ 2	○ 3	○ 4	○ 5
Surgery would be a last resort	○ 1	○ 2	○ 3	○ 4	○ 5
Surgery will cause a drastic change in my eating habits	○ 1	○ 2	○ 3	○ 4	○ 5
Surgery will cause a drastic change in my lifestyle	○ 1	○ 2	○ 3	○ 4	○ 5
People will judge me if I get bariatric surgery	○ 1	○ 2	○ 3	○ 4	○ 5
My family approves of surgery	○ 1	○ 2	○ 3	○ 4	○ 5
My partner approves of surgery	○ 1	○ 2	○ 3	○ 4	○ 5
My friends approve of surgery	○ 1	○ 2	○ 3	○ 4	○ 5
I have lost weight in the past but cannot keep it off	○ 1	○ 2	○ 3	○ 4	○ 5
I believe surgery will be effective in helping me reach my goal weight	○ 1	○ 2	○ 3	○ 4	○ 5
I would get surgery if the costs were covered	○ 1	○ 2	○ 3	○ 4	○ 5
I would pay for surgery myself	○ 1	○ 2	○ 3	○ 4	○ 5

How much weight do you think surgery would help you lose? ☐☐☐ pounds

Appendix C: Lifestyle and Weight Predictors of a Healthy Overweight Profile over a 20 Year Follow-Up

In Press at Obesity (Accepted Feb 20, 2015)

Lifestyle and Weight Predictors of a Healthy Overweight Profile over a 20 year Follow-up

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Metabolic Status over a 20 year Follow-up

What is already known about this subject?

- Overweight and obesity is positively associated with several disease risk factors.
- There are some overweight/obese individuals who do not demonstrate these typical risk factors.
- Physical activity, cardiorespiratory fitness, weight, and diet composition are associated with CVD risk.

What does this study add?

- This paper examines the lifestyle and weight predictors of a healthy overweight and obese profile over a 20 year follow-up.
- Changes in cardiorespiratory fitness and weight are associated with a healthy metabolic status and changes in physical activity and macronutrient intake are not.

Metabolic Status over a 20 year Follow-up

Abstract

Objectives: The longitudinal and independent associations of modifiable risk factors on the transition to metabolically healthy overweight/obese (MHO) versus metabolically abnormal overweight/obese (MAO) are unknown. The purpose of this study is to determine the independent associations of changes in physical activity, cardiorespiratory fitness (CRF), body weight and diet composition on the transition to MHO versus MAO.

Methods: 1358 adults from the CARDIA study who were healthy at baseline and overweight/obese at the 20 year follow-up were included in the current analyses.

Results: At follow-up, 47% of participants were MHO. After adjusting for changes in CRF, diet and weight change, physical activity and macronutrient intake were not independently associated with MHO ($p>0.05$). Individuals who were unfit at follow-up were less likely to be MHO at follow-up compared with individuals who remained fit. Individuals who gained weight or cycled their weight from baseline to follow-up were less likely to be MHO at follow-up compared with individuals who maintained a stable weight or lost weight.

Conclusion: Focusing on having a high CRF and strategies to limit weight gain may be important in overweight and obese individuals in early to mid-adulthood in order to maintain a metabolically healthy profile.

Metabolic Status over a 20 year Follow-up

Introduction

It is well established that obesity is positively associated with several cardiovascular disease (CVD) risk factors [1,2]. However, there is a subgroup of obese individuals who appear to be 'protected' from the common ill effects of obesity such as insulin resistance, hyperglycemia, hypertension and dyslipidemia [3]. These 'Metabolically Healthy Obese' (MHO) individuals display a metabolic profile that is nearly indistinguishable from that of healthy normal-weight individuals [3–5]. Despite the clinical awareness of MHO individuals, factors underlying the apparently protective profile are not well established.

As the global prevalence of overweight and obesity is rising in both adult and youth populations[6,7], it is important to examine what factors distinguish those who will become MHO versus the more common form of obesity that is associated with metabolic abnormalities (MAO). While physical activity, cardiorespiratory fitness (CRF), weight and diet composition have been indicated to be associated with CVD risk[8–11], research has yet to demonstrate whether changes in these factors can predict the development of MHO versus MAO. Therefore, the purpose of the current investigation is to track metabolically healthy individuals who were overweight/obese after a 20 year follow-up and to examine whether changes in physical activity, fitness, body weight and diet composition predict the transition to MHO versus MAO.

Metabolic Status over a 20 year Follow-up

Methods

Study Population & Database

The CARDIA study is a multi-center, longitudinal study designed to investigate the development and progression of CVD risk factors in young adults. In 1985-1986, a cohort of 5,115 participants from Birmingham, AL; Chicago, IL; Minneapolis, MN; and Oakland, CA were randomly sampled and balanced for age (18 to 24 years and 25 to 30 years old), sex, ethnicity (African-American and White), and educational status (high school graduate or less, and more than high school). Further details of the CARDIA eligibility criteria, recruitment process, and baseline demographic characteristics have been published elsewhere [12,13]. This current study was reviewed and approved by the York University Research Ethics Board. Limited data access was obtained through the National Heart, Lung, and Blood Institute (NHLBI) of the National Institutes of Health (NIH). This manuscript was prepared using research materials obtained from the NHLBI Data Repository Information Coordinating Center and does not necessarily reflect the opinions or views of the CARDIA investigators or the NHLBI.

Participants

Of the 5,115 individuals in the original sample at year 0, approximately 31% (n=1,569) were lost to follow-up by year 20 and were not included in the current analysis. Participants were excluded if they did not attend at least one other examination (year 5, year 10, and/or year 15) (n = 92) to determine weight change. Participants were also excluded if they reported exceedingly high (men ≥8,000; women ≥6,000 kcal) or low (men ≤800; women ≤600 kcal) energy intakes (n = 104), had 2 or more CVD risk factors at baseline (n = 627), were pregnant at baseline (n = 35),

had a body mass index (BMI) of <25 kg/m^2 at follow-up (n = 1,029), or had missing data for CRF (n = 707), physical activity (n = 21), BMI (n = 31), dietary data (carbohydrate-, fat- or protein-intake) (n = 407) or smoking status (n = 54) at baseline or follow-up.

Metabolic Measurements and Demographic Data

Age, sex, ethnicity, socioeconomic status, cigarette smoking status, alcohol consumption, family history and medication use were assessed by interviewer–administered questionnaires [12]. All outcomes variables were collected according to the standardized CARDIA protocol and processed at central laboratories previously described elsewhere [12]. Measured height and weight was used to calculate BMI (kg/m^2) and weight change.

Individuals were classified as MAO if they had a BMI ≥25 kg/m^2 and had two or more of the following sub-clinical CVD risk factors at follow-up: triglycerides ≥ 1.7 mmol/L; HDL cholesterol < 1.04 mmol/L for men, < 1.29 mmol/L for women; LDL cholesterol ≥ 4.1 mmol/L or taking cholesterol lowering medication; systolic blood pressure ≥ 130 mmHg or diastolic blood pressure ≥ 85 mmHg or taking hypertension medication; fasting glucose ≥ 5.6 mmol/L or taking blood glucose lowering medication; or Homeostasis Model Assessment of Insulin Resistance (HOMA-IR) ≥ 2.5. Conversely, participants were classified as MHO if they had a BMI ≥25 kg/m^2 and had one or fewer of the six aforementioned CVD risk factors at follow-up.

Assessment of Physical Activity & Cardiorespiratory Fitness

Physical activity was assessed using the CARDIA Physical Activity Questionnaire, which is an interviewer-based self-report questionnaire of frequency of participation in moderate (3-6 metabolic equivalent of tasks [METs]) and vigorous intensity activities (>6 METs).

Separate moderate- and vigorous-intensity activity scores (expressed in exercise units; EUs) were computed as the product of the frequency and intensity of the activity [14]. Physical activity was subsequently categorized into sex-specific tertiles (inactive, moderately active and active). For these analyses, the moderately-active and active categories (males ≥ 364 EU, females ≥ 192 EU) were collapsed as previous studies have demonstrated that the greatest improvement in cardio-metabolic risk factors is found between inactive and moderately active individuals[15,16].

CRF was measured using a graded maximal exercise treadmill test[12]. CRF was subsequently categorized into sex-specific tertiles (unfit-, moderately-fit and fit). Moderately fit and fit categories (baseline males ≥ 689 seconds, females ≥ 435 seconds; follow up males ≥ 466 seconds, females ≥ 254)were collapsed for this analysis as previous studies have demonstrated that the greatest protective health benefits are found between unfit and moderately fit individuals[17,18].

Weight Changes

Weight changes between examinations (years 0, 5, 10 and 20) were divided into stable weight, weight loss and weight gain categories**.** Weight change of <5% of body weight between all available time points with an overall weight change of <15% from baseline was classified as stable weight. Weight losers were defined as losing weight without gaining weight between any of the time points. Due to a low number of weight losers (n=23), the stable weight and weight loser groups were collapsed and classified as stable weight. Weight gainers were defined as gaining ≥5% body weight without losing ≥5% body weight between any of the time points, and had ≥15% overall increase in body weight from baseline to follow-up. Participants were

classified as weight cyclers if they experienced both weight gain (>5%) and weight loss (>5%) between examinations.

Dietary Intake

Dietary data were obtained using the CARDIA Diet History Questionnaire[19], which is an interviewer-administered questionnaire of food intake in the past month. Carbohydrate, fat and protein consumed (g/day) were converted into caloric values and percentage of total caloric intake. Macronutrient intake was subsequently divided into two categories: high intake (carbohydrates ≥65%, fats ≥35% or protein ≥15%) and low intake (carbohydrates <65%, fats <35% and protein <15%)[20].

Statistical Analysis

Differences in baseline and follow-up characteristics stratified by metabolic status (MHO and MAO) were assessed using repeated measures analysis of variance (ANOVA) for the continuous variables and chi-square tests for the categorical variables. Log-binomial regression was performed to estimate the longitudinal associations of physical activity, CRF, weight cycling and diet composition (carbohydrate-, fat- and protein-intake) on the relative risk (RR) of becoming MHO at the 20 year follow up adjusting for age, sex, ethnicity, education, smoking status, alcohol consumption and baseline BMI (Model 1). The mutually adjusted model was further adjusted for changes in physical activity, CRF, weight and diet composition where applicable (Model 2). All statistical analyses were performed using SAS v9.4. Statistical significance was set at an alpha of 0.05.

Results

Table 1 presents the baseline and follow-up characteristics of participants stratified by metabolic status at follow-up. Of the 1,358 adults who became overweight or obese, 47% (642) were MHO. Individuals who were MHO at follow-up had a lower baseline BMI and caloric intake and higher baseline protein intake than those who were MAO at follow-up ($P<0.05$). At follow-up, those who were MHO also had a lower BMI, and higher levels of physical activity and CRF, lower carbohydrate intake and a smaller increase in BMI from baseline to follow-up as compared to those who were MAO at follow-up ($P<0.05$).

After adjustment for age, sex, ethnicity, education, smoking status, alcohol consumption and baseline BMI (Model 1), only individuals who were active at baseline but became inactive were less likely to be MHO at follow up (active-inactive: RR (95%) = 0.85, 0.75-0.95) when compared with individuals who remained active. After accounting for changes in CRF, diet and body weight in the mutually adjusted model (Model 2), physical activity was no longer associated with becoming MHO (**Figure 1A**, $P> 0.05$). In both models, remaining inactive or becoming active at follow up was not associated with MHO at follow up ($P> 0.05$). Regardless of baseline CRF, individuals who were unfit at follow-up (fit-unfit: RR (95%) = 0.58, 0.52-0.66; unfit-unfit: RR (95%) = 0.67, 0.58−0.76) were less likely to be MHO at follow-up compared with individuals who remained fit. Similar results for CRF were observed in model 2 **(Figure 1B)**. Individuals who gained weight (RR (95%) = 0.54, 0.43-0.67) or cycled their weight (RR = (95%) 0.74, 0.57−0.94) from baseline to follow-up were less likely to be MHO at follow-up compared with individuals who maintained a stable weight or lost weight. Similar results were observed in model 2 **(Figure 1C)**. Macronutrient intake was not associated with becoming MHO in either model **(Table 2)**.

Discussion

To our knowledge this is the first longitudinal study to demonstrate that CRF and weight changes are both independently associated with the maintenance of a metabolically healthy profile, and that physical activity and diet are not associated with MHO status. This may suggest that focusing on maintaining a high level of CRF and limiting weight gain in overweight and obese individuals in early adulthood may be more important factors to consider when it comes to maintaining metabolic health in obesity.

Changes in physical activity were associated with the maintenance of a metabolically healthy profile in overweight or obese individuals. Previous research offers conflicting results regarding physical activity and MHO[21,22]. However, these studies only examined physical activity at one time point and did not track changes in physical activity over time. In the current study, only the individuals who were active at baseline but became inactive, and not those who were consistently inactive, were less likely to be MHO at follow up when compared to those who remained active. These findings are analogous to observations in the Harvard Alumni Study which report that former university athletes who subsequently decreased sports play were at elevated morality risk compared to those who chronically participated in no sports[23]. However, these associations were no longer significant after adjusting for changes in CRF, BMI and macronutrient intake. Thus, measuring physical activity at one time point may be insufficient in optimally predicting the development of a MHO profile and furthermore, self-reported physical activity appears to be an inferior predictor for MHO when compared to CRF.

Metabolic Status over a 20 year Follow-up

Previous research reports that low CRF is associated with metabolic syndrome[24], and that MHO women have significantly higher CRF than obese women with metabolic syndrome[25]. In the current study, CRF was also a significant predictor of the maintenance of a metabolically healthy profile, even after adjusting for changes in physical activity, weight and diet. More specifically, individuals that had low CRF at follow-up were less likely to be MHO compared to individuals that maintained or achieved a high level of CRF at follow-up. These results suggest that having a high level of CRF may be more important than high levels of physical activity for metabolic health in overweight and obese individuals. However, a high CRF is generally attained through engaging physical activity[24,25], and thus this may highlight the limitations of using self-report physical activity. Alternatively, individuals simply may not have engaged in the types of activities that are associated with increases in CRF. Studies have demonstrated that individual response to a given training intervention can range from no change to a doubling in CRF (VO_2max)[26,27]. These differences are generally attributed to genetic variability, but suggest that individuals with the greatest improvement in CRF with physical activity may also have the greatest health benefits and are more likely to maintain a healthy profile with overweight or obesity. However, it is important to note that we defined high CRF as being in the upper two tertiles and the relatively low levels of CRF necessary to attain health benefits aligns with previous studies which demonstrate the largest gains in health lies between those who are in the lowest fitness quintile and the upper 80%[28].

Individuals that gained or cycled weight were less likely to be MHO independent of changes in physical activity, CRF and diet when compared to those who maintained a stable weight or lost weight. These results extend previous findings demonstrating that both weight

gain and weight cycling are associated with metabolic syndrome[9,11]. The negative effects of weight cycling may be in part due to the reported detrimental effects on body composition[29]. Weight cyclers experience greater reductions in lean mass during weight loss and a greater proportion of fat mass gained during weight regain compared to non-weight cyclers[29]. As only 5-10% of individuals maintain clinically significant weight loss for more than 1 year[30], our findings suggests that it may be more beneficial for individuals to focus on limiting weight gain as opposed to repeatedly failing at weight loss.

Changes in diet composition were not associated with the maintenance of a metabolically healthy profile. Although previous studies report that diet composition is associated with several CVD risk factors [31,32], the relationship of macronutrient intake with the clustering of these CVD risk factors is still unclear [33]. For instance, there are studies that indicate high carbohydrate intake is a risk factor for having metabolic syndrome[34], while others do not[33]. However, similar to the current analyses, in studies examining MHO specifically, there are often no differences in macronutrient intake between MHO and MAO individuals [21,35]. However, this area may require further study as the association between diet composition and health risk factors may require more holistic examination of dietary factors such as fibre, glycemic load, and sodium content in addition to macronutrient content. Alternatively, the general lack of association between dietary factors and the MHO phenotype may suggest that there is no single dietary factor that is responsible for this unique healthy profile.

Several limitations of the present study warrant mention. There are several definitions of MHO used in previous studies and thus comparisons between results must be made cautiously[36,37]. Information as to why participants were lost to follow-up was unavailable.

Excluded individuals may have had the highest health risk (e.g. low physical activity, low CRF, greater disease etc.), which may have minimized the observed associations. Physical activity and dietary data was obtained using self-report. Another shortcoming was that we were unable to distinguish intentional from unintentional weight loss. Also, all variable changes that occurred in between assessments were not accounted for. However, a major strength of this study is the tracking of these variable changes over a 20 year period of time with direct assessment of weight and health risk factors.

In summary, CRF and changes in weight are independently associated with the maintenance of a MHO profile whereas physical activity and macronutrient intake were not. Thus, it may be more important for individuals who develop overweight or obesity in early-mid adulthood to focus on maintaining a high CRF and limiting weight gain to maintain a metabolically healthy status.

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Metabolic Status over a 20 year Follow-up

Table 1 – Baseline and follow-up characteristics in 1,358 adults who were overweight/obese at follow-up, stratified by follow-up metabolic status

	Baseline		Follow-up	
Total sample (n=1,358)	MHO at follow-up	MAO at follow-up	MHO at follow-up	MAO at follow-up
n (%)	642 (47%)	716 (53%)		
Sex (% male)	43.0	50.8	--	--
Age (years)	25.0 ± 0.1	24.9 ± 0.1	--	--
BMI (kg/m^2)	24.2 ± 0.1	24.8 ± 0.1*	29.6 ± 0.2	32.4 ± 0.2*
Active (%)	434 (68%)	477 (67%)	365 (57%)	352 (49%)*
High CRF (%)	460 (72%)	458 (64%)*	510 (79%)	400 (56%)*
Caloric Intake (kcal)	2652 ± 50	2807 ± 47*	2293 ± 41	2345 ± 38
Dietary Carbohydrates (%)	46.3 ± 0.3	46.7 ± 0.3	46.2 ± 0.4	47.4 ± 0.4*
Dietary Fat (%)	37.2 ± 0.2	37.1 ± 0.2	36.8 ± 0.3	36.4 ± 0.3
Dietary Protein (%)	14.9 ± 0.1	14.6 ± 0.1*	15.5 ± 0.1	15.6 ± 0.1
BMI Change (kg/m^2)	--	--	5.4 ± 0.2	7.6 ± 0.1*

Data are presented as mean (SD) unless otherwise indicated.
* Significantly different from MHO at follow-up ($P<0.05$)

MHO: Metabolically Healthy Obese
MAO: Metabolically Abnormal Obese
BMI: Body Mass Index

Metabolic Status over a 20 year Follow-up

Table 2 – Relative Risk for becoming MHO with changes in diet composition (fat, carbohydrate, and protein intake)

	Model 1	Model 2
Fat		
Low-Low	1.01 (0.88-1.14)	1.01 (0.89-1.14)
Low-High	1.05 (0.90-1.23)	1.01 (0.89-1.14)
High-Low	0.99 (0.88-1.11)	0.99 (0.88-1.10)
High-High	1	1
Carbohydrates		
Low-Low	1	1
Low-High	0.95 (0.81-1.10)	0.96 (0.85-1.09)
High-Low	1.02 (0.86-1.19)	1.04 (0.90-1.19)
High-High	0.92 (0.79-1.05)	0.97 (0.85-1.11)
Protein		
Low-Low	0.95 (0.83-1.10)	0.96 (0.86-1.08)
Low-High	0.97 (0.84-1.12)	0.98 (0.88-1.09)
High-Low	1.03 (0.88-1.21)	0.99 (0.87-1.12)
High-High	1	1

Model 1: Simple Model - adjusted for age, sex, ethnicity, smoking status, education, alcohol consumption, and baseline BMI
Model 2: Mutually Adjusted Model - adjusted for age, sex, ethnicity, smoking status, education, alcohol consumption, baseline BMI, physical activity, CRF, weight change, and diet where applicable
*Significantly different from reference group ($P<0.05$)

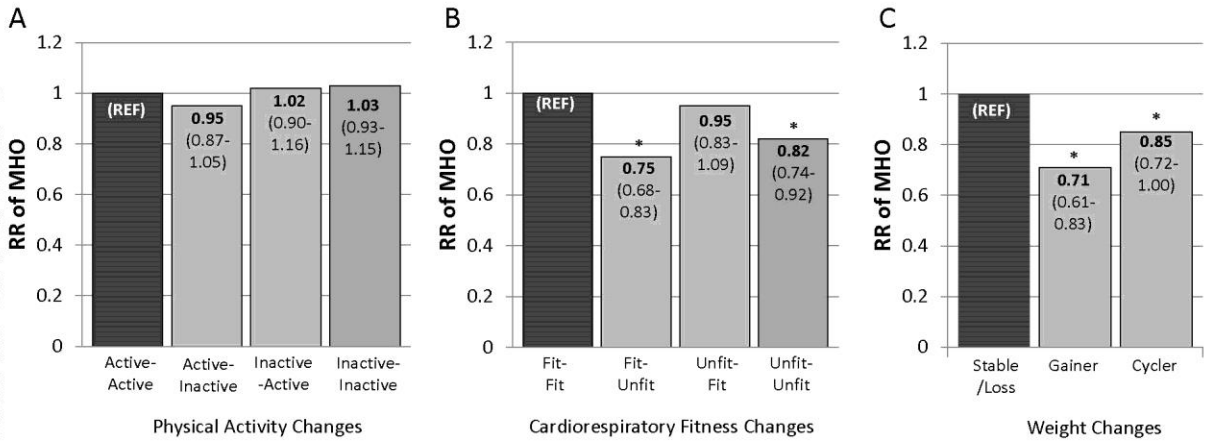
Metabolic Status over a 20 year Follow-up

Figure Legends

Figure 1. Relative Risk for becoming MHO with changes in physical activity (A), fitness (B) and weight (C) after adjusting for age, sex, ethnicity, education, smoking status, alcohol consumption, baseline BMI, and changes in physical activity, fitness, weight and diet composition in 1,358 overweight/obese adults.

MHO: Metabolically Healthy Overweight/Obese; RR: Relative Risk

* Significantly different than reference group ($P < 0.05$)


A
RR of MHO
1.2
1
0.8
0.6
0.4
0.2
0
(REF)
0.95 (0.87-1.05)
1.02 (0.90-1.16)
1.03 (0.93-1.15)
Active-Active
Active-Inactive
Inactive-Active
Inactive-Inactive
Physical Activity Changes
B
RR of MHO
(REF)
0.75 (0.68-0.83)
0.95 (0.83-1.09)
0.82 (0.74-0.92)
Fit-Fit
Fit-Unfit
Unfit-Fit
Unfit-Unfit
Cardiorespiratory Fitness Changes
C
RR of MHO
(REF)
0.71 (0.61-0.83)
0.85 (0.72-1.00)
Stable/Loss
Gainer
Cycler
Weight Changes