

Exploring Cause-Specific Mortality, Weight Management Goals, Motivations, and Approach Selection.

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General Abstract

Obesity is a chronic and multifactorial disease that is associated with increased morbidity and mortality. Study 1 investigated differences in cause-specific mortality risks between obesity classes stratified by age and sex. Cox proportional hazard ratios were used to analyze data from NHANES Continuous (1999 to 2018) with mortality follow-up through Dec 31, 2019. Obesity class III is strongly associated with higher mortality risk than class I obesity in adults younger than 65 years of age and to a lesser degree in older men, while there were no significant associations in older women. Mortality risks were generally not different between obesity class I and II. Study 2 investigated differences in the weight loss by weight management goals, approaches employed, and the desired weight loss for adults attempting weight loss or preventing weight gain using NHANES Continuous (2007 to 2012). Generalized linear models with least squared adjusted means and Bonferroni post hoc tests were used. Both men and women tended to gain weight despite wanting to lose a significant amount of weight and employing several weight management approaches. This highlights that weight management approaches may have limited success in preventing weight gain or achieving the desired weight loss in the general population regardless of the approach used. Study 3 explored differences in weight loss and treatment time with health, mobility, and/or esthetics motivations for attempting weight loss among adults who participated in a publicly funded obesity management program at the Wharton Medical Clinic using least squared adjusted means. Despite small differences in treatment time and weight loss goals, differences in the motivations for attempting weight loss were not significantly associated with differences in the weight loss achieved. Overall, this thesis suggests that mortality rates for different specific causes are only elevated for severe obesity and disproportionately affects adults younger than 65 years of age. However, lifestyle interventions for obesity management may be

limited in their effectiveness, and individual motivations, goals or approaches may not lead to a meaningful or sustained weight loss, highlighting the need for more effective obesity management approaches.

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General Introduction:

Obesity is a complex and chronic medical condition that exerts detrimental effects on life expectancy, health status, and the likelihood of enduring medical complexities.¹ Over the recent decades, there has been a notable increase in the prevalence of obesity worldwide, with approximately 650 million adults falling in the obesity category, and an additional 1.9 billion individuals being classified as having overweight.² The prevalence of obesity in Canada has increased from 22.2% to 27.2% between 2005 and 2018, with an observed increase in both women and men, regardless of age, across all providences and territories.³ While there has been a slight decrease in the prevalence of obesity in Canada over the recent years,⁴ obesity still remains a significant public health concern.

Obesity negatively affects physical and psychological health, contributing to increased morbidity and mortality.¹ Obesity is associated with an increased risk of all-cause mortality compared to normal weight, as well as increased risk of other health complications, such as hypertension, glucose intolerance, type II diabetes, dyslipidemia, cardiovascular disease, coronary heart disease, stroke, dementia and cancer.⁵⁻⁷ Thus, weight loss is often recommended for individuals with obesity in order to improve health.¹

Literature review

Obesity and Mortality

Obesity stands as the fifth leading global cause of death, concurrently fueling the development of the leading cause of death worldwide, cardiovascular diseases.^{8,9} Notably, in 2019, 23.1% of total deaths in the United States were due to diseases of the heart, 21.0% were due to cancer, 5.3% were due to cerebrovascular diseases, 5.5% were due to chronic lower

respiratory diseases, and 3.1% were due to diabetes mellitus.¹⁰ It is estimated that obesity class I may decrease life expectancy by 2-4 years, while obesity class III may reduce it by 8-10 years.¹¹ This has raised concerns that obesity and its associated complications might slow or even reverse the progress made in life expectancy over recent decades.⁷

Body mass index (BMI) is one of the most commonly used anthropometric measures for assessing obesity.¹² BMI was developed in the early 19th century by a Belgian mathematician and statistician, Adolphe Quetelet, in an effort to find a mathematical function that has a linear association between height and weight, in order to describe the “average man”.^{13,14} BMI is calculated by dividing individual’s weight by their height squared (kg/m^2).^{13,14} BMI cut-offs were not intended to be used as measure of individuals fatness or obesity, but rather it was intended to be used as a measure of health for population-level studies.^{12,14} However, because of it has strong correlation with major health outcomes and fat mass,¹⁵ BMI gained popularity as a simple, quick and non-invasive way to measure and define overweight and obesity,^{12,16} with health agencies such as Health Canada,¹⁷ Centers for Disease Control and Prevention (CDC)¹⁸ and World Health Organization (WHO)¹⁹ incorporating BMI into their guidelines. The specific cut-off values for BMI used to denote overweight and obesity has changed over the past over time, and different health agencies and countries can use different cut-off points for their specific population.¹⁴ The current standard BMI classification as outlined by the CDC and Health Canada include: underweight - below 18.5 kg/m^2 ; normal weight - 18.5 to 24.9 kg/m^2 ; overweight – 25.0 to 29.9 kg/m^2 ; obesity class I - 30 to 34.9 kg/m^2 ; obesity class II - 35 to 39.9 kg/m^2 ; obesity class III - 40 kg/m^2 and above.¹⁸

BMI is not without limitations. One of the main limitations of BMI is that it is not a direct measure of body composition and cannot distinguish between fat mass and fat free mass

and may therefore incorrectly classify individuals as having obesity.^{12,14} For instance, an athlete with very high levels of muscle mass and low levels of body fat, could be mis-classified as someone with obesity using BMI, despite their low levels of adiposity. Moreover, higher levels of central or abdominal fat have been shown to be more strongly associated higher mortality risk and disease;²⁰ however, BMI does not account for fat distribution. Even for a given BMI, those with an elevated waist circumference are at higher mortality risk as compared to those with a lower waist circumference.²¹ Because of these limitations, BMI alone may be a poor indicator of an individual's health status, but are a more appropriate measure for population studies.^{12,14} It has been suggested that the use of other anthropometric or body composition assessment tools, such as waist-to-hip ratio, bioelectrical impedance analysis (BIA) or dual-energy X-ray absorptiometry (DXA), combined with BMI could provide a better overall picture of an individual's health status in clinical setting.^{12,14} However these methods are not without their own limitations. In body composition research there is no singular gold standard that is agreed upon and universally used.²² Often the 5-compartment model is used for research, but is costly and resource intensive as it uses DXA, BIA and hydrostatic weighing or air displacement plethysmography together to assess fat mass, fat-free mass, total body water, protein mass and mineral mass.²³ More commonly, the 2-compartment model is used (fat versus fat free mass) using a single body composition tool.²³ However, all of these body composition tools are indirect predictors of fat mass and many also do not directly assess differences in body fat distribution. Of the most commonly used, DXA can provide predictions of total and regional fat mass and is often called the gold-standard for body composition.²⁴ However, this measure is associated with radiation exposure and is expensive to use.^{22,23} It is also important to consider that different body composition assessment methods and even devices using a similar method (i.e. different models

of BIA) can give different body fat percentages for a given individual that can differ by over 5%.²⁵ As such, there are no wide-spread accepted fat mass cut-offs in the literature. For this reason, incorporating body fat assessment tools are also problematic in clinical care.

Other obesity assessment tools such as Edmonton Obesity Staging System (EOSS), which considers individual's physical, psychological, and metabolic condition to determine the obesity classification and optimal treatment, and has been suggested to be used for clinical use.¹ Obesity is commonly defined as “a complex chronic disease in which abnormal or excess body fat (adiposity) impairs health, increases the risk of long-term medical complications and reduces lifespan.”¹ This would mean that elevated fat mass in conjunction with obesity-related comorbidities should be used to diagnose obesity. According to EOSS, only those with an elevated BMI in conjunction with clinically diagnosed obesity comorbidities would have obesity and be prescribed obesity management.

When examining the association between BMI and mortality, there are numerous studies have shown a positive association between obesity and all-cause mortality, with some suggesting a J-shaped pattern of association.^{5,6,11,26–32} There is more limited research suggesting that the association between BMI and mortality rates may differ depending on the specific cause.^{6,11,27} One study reports a J-shaped association between BMI with cancer, cardiovascular, respiratory, blood and endocrine, digestive, musculoskeletal, and urogenital causes of death, with a nadir at 21–25 kg/m².²⁷ However, another study suggest the nadir of the J-shaped association for cancer lies in the overweight BMI range.⁶ Thus, the pattern of association between BMI and mortality may differ depending on the outcome in question. Further, very few studies have examined this association when stratified for age, sex and the obesity classes as defined by the Centers for Disease Control and Prevention (CDC).¹⁸ In studies that have examined BMI and all-cause

mortality in older populations suggest there is no association,^{5,28,31,33} or even a negative association.³⁴ One possible explanation for these age differences in mortality risk with BMI could be survivor bias. Individuals with obesity who develop severe cardiometabolic complications may die earlier and therefore are less likely to survive into older age.³⁵ As a result, the population of older adults with obesity may represent a healthier subset of individuals who were able to remain healthy and survive despite having obesity.³⁵ Additionally, weight loss among other adult may be associated with increased mortality.^{36,37} Old age is associated with sarcopenia, muscle loss and increased frailty. Similarly, losing weight is also associated with loss of muscle mass which can lead to loss of strength and functionality, which could increase the risk of fall and increase the mortality risk particularly in older individuals who are more likely to already have lower levels of muscle.³⁶ Further, higher fat mass in older individuals may benefit survival in times of disease.³⁸ For example, pneumonia, cancer and myocardial infarction are often associated with weight loss during the disease process and thus higher levels of fat mass may act as an energy reserve that would benefit survival. Therefore, older adults who have higher body weight may have lower mortality risk compared with those who lower body weight because they have more resources to lose before the loss of fat energy or lean tissue becomes critical and be in better overall health.³⁶

Another question that remains is whether there are differences in mortality risk across the obesity sub-classes. The majority of the studies have used normal weight as the reference group and did not directly assess the association within obesity classes. Individuals with class III obesity tend to have more physical limitations and difficulties with daily activities compared to those with obesity class I and II.^{39,40} Further, class II and III obesity is more prevalent in women than men,⁴¹ and there may be age related differences in mortality risk.⁴² This raises the question

of whether cause-specific mortality rates may differ between obesity classes by age and sex. Therefore, selection of obesity class I as the reference group, combined with stratification by age and sex, may allow for a more clinically meaningful assessment of the association between BMI and cause-specific mortality within the obesity spectrum.

Obesity Risk Factors

Changes in body weight occur due to an imbalance between the energy consumed and the energy expended. When the intake of energy surpasses the expenditure, it leads to weight gain, while weight loss occurs when the energy expenditure exceeds intake.⁴³ Traditionally, a common starting point in obesity management is lifestyle intervention, which involves modifying one's diet and increasing physical activity.⁴⁴ However, other underlying factors, such as genetics, biology, metabolism, behaviour, socioeconomic status, and the environment, may also collectively contribute to the development of obesity.¹ Children with parents with overweight or obesity are more likely to develop overweight.⁴⁵ This could be due to genetic, social or environmental factors. Children may inherit genes and adopt their parent's physical activity and eating behaviours that may increase their risk for obesity.⁴⁶ Genetics are reported to account for about 40 to 50% of the variations in body weight.⁴⁷ Biological factors such as abnormalities in satiety and hunger hormones, such as glucagon-like peptide 1, cholecystokinin, peptide YY, ghrelin, or insulin have been associated with over eating and lower energy expenditure in those with obesity.^{48,49} Other factors such as cultural values and practices, excessive maternal weight gain, or lack of breastfeeding are also associated with unhealthy overeating and weight gain.^{50,51} Similarly, environmental and socio-economic factors such as living in a neighbourhood with low walkability or access to recreational facilities,⁵² lower education,⁵³ higher job insecurity,⁵⁴ lower financial security,⁵⁵ and higher food insecurity,⁵⁶ are found to be associated with higher obesity.⁵²

Certain mental health conditions such as depression, anxiety, or bipolar disorder have also been shown to associated with higher odds of obesity.⁵⁷ Psychosocial factors such as having higher levels of body dissatisfaction, conscientiousness, extraversion, or neuroticism have also been found to be associated with higher body weight.⁵⁷

Some of these underlying factors associated with obesity may also interact, reinforcing their affects, collectively lead to development of obesity. For example, genetic predisposition may lead dysregulation of appetite simulating hormones, leading to increased appetite and attraction to calorie dense foods that can be compounded by low socioeconomic status and food availability, and ultimately resulting in changes in feeding behaviour and weight gain.⁴⁹ Socioeconomic disadvantages, such as financial insecurity may lead to higher stress levels or emotional distress, which may lead to maladaptive coping mechanisms, such as eating to supress negative emotions or stress eating, ultimately leading to higher calorie intake, weight gain and obesity.⁴⁹ Additionally, there may be other physiological factors that may create difficulties in losing weight and maintaining weight after weight loss. According to set point theory, body weight is regulated around a set point, and may respond to weight loss with compensatory mechanisms that would impair weight loss, such as increased appetite and adaptive thermogenesis, in order to bring the body weight back to the initial point and preventing weight loss.^{58–60}

Because of the complexity of the factors underlying obesity and weight gain, this likely necessitates a multifaceted approach to obesity management.¹ As a result, other approaches such as cognitive-behavioural therapy, pharmacotherapy, and/or bariatric surgery are also used alongside lifestyle intervention in obesity management.⁶¹ Nevertheless, the effectiveness of such approaches remains limited due to the modest weight reduction achieved through lifestyle

modifications and pharmacotherapy and the limited availability of bariatric surgery among eligible individuals.⁶¹ Newer weight loss medications, such as semaglutide and tirzepatide, which act on several regions of the brain involved in controlling appetite, food cravings and eating behaviour, resulting in reduced hunger, increased satiety, and lower food intake,⁶² and show more promising weight loss results (15% to 21% versus 5% to 10% mean weight loss) as compared to lifestyle interventions or older obesity medications.^{62,63} However, the high cost associated with such medications, which many may not be covered through health insurance, is still a significant barrier for use and adherence to these medications.⁶³ Thus, further research is necessary to gain a deeper understanding of the risks associated with obesity, as well as exploring factors that are associated with superior obesity management outcomes.

Canadian Clinical Obesity Guidelines

In recent years, Canada has changed its obesity guidelines for clinical practice, from a more hierarchical obesity management system to a more individualized, patient centric approach. Within the framework of the previous obesity management pyramid hierarchical system, patients would begin with lifestyle interventions, such as diet and physical activity.⁴⁴ However, if sufficient weight loss was not achieved, then pharmacotherapy would be recommended to the patients.⁴⁴ If sufficient weight loss was not achieved with pharmacotherapy, then bariatric surgery would be recommended as the final resort, depending on patients' eligibility.⁴⁴ This step-wise progression of care is based on the assumption that sufficient weight loss could be achieved through lifestyle interventions and behaviour change. However, lifestyle interventions often show very limited success rates.^{61,64} The contemporary Canadian clinical obesity guidelines, however, has recognized this limitation associated with lifestyle intervention, and has moved away the approach from this step-wise progression to a more individualized treatment strategy

that is also used by other chronic disease models such as diabetes and cardiovascular disease clinical care guidelines.^{65,66}

Under the new Canadian clinical obesity guidelines, medical nutrition therapy and exercise should be recommended to everyone, regardless of their BMI, for their health benefits and not weight loss specifically.¹ In addition to nutrition and exercise, patient may also be recommended psychological, medical and surgical interventions either individually, or in combination with each other, depending on their preferences and individual conditions.¹ The updated guidelines recommend pharmacotherapy for individuals with a BMI of above 30 kg/m² or 27 kg/m² with obesity related complications, while bariatric surgery is recommended for individuals with a BMI of above 40 kg/m² or 35 kg/m² with obesity related complications.¹

Weight Loss Goals, Strategies and Outcomes

Given the growing prevalence of obesity and its associated complications, overweight and obesity are now widely recognized as significant health concerns. For many individuals living with overweight and obesity, improving their overall health and well-being often serves as a primary motivation for pursuing weight loss.⁶⁷ A weight loss of 5-10% of body weight, has been associated with significant improvements in physical and psychological health.⁶⁸ However, the weight loss achieved through different interventions varies considerably. On average, lifestyle interventions lead to a modest reduction in weight, approximately 3 to 5% of body weight, while medications are associated with a weight loss of 5.0-12.5%, and bariatric surgery with an average weight loss of 20-40%.^{1,69,70} However, individuals with overweight and obesity have a goal weight loss of 22-35%, a weight loss that far exceeds what is normally achieved by

these lifestyle interventions and is generally more commonly observed with bariatric surgery.^{68,71,72}

Setting a goal for weight loss could be an important initial step in the process, potentially motivating individuals throughout their weight loss journey. One study reports cardiac rehabilitation patients who had set a weight loss goal, lost more weight in a weight loss program compared to those who did not.⁷³ Some studies have shown that setting greater goals is associated with more weight loss in the short term.^{72,74–76} Alternatively, others found no such association.^{68,71} These inconsistencies could arise from differences in methodologies, population sizes, and durations. However, this may suggest that individuals with greater weight loss goals might take more action and invest more effort in their weight loss endeavours.^{68,74} Linde and colleagues, for example, found no direct association between weight loss goals and weight loss outcome;⁶⁸ however, they did observe a positive association between greater goals with the expectation to use specific strategies such as engaging in physical activity, consuming a well-balanced diet, and having smaller portions.⁶⁸

Some studies have explored the strategies individuals use to lose weight. The prevalence of those wanting to lose weight tends to be higher among those with higher BMIs.^{77–79} One study reports that among those attempting to lose weight, 90% used strategies to modify their diet, such as consuming fewer calories and reducing fat intake.⁷⁷ However, the prevalence of engaging in physical activity (46% men, 35.6% women) or using a combination of diet modification and exercise (28.6% men, 26.6% women) for weight loss was much lower.⁷⁷ Additionally, it is reported that women are more likely to use dietary strategies to lose weight, whereas men are more likely to use physical activity for weight loss.^{77,79}

Although some studies have examined weight loss goals, strategies, and outcomes, there has been little description of how the magnitude of someone's desired weight loss may influence their weight loss-specific practices such as dieting and exercising. This raises the question, whether having greater desired weight loss can lead to is associated with differences in the number and type of weight loss strategies used and ultimately greater weight loss achieved in women and men.

Weight Loss and Motivation

The increasing rates of obesity and its complications highlights the need for more effective obesity and weight management strategies in the face of this global epidemic. Dietary and lifestyle interventions often serve as initial line of treatment; however, they show limited success rates and may not lead to sustained long-term weight maintenance.⁶⁴ In fact, studies have shown that up to 70–80% of individuals tend to regain the weight they initially lost through lifestyle changes within a year.⁸⁰

Behaviour change theories may provide a useful framework for understanding the psychology and motivation behind weight management and achieving a sustained lifestyle change. For instance, the Transtheoretical Model (TTM) describes the stages of change in the process of intentional behaviour change, and can be used to conceptualize the process and individual undergoes in order to achieve a sustained positive behavioural changes such as dietary or physical activity practices in order to achieve weight management.^{81,82} Some studies of have examined the use of TTM in weight management,^{81,82} and while stage appropriate interventions may be more effective in creating behaviour and lifestyle change, the weight loss associated with

incorporating TTM into behavior change interventions may be modest (0.2 kg to 2.1 kg at 24 months).⁸¹

The motivation driving weight management, may also play an important role in lifestyle changes and resulting weight loss. The most commonly cited primary motivations for weight loss are improving one's health followed by improving one's appearance.^{67,83–86} Some other motives for losing weight include, social pressure, improved energy, improved social life, improved performance, improved self-esteem, special event, etc.⁸⁷ Numerous studies have shown a strong association between the primary motivations for losing weight and the resulting outcomes.^{67,84–86} Health, as the primary motivation, has been associated with favourable weight loss outcomes,^{67,84,86} while appearance has been associated with negative outcomes,^{67,84,87} and the effect of having other weight loss motivations is not clear. Having an aesthetic motivation for weight loss is more common in women than men.^{67,85,88} This may be important as the length of the treatment has been shown to be a key factor influencing weight loss success and having aesthetic motivation has been associated with greater discontinuation of the treatment.^{67,89,90} One study reports that 24%, 41%, and 65% of patients discontinued the treatment at 6, 12, and 24 months, respectively.⁶⁷ Aesthetic motivation was associated with increased discontinuation rates, while health motivation was associated with decreased discontinuation rates.⁶⁷ Although there is some evidence suggesting that these primary motivations such as health or esthetics may impact weight loss results, most studies focused on one primary motivation. Therefore, there is limited data on how having multiple motivations may influence weight loss outcomes and treatment continuation.

Although some existing evidence indicates that an individual's primary motivation may influence weight loss outcomes, the association between weight loss motivations, weight loss

outcomes, and their connection with treatment continuation is not fully understood. Therefore, a better understanding of how having one or multiple primary motivations for weight loss may influence weight loss outcomes could provide some insight for improving the efficacy of lifestyle interventions.

Summary

Obesity is a significant public health concern and is associated with increased risk for various causes of mortality.^{6,11,27} However, there is limited data on how cause specific mortality differ between obesity classes, stratified by age and sex. Improving health and aesthetics are the primary goals for individuals pursuing weight loss;^{67,83–86} moreover, lifestyle interventions are often the first measures used for achieving those weight loss goals and treating overweight and obesity.⁶⁴ However, how the magnitude of someone's desired weight loss may influence their weight loss-specific practices, or how their motives influence, treatment continuation and ultimately their weight loss outcome, is not fully understood. Therefore, the objective of this dissertation is to investigate:

- 1) The differences in cause-specific mortality between obesity classes by age and sex;
- 2) The association between weight management goals, approach selection and weight outcomes;
- 3) The association between motivational factors, with treatment continuation and weight outcome.

The Association Between Obesity Class and Cause-Specific Mortality by Age and Sex in U.S. Adults.

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Abstract:

Objective: To investigate differences in cause-specific mortality risks between obesity classes stratified by age and sex, using a nationally representative sample of the United States population.

Methods: Differences in mortality risk by standard body mass index (BMI) categories with examination of obesity classes I to III, stratified by age and sex was examined using Cox proportional hazard ratios with data from NHANES Continuous (1999 to 2018) with mortality follow-up through Dec 31, 2019.

Results: Among adults younger than 65 years of age, obesity class III was associated with higher all-cause, cardiovascular, non-cardiovascular/non-cancer, hypertension and diabetes-related mortality compared to class I. Among older adults, there were fewer significant associations with only cardiovascular and diabetes-related mortality risks being elevated in men with obesity class III, and none in women. There were no differences in mortality risks between obesity class I and II, except for diabetes-related mortality in adults younger than 65 years of age and older men.

Discussion: Obesity class III is strongly associated with higher mortality risk in adults and to a lesser degree in older men, while there were no significant associations in older women. Mortality risks were generally similar between obesity class I and II. Therefore, adults younger than 65 years of age with severe obesity may benefit more from aggressive obesity management.

Introduction:

Obesity is a significant public health concern as it negatively affects physical and psychological health, contributing to increased morbidity and mortality.¹ It has been well established that obesity is associated with several health complications, such as hypertension, glucose intolerance, type II diabetes, dyslipidemia, cardiovascular disease, coronary heart disease, stroke, dementia and some cancers.⁵⁻⁷ Currently, obesity stands as the fifth leading global cause of death, and is a contributor to the development of several significant causes of death such as cardiovascular diseases,^{8,9} some cancers^{27,91} and other mortality outcomes.^{27,42} This has raised concerns that obesity and its complications might slow or even reverse the progress made in life expectancy over recent decades.⁷ Notably, it is estimated that obesity class I may decrease life expectancy by 2-4 years, while obesity class III may reduce it by 8-10 years.¹¹ This suggests a trend of increasing mortality rates with increasing severity of obesity.²⁶ Though the differences in mortality risk between obesity classes is not clearly demonstrated, particularly for different mortality outcomes.

There is a substantial body of evidence indicating that obesity is associated with higher all-cause mortality rates.^{5,6,11,26-32} However, the pattern of association between BMI and mortality rates may differ depending on the specific cause.^{6,11,27} Further, the majority of the studies did not directly look at differences between obesity classes as defined by the Centers for Disease Control and Prevention (CDC).⁹² Most studies have examined obesity as a whole as compared to normal weight, and did not examine differences between the obesity classes. Indeed, individuals with class III obesity tend to have more physical limitations and difficulties with daily activities than those with class I and II obesity.^{39,40} Moreover, there may be sex differences as class II and III obesity are more prevalent in women than men.⁴¹ Further, many

studies did not stratify by both age and sex, which is important given the clear differences in mortality risk for obesity between younger and older populations.⁴² Given that the suggested obesity therapies are often dependent upon the severity of obesity, it is important to examine the question of whether cause-specific mortality rates may differ between obesity classes by age and sex groups.

Methods:

Data was obtained from adults over 20 years of age in the United States, participated in the National Health and Nutrition Examination Survey (NHANES) Continuous between 1999 to 2018 surveys with mortality follow-up to Dec 31, 2019 (n=55,081). A detailed explanation of the data collection methods has been previously reported.^{93,94} Prior to participating, all individuals provided written informed consent, and the methods used were approved by the National Centre for Health Statistics.⁹⁴ The National Centre for Health Statistics used probabilistic record matching with death certificate data from the National Death Index (NCHS Linked Mortality File) until December 31, 2019, to obtain mortality information for participants in the NHANES Continuous survey. Primary causes of deaths were recorded as: diseases of the heart; malignant neoplasms; cerebrovascular diseases; chronic lower respiratory diseases; diabetes mellitus; accidents; Alzheimer's; influenza and pneumonia; nephritis, nephrotic syndrome, and nephrosis; and other causes. Hypertension-related and diabetes-related death were classified if hypertension or diabetes were listed as one of the up to 20 contributing causes of death on the death certificate. Because the current analysis included only publicly available data, ethics approval from our institutional Research Ethics Board was not required.

Participants with missing education (n=10,454), height, weight or BMI (n=2634), or mortality follow-up (n=90), were excluded from the analysis, leaving a total of 41,903 patients were included in the analysis. A trained technician conducted measurements of height and weight during the physical examination.⁹⁴ Standing height was measured using a fixed stadiometer, and body weight was measured using an electronic load-cell scale while wearing underwear, a paper gown and paper pants. Body mass index (BMI) was calculated⁹⁴ and categorized using CDC cut-offs¹⁸: underweight - below 18.5 kg/m²; normal weight - 18.5 to 24.9

kg/m²; overweight - 25.0 to 29.9 kg/m²; obesity class I - 30 to 34.9 kg/m²; obesity class II - 35 to 39.9 kg/m²; obesity class III - 40 kg/m² and above.

Questionnaires were used to assess age, sex, smoking status, education level and ethnicity.⁹⁴ Age was reclassified into two groups, adults younger than 65 years of age (18-64 years of age) and older adults (65+ years of age). Educational level was recorded as: Less than 9th grade; 9-11th grade (Including 12th grade with no diploma); High school graduate/GED or equivalent; Some college or Associate of Arts degree; and College graduate or above; and education was re-categorized as the presence or absence of post-secondary education (i.e. more than high school). The ethnic categories were collected as: Mexican American; Other Hispanic; non-Hispanic white; non-Hispanic black; and other non-Hispanic race including non-Hispanic multiracial, and were re-categorized as white and non-white.

Statistical Analysis

The data from Continuous NHANES was weighted to be nationally representative of the United States population. The weighted means or prevalence with standard errors were calculated and reported within each age- and sex-stratified BMI category. Due to the small sample size of the underweight BMI group, this group was excluded from the analysis of BMI group differences in mortality rates.

Due to a violation in proportionality assumptions, the follow-up times were truncated to 200 months. Cox proportional hazards ratio (HR) with consideration of competing interests using the Fine and Gray method was performed to assess differences in specific-cause mortality risk by BMI classes with class I obesity as the referent group. Due to sample size, mortality causes were grouped into three larger categories. Mortality from diseases of the heart and cerebrovascular

diseases were combined to represent mortality from cardiovascular diseases, and all other deaths (chronic lower respiratory diseases; diabetes mellitus; accidents; Alzheimer's; influenza and pneumonia; nephritis, nephrotic syndrome, and nephrosis; and other causes), with the exception of malignant neoplasms, were combined to represent mortality from non-cardiovascular/non-cancer reasons. Diabetes and hypertension related mortality were also examined using Cox proportional hazards regression. Hazards ratio models were adjusted for ethnicity, education and smoking. All results were stratified based on sex and age group.

All statistical analyses were performed using SAS software version 9.4 and a significance threshold of $P < 0.05$.

Results:

Table 1 presents the participant characteristics. The sex and BMI class all-cause mortality rates for young adults ranged between 2.4% to 13.2% and between 22.2% to 61.6% in older adults. All-cause mortality rates in adults younger than 65 years of age generally did not differ for most BMI categories as compared to class I obesity. In adults younger than 65 years of age, only obesity class III had a significantly higher prevalence of all-cause mortality as compared to class I obesity. Among older adults, the underweight and normal weight categories had the highest prevalence of all-cause mortality, while obesity class I had lowest prevalence of mortality among older men and obesity class II had the lowest prevalence in older women.

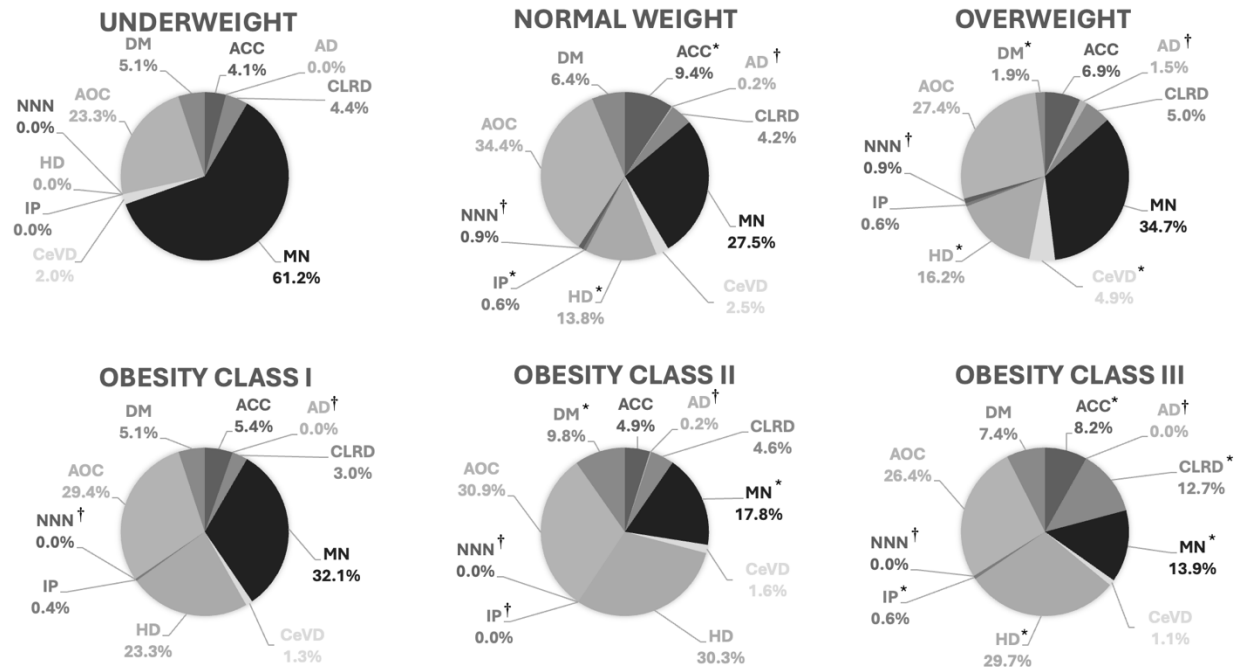
Table 1: Characteristics of participants stratified by sex, age and BMI class.

	Underweight	Normal Weight	Overweight	Obesity Class I	Obesity Class II	Obesity Class III
Males under 65 years of age						
N (n, %)	197.0 (1.3)	4115.0 (27.1)	5651.0 (37.2)	3202.0 (21.1)	1204.0 (7.9)	824.0 (5.4)
Age, years	35.1 $\pm$ 1.4 *	37.7 $\pm$ 0.3 *	42.3 $\pm$ 0.2	43.0 $\pm$ 0.3	42.7 $\pm$ 0.5	42.3 $\pm$ 0.5
BMI, kg/m2	17.6 $\pm$ 0.1 *	22.6 $\pm$ 0.04 *	27.4 $\pm$ 0.03 *	32.2 $\pm$ 0.03	37.0 $\pm$ 0.1 *	45.4 $\pm$ 0.2 *
White Ethnicity (%)	62.1 $\pm$ 4.5	65.0 $\pm$ 1.3	64.9 $\pm$ 1.4	65.5 $\pm$ 1.6	64.4 $\pm$ 2.0	63.9 $\pm$ 2.6
Higher Education (%)	46.8 $\pm$ 4.5 *	57.7 $\pm$ 1.5	59.5 $\pm$ 1.3	58.2 $\pm$ 1.0	58.8 $\pm$ 2.0	52.9 $\pm$ 2.2 *
Smoker (%)	41.6 $\pm$ 4.6 *	35.6 $\pm$ 1.3 *	23.5 $\pm$ 0.8	22.9 $\pm$ 0.8	16.1 $\pm$ 1.2 *	19.6 $\pm$ 1.7
Mortality Rate (%)	13.2 $\pm$ 3.3 *	4.5 $\pm$ 0.4	4.2 $\pm$ 0.3	4.8 $\pm$ 0.4	5.4 $\pm$ 0.8	8.7 $\pm$ 1.3 *
Average follow up time, months	98.9 $\pm$ 6.6	107.4 $\pm$ 1.6 *	106.0 $\pm$ 1.3 *	98.6 $\pm$ 1.9	94.3 $\pm$ 2.6	88.6 $\pm$ 3.0 *
Females under 65 years of age						
N (n, %)	340.0 (2.0)	4834.0 (29.0)	4553.0 (27.3)	3351.0 (20.1)	1908.0 (11.5)	1673.0 (10.0)
Age, years	36.1 $\pm$ 0.9 *	39.5 $\pm$ 0.3 *	42.3 $\pm$ 0.3 *	43.5 $\pm$ 0.3	42.6 $\pm$ 0.4	42.9 $\pm$ 0.4
BMI, kg/m2	17.5 $\pm$ 0.1 *	22.2 $\pm$ 0.03 *	27.4 $\pm$ 0.03 *	32.3 $\pm$ 0.03	37.2 $\pm$ 0.05 *	46.0 $\pm$ 0.1 *
White Ethnicity (%)	72.9 $\pm$ 2.2 *	69.1 $\pm$ 1.2 *	62.8 $\pm$ 1.7 *	58.5 $\pm$ 1.8	60.4 $\pm$ 1.8	58.1 $\pm$ 2.1
Higher Education (%)	61.8 $\pm$ 3.6	70.9 $\pm$ 1.1 *	63.5 $\pm$ 1.1	58.3 $\pm$ 1.4	55.3 $\pm$ 1.4	60.7 $\pm$ 1.4
Smoker (%)	35.0 $\pm$ 3.8 *	21.1 $\pm$ 1.0	20.2 $\pm$ 0.8	20.6 $\pm$ 0.9	20.0 $\pm$ 1.1	18.8 $\pm$ 1.2
Mortality Rate (%)	5.0 $\pm$ 1.5	2.6 $\pm$ 0.2	2.4 $\pm$ 0.3	3.0 $\pm$ 0.3	4.1 $\pm$ 0.6	5.2 $\pm$ 0.6 *
Average follow up time, months	109.2 $\pm$ 4.2	108.6 $\pm$ 1.5 *	104.4 $\pm$ 1.3	101.2 $\pm$ 1.5	102.3 $\pm$ 2.0	92.8 $\pm$ 2.6 *
Males over 65 years of age						
N (n, %)	63.0 (1.3)	1292.0 (25.9)	2064.0 (41.4)	1082.0 (21.7)	351.0 (7.0)	134.0 (2.7)
Age, years	73.1 $\pm$ 0.9	73.7 $\pm$ 0.3 *	73.0 $\pm$ 0.2 *	72.2 $\pm$ 0.2	70.9 $\pm$ 0.4 *	70.4 $\pm$ 0.6 *
BMI, kg/m2	17.3 $\pm$ 0.1 *	22.9 $\pm$ 0.1 *	27.4 $\pm$ 0.04 *	32.1 $\pm$ 0.1	37.0 $\pm$ 0.1 *	43.8 $\pm$ 0.6 *
White Ethnicity (%)	63.9 $\pm$ 7.7 *	72.6 $\pm$ 1.8 *	82.0 $\pm$ 1.2	81.9 $\pm$ 1.4	86.5 $\pm$ 1.9	77.3 $\pm$ 4.3
Higher Education (%)	48.2 $\pm$ 9.5	55.6 $\pm$ 2.2	56.0 $\pm$ 1.5	54.1 $\pm$ 2.4	56.2 $\pm$ 4.0	54.3 $\pm$ 5.1
Smoker (%)	55.5 $\pm$ 9.6 *	15.8 $\pm$ 1.4 *	10.1 $\pm$ 1.0 *	6.1 $\pm$ 0.9	10.2 $\pm$ 2.3	7.7 $\pm$ 4.3
Mortality Rate (%)	49.2 $\pm$ 9.1 *	39.2 $\pm$ 1.8 *	32.1 $\pm$ 1.5	30.8 $\pm$ 1.8	31.8 $\pm$ 3.7	35.7 $\pm$ 5.8
Average follow up time, months	64.1 $\pm$ 6.2 *	78.6 $\pm$ 2.0	80.4 $\pm$ 2.0	77.2 $\pm$ 2.4	76.7 $\pm$ 3.8	67.4 $\pm$ 5.5
Females over 65 years of age						
N (n, %)	85.0 (1.7)	1361.0 (26.9)	1657.0 (32.7)	1126.0 (22.2)	536.0 (10.6)	300.0 (5.9)
Age, years	74.7 $\pm$ 0.8 *	74.4 $\pm$ 0.2 *	73.8 $\pm$ 0.2 *	73.1 $\pm$ 0.2	71.9 $\pm$ 0.3 *	71.5 $\pm$ 0.4 *
BMI, kg/m2	17.2 $\pm$ 0.2 *	22.5 $\pm$ 0.1 *	27.4 $\pm$ 0.1 *	32.1 $\pm$ 0.1	37.0 $\pm$ 0.1 *	44.6 $\pm$ 0.4 *
White Ethnicity (%)	85.2 $\pm$ 2.8 *	82.3 $\pm$ 1.1 *	79.8 $\pm$ 1.4	77.7 $\pm$ 1.7	74.0 $\pm$ 2.2	75.4 $\pm$ 2.6
Higher Education (%)	46.3 $\pm$ 6.5	52.1 $\pm$ 1.9 *	47.0 $\pm$ 1.8	46.7 $\pm$ 1.8	44.8 $\pm$ 2.9	47.7 $\pm$ 4.2
Smoker (%)	21.0 $\pm$ 5.4 *	9.9 $\pm$ 1.0 *	7.4 $\pm$ 0.8	5.5 $\pm$ 0.8	4.8 $\pm$ 1.2	94.7 $\pm$ 1.6
Mortality Rate (%)	61.6 $\pm$ 6.7 *	35.5 $\pm$ 1.6 *	28.3 $\pm$ 1.5	27.6 $\pm$ 1.7	22.2 $\pm$ 2.0 *	28.0 $\pm$ 3.0
Average follow up time, months	78.3 $\pm$ 6.8	83.7 $\pm$ 2.1	84.0 $\pm$ 1.7	82.5 $\pm$ 2.3	79.8 $\pm$ 2.9	81.9 $\pm$ 3.8

BMI= Body Mass Index. Values reported are means $\pm$ standard error or prevalence (%) $\pm$ standard error.

*= significantly different from Obesity Class I (P<0.05).

a) Males



b) Females

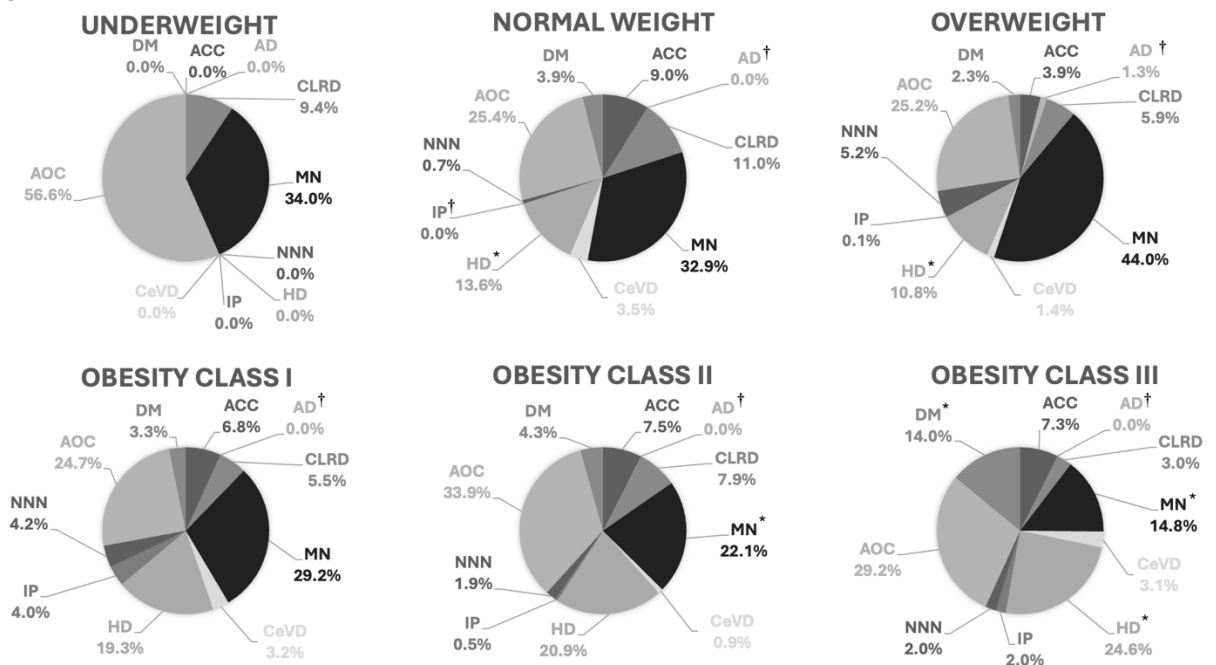
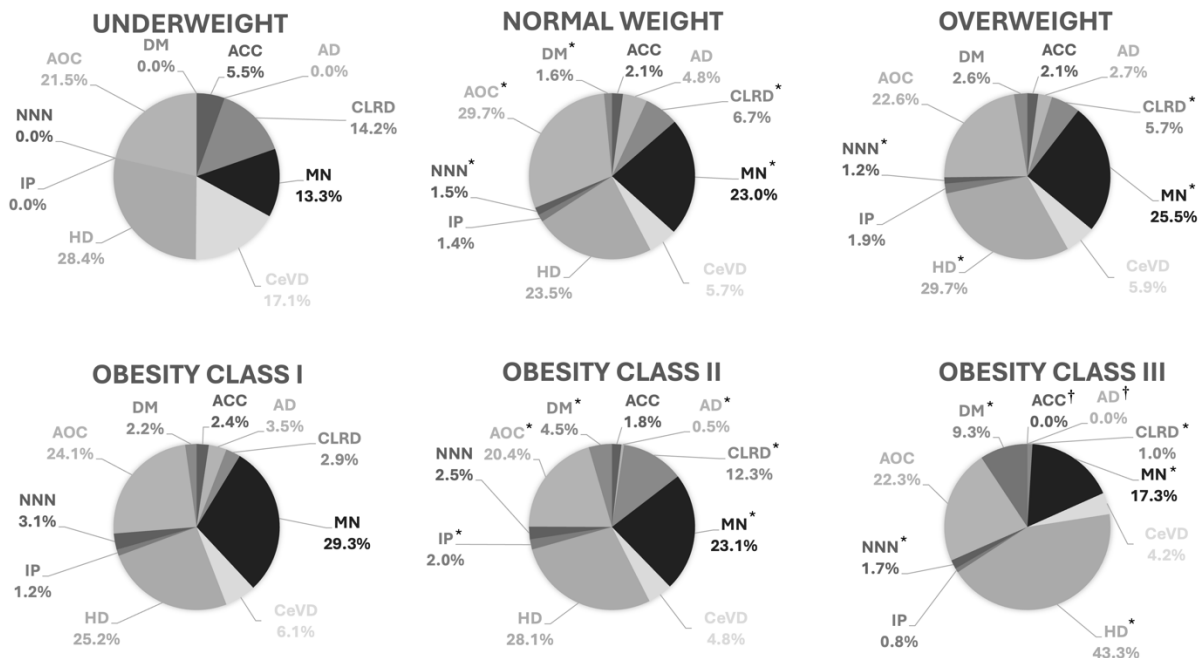


Figure 1 Legend. Differences in prevalence of mortality due to a specific cause among a) men and b) females younger than 65 years of age by BMI class. Values represent weighted prevalence. ACC= Accidents. AD= Alzheimer's disease. CLRD= Chronic lower respiratory diseases. MN= Malignant neoplasms. CeVD=

Cerebrovascular diseases. HD= Diseases of heart. IP= Influenza and pneumonia. NNN= Nephritis, nephrotic syndrome and nephrosis. DM= Diabetes mellitus. AOC= All other causes. *= significant difference Obesity Class I. †= Unable to analyze the difference due to zero observations in that cause of death-BMI category group.

Figure 1 shows the prevalence of the various causes of mortality among younger men and women by BMI class. Malignant neoplasms and diseases of the heart were the most common causes of mortality among adults younger than 65 years of age (**Figure 1a** and **1b**). Though the significance of the differences in the prevalence of the various cause-specific mortality types between BMI classes varied by mortality type, most follow a similar pattern of association, with normal weight and overweight groups being at a lower mortality risk than obesity class I, while obesity class III had higher mortality rates, with the exception of malignant neoplasms mortality that was not associated with BMI ($P<0.05$, **Figure 1a**). In younger men, obesity class II had a greater prevalence of deaths due diabetes mellitus (9.8% versus 5.15%; $P<0.001$) and but a lower prevalence of death due to malignant neoplasms (17.8% versus 32.1%; $P<0.001$) compared to class I, while class III was associated with a higher prevalence of death due to diseases of the heart (29.7% versus 23.3%; $P<0.02$) and lower prevalence of death due to malignant neoplasms (13.9% versus 32.1%; $P<0.001$, **Figure 1a**). In younger women, obesity class III was associated with a higher prevalence of death due to diabetes mellitus (14.0% versus 3.3%; $P<0.001$) and diseases of the heart (24.6% versus 19.3%; $P<0.01$), while obesity class II was only associated with a lower prevalence of death due to malignant neoplasms compared to class I (14.8% versus 29.2%; $P<0.001$, **Figure 1b**).

a) Older Males



b) Older Females

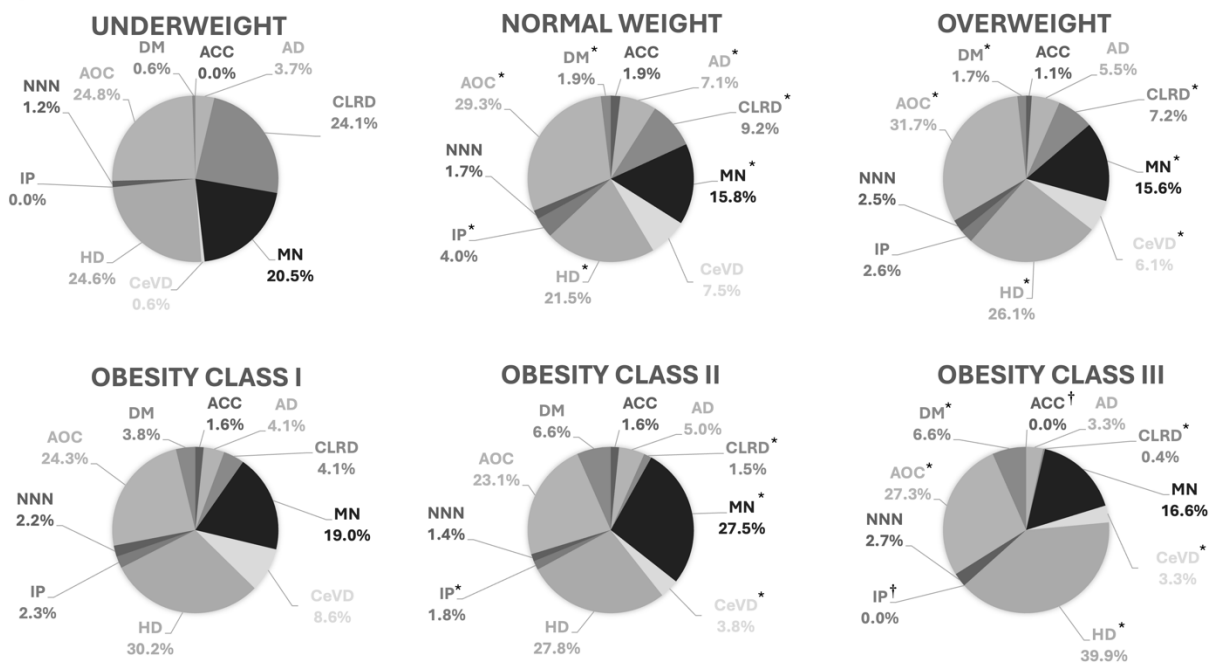


Figure 2 Legend. Differences in prevalence of mortality due to a specific cause among a) men, and b) females older than 65 years of age, by BMI class. Values represent weighted prevalence. ACC= Accidents. AD= Alzheimer's disease. CLRD= Chronic lower respiratory diseases. MN= Malignant neoplasms. CeVD= Cerebrovascular diseases. HD= Diseases of heart. IP= Influenza and pneumonia. NNN= Nephritis, nephrotic syndrome and nephrosis. DM=

Diabetes mellitus. AOC= All other causes. *= significant difference Obesity Class I. †= Unable to analyze the difference due to zero observations in that cause of death-BMI category group.

Figure 2 shows the prevalence of the various causes of mortality among older men and women by BMI class. The most common causes of death among older adults were also malignant neoplasms and diseases of the heart (**Figure 2a** and **2b**). Older men with obesity class II had a significantly higher prevalence of death due to diabetes mellitus (4.5% versus 2.2%; $P<0.001$), and chronic lower respiratory diseases (12.3% versus 2.9%; $P<0.001$) and had a lower prevalence of death due to malignant neoplasms (23.1% versus 29.3%; $P<0.01$), compared to obesity class I (**Figure 2a**). Older women with obesity class II had a higher prevalence of death due to malignant neoplasms (27.5% versus 19.0%; $P<0.001$) and lower prevalence of death due to chronic lower respiratory diseases (1.5% versus 4.1%; $P<0.05$) compared to class I. Both older men and women with obesity class III had a significantly higher prevalence of death due to diseases of the heart (men: 43.3% versus 25.2%; $P<0.001$; women: 39.9% versus 30.2%; $P<0.001$), and diabetes mellitus (men: 9.3% versus 2.2%; $P<0.05$; women: 6.6% versus 3.8%; $P<0.05$, **Figure 2a** and **2b**). Older men had a lower prevalence of death due to malignant neoplasms (17.3% versus 29.3%; $P<0.001$) and chronic lower respiratory diseases (1.0% versus 2.9%; $P<0.002$), compared to those with class I (**Figure 2a** and **2b**).

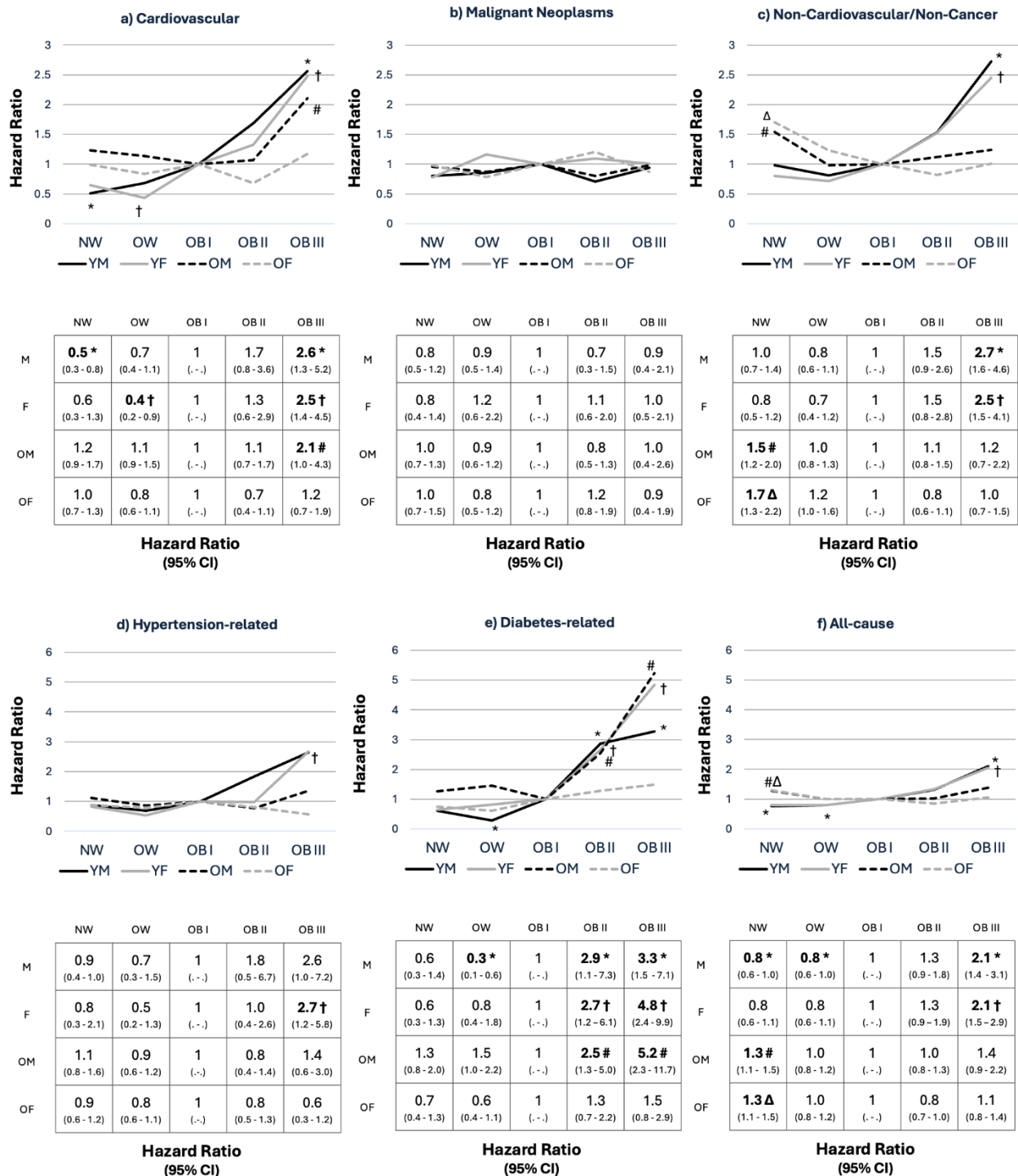


Figure 3 Legend. Differences in hazard ratios of mortality due a) cardiovascular diseases, b) malignant neoplasms, c) non-cardiovascular diseases/non-cancer causes, and d) hypertension-related causes, e) diabetes-related causes, and f) all-cause by age, sex, and BMI class. Values represent adjusted hazard ratios adjusted for ethnicity, education,

and smoking. NW= Normal weight. OW= Overweight. OB I= Obesity class I. OB II= Obesity class II. OB III= Obesity class III. M= Males under 65 years of age. F= Females under 65 years of age. OM= Males over 65 years of age. OF= Females over 65 years of age. *= significant difference from younger males with obesity class I. †= significant difference from younger females with obesity class I. #= significant difference from older males with obesity class I. Δ= significant difference from older females with obesity class I.

Figure 3 shows the differences in hazard ratios of mortality due to: cardiovascular diseases (**Figure 3a**), malignant neoplasms (**Figure 3b**), non-cardiovascular/non-cancer causes (**Figure 3c**) hypertension-related causes (**Figure 3d**), diabetes-related causes (**Figure 3e**), and all-cause (**Figure 3f**) mortality by age group, sex, and BMI class adjusted for ethnicity, education, and smoking. The HR for all-cause mortality was positively associated with BMI class in younger individuals ($P<0.0001$). Both younger men and women with obesity class III had an HR of 2.1 for all-cause mortality compared to those with obesity class I ($P<0.05$, **Figure 3f**). BMI was not significantly associated with all-cause mortality in older men ($P>0.15$), while there was a negative association in older women ($P<0.002$). There were no significant differences between obesity classes among older men or women. This suggests that severe obesity may be a significant risk factor among younger individuals, but not older adults.

A positive association was also observed between BMI and cardiovascular mortality among adults younger than 65 years of age ($P<0.0001$), but not older men ($P>0.93$), and women ($P>0.90$; **Figure 3a**). Younger men and women and older men with obesity class III had significantly higher cardiovascular mortality risk, respectively, compared to those with obesity class I (HR = 2.1-2.6, $P<0.05$, **Figure 3a**). No differences were observed between obesity classes among older women ($P>0.08$). This suggests that within obesity classes, adults younger than 65

years of age and older men with severe obesity are at significantly higher risk of cardiovascular mortality.

In the current study, no significant associations between BMI and mortality due to malignant neoplasms was observed in either younger or older adults ($P>0.30$, **Figure 3b**). Among adults younger than 65 years of age a positive association between BMI and non-cardiovascular/non-cancer mortality was observed ($P<0.002$). There were also differences between obesity classes with mortality risk due to non-cardiovascular/non-cancer causes being approximately 2.7 and 2.5 times higher for younger men and women with obesity class III, respectively, compared to obesity class I ($P<0.05$, **Figure 3c**). Conversely, a negative association between BMI and non-cardiovascular/non-cancer mortality was observed among older adults ($P<0.05$). However, mortality risk due to non-cardiovascular/non-cancer causes was not different between obesity classes ($P>0.24$, **Figure 3c**). This suggests that severe obesity is a significant risk factor for non-cardiovascular/non-cancer mortality among younger individuals, but not older adults.

Mortality risk for death due to hypertension-related causes was positively related with BMI among adults younger than 65 years of age ($P<0.03$). Younger women with obesity class III had a significantly higher hypertension-related mortality risk compared to those with class I obesity ($P<0.05$, **Figure 3d**). However, no differences were observed between obesity classes in younger men ($P>0.05$, **Figure 3d**). Among older adults, there were no significant associations between BMI and hypertension-related mortality ($P>0.68$), and no significant differences between obesity classes were observed ($P>0.13$). This suggests that severe obesity might be a more significant risk factor for hypertension-related mortality among adults younger than 65 years of age, and in particular women.

A positive association between BMI and diabetes-related mortality risk was observed in both younger and older adults ($P < 0.02$). Younger men and women with obesity class II and III had a higher mortality risk due to diabetes-related causes compared to those with class I obesity (HR = 2.7 to 4.8, $P < 0.05$, **Figure 3e**). Similarly, older men with obesity class II and III had a higher diabetes-related mortality risk compared to those with class I obesity (HR of 2.5 to 5.2, $P < 0.05$, **Figure 3e**). No significant differences were observed between obesity classes in older women ($P > 0.24$, **Figure 3e**). This suggests that obesity is associated with step-increases in diabetes mortality risk with increasing BMI category among adults younger than 65 years of age, as well as older men, but not women.

Discussion:

This study examined the differences in mortality risks between BMI classes, stratified by age and sex. There were very few differences in mortality risks between class I and class II obesity, while class III is associated with significantly higher mortality, compared to class I in adults younger than 65 years of age and to a lesser degree in older men, there were very few differences in older women. Though there were subtle variations between the various causes of death, obesity class III was associated with higher mortality risk for cardiovascular, non-cardiovascular/non-cancer, hypertension-related, diabetes-related and all-cause mortality causes in adults younger than 65 years of age. Severe obesity was less consistently associated with mortality risk in older adults.

Obesity has been shown to be associated with significantly higher all-cause mortality within different populations, with some suggesting a J-shaped or linear pattern of association.^{5,6,11,26–32} However, no other study directly examined differences between the obesity classes, while stratifying by both age and sex. Other studies have generally used normal weight as reference group and did not examine the differences between obesity classes.^{26,28} Determining differences in risk between obesity sub-classes would be important in verifying the appropriateness of current BMI obesity class cut-points. In the current study, it was observed that all-cause mortality was positively related with BMI only in adults younger than 65 years of age. While there were no differences in all-cause mortality between class I and class II obesity, obesity class III was associated with significantly higher all-cause mortality risk compared to obesity class I. Some studies have previously examined the association between all-cause mortality and BMI using models stratified by either sex or age, but not both.^{26–28} This may be important as we observe clear differences in how BMI is associated with all-cause mortality

between younger and older adults and to a lesser degree sex. Some studies report elevated all-cause mortality risk in men with obesity class II and women with obesity class II and III compared to those with normal weight,²⁸ while others report elevated all-cause mortality risks for both men and women for all obesity classes compared to normal weight.²⁶ However, these studies did not directly examine the differences between obesity classes. Among older adults, the results have been more divided with some studies reporting no association,^{5,28,31,33} a negative association,³⁴ and positive association between all-cause mortality risk and BMI.^{26,29} We also observe no association between all-cause mortality and BMI in older men and a negative association in older women. This suggests that severe obesity is a significant risk factor for all-cause mortality among younger individuals, but this association may change with age and may differ by sex.

Cardiovascular deaths are one of the leading causes of death in the world.⁹ Some studies report elevated cardiovascular mortality with overweight and obesity,^{6,11,26,30,95} while others report cardiovascular mortality is only elevated in obesity class II and III compared to normal weight.²⁸ One study suggests the significantly higher cardiovascular mortality risk with obesity class II and III as compared to normal weight is consistent between middle age (aged 45 to 64 years old) and older adults (older than 65 years of age).²⁸ However, no study has directly examined differences in cardiovascular mortality risk between the obesity classes. In this study, no differences in cardiovascular risk between class I and II were observed in younger or older adults, while only obesity class III was associated with significantly higher risk of cardiovascular mortality in adults younger than 65 years of age and older men, but not older women.

Elevated cancer mortality rate has also been positively associated with BMI and obesity.^{6,7,27,30,91,96,97} However, again no other study directly examined differences in cancer

mortality risk between the obesity classes. Some studies report a J-shape relationship between BMI and cancer mortality risk,^{26,27} while others found no association between obesity and cancer mortality risk.^{42,98–100} We also observed no association between BMI and cancer mortality in both younger and older men and women. Even within studies that report a significant association between obesity and cancer mortality suggest a relatively lower mortality risk (hazard ratio <2.0) compared to other causes of death.^{26,27} This is likely due to the differences in risk for the various types of cancer and obesity. While obesity is associated with some cancers such as liver and colorectal cancers, it is not associated with other cancers that have higher mortality risk such as lung and brain cancers.^{27,91,97} Therefore, further research, with larger sample sizes may be necessary to fully understand differences in cancer mortality risk and the specific cancer subtypes, between obesity classes, among younger and older men and women.

A number of studies have investigated the association between non-cardiovascular/non-cancer mortality risks with BMI.^{33,34,42,100} Some studies suggest higher mortality risk with obesity in younger adults compared to normal weight.⁴² In the present study, adults younger than 65 years of age with class III obesity had significantly higher non-cardiovascular/non-cancer mortality risk compared to class I, but with no differences with class II. This category of mortality is more heterogeneous in nature with causes that include chronic lower respiratory diseases; diabetes mellitus; accidents; Alzheimer's; influenza and pneumonia; nephritis, nephrotic syndrome, and nephrosis; and other causes. These causes of death vary in the strength of their association with obesity, with some causes being strongly associated (i.e. diabetes, influenza and pneumonia, and respiratory diseases, nephritis, nephrotic syndrome, and nephrosis), while others such as Alzheimer's Disease, neurological, accidents, and self-harm causes of death are less strongly or not related.²⁷ Among older adults, no differences in non-

cardiovascular/non-cancer mortality risks were observed between obesity classes, while normal weight was associated with a significantly higher mortality risk. Other studies have also suggested higher non-cardiovascular and/or non-cancer mortality risk in older adults with normal weight, compared to those with overweight and obesity.^{33,34} The lower mortality risk observed in older adults with higher BMIs may be due to the protective effects of excess body fat³⁴ or higher fat-free mass that is also associated with higher BMIs.¹⁰¹ Thus, the elevated non-cardiovascular/non-cancer mortality risk among those with normal weight may be reflective of the underlying frailty in this population.³³ This suggests that adults younger than 65 years of age may benefit more from aggressive obesity management and weight loss strategies, while older adults would be better served with weight maintenance approaches.

Hypertension and type II diabetes are comorbidities that are strongly associated with obesity and contribute to the development of cardiovascular disease mortality risk.^{9,102} As with the other mortality analyses, obesity class III was more consistently associated with hypertension-related mortality risk in adults younger than 65 years of age than in older adults. Type II diabetes is one of the most strongly obesity-related comorbidities and this was the only mortality outcome where we observed a significantly higher mortality risk for obesity class II as compared to obesity class I in adults younger than 65 years of age. The association between obesity and type II diabetes mortality outcomes was not as clear in older adults. A number of studies have examined the association between BMI and all-cause mortality in patients with diabetes, however the results have been inconsistent. One study reports that patients with type II diabetes and obesity class I, II and III did not have significantly different mortality risk as compared to normal weight patients with type II diabetes, though they may have been underpowered as the sample size of the deaths in the obesity sub-classes were relatively small

(n= 1 to 69).¹⁰³ Other studies report higher diabetes mortality rates in obesity class III compared to class I ^{104,105} or II ¹⁰⁴ among those with type II diabetes. Conversely, another study found a negative association between BMI, and mortality risk among patients with type II diabetes, despite having a predominating middle-aged sample.¹⁰⁶ However, these studies also lacked age and sex stratification, which leaves the questions whether these associations differ between younger and older men and women.

Across the various causes of mortality, there were minimal differences between class I and class II obesity, while class III was more consistently associated with significantly higher mortality risk in adults younger than 65 years of age and older men. Though BMI is generally positively associated with several health risk factors and many of the mortality outcomes examined here, it is unclear whether obesity class I and II cut-offs discriminate two distinctly different health risk groups that require differentiation. Indeed, BMI cut-offs have been revised over time to reflect the changing association between BMI and health risk over time. There is evidence to suggest that the risk for certain obesity comorbidities such as hypertension and dyslipidemia may be decreasing over time, while the risk for diabetes may be increasing.¹⁰⁷ Additionally, advancement of medicine, better screenings and more effective treatments, may also affect the prevalence of these chronic conditions associated with obesity and ultimately affect the associated mortality risks.¹⁰⁷ This study provides evidence to suggest that mortality outcomes are similar between obesity class I and II, while obesity class III is clearly associated with elevated mortality risk and may require more aggressive obesity management approaches. More research is necessary to determine the most currently appropriate BMI cut-offs to delimitate obesity sub-classes that differ in health risk.

Strengths and limitations

One notable strength of this study is a large, weighted sample to reflect the United States population. However, this study has several limitations that should be taken into account. BMI was measured only at the baseline. In the current study, the models were not adjusted for physical activity, as those with severe obesity may experience physical limitation that limits their ability to exercise.^{39,40} Moreover, the models were also not adjusted for use of medication as adjustment for obesity related conditions may represent an over-adjustment for conditions that lie on the causal pathway between obesity and mortality risk. Additionally, use of BMI as a measure of obesity also has a limitation, as BMI does not differentiate between fat mass and fat free mass.¹⁰⁸ Fat free mass and fat mass relate to mortality outcomes differently,¹⁰⁹ and the negative consequences of low fat free mass may be of greater concern in older individuals.^{110,111} Recent and previous weight loss or gain, as well as body shape may also alter the association between BMI and mortality and this was not considered in this study.²⁹ The prospective cohort design of the study with mortality follow-up, and lack of follow up BMI measurements, limits the ability to infer causal association between the variables. Consequently, further research is necessary to explore the relationship between BMI classes and mortality, in different sub populations, such as patients with pre-existing conditions.

Among adults younger than 65 years of age, obesity class III is generally associated with the highest mortality risks, while there were minimal differences between obesity class I and II. This study contributes to the growing literature that suggests that obesity is associated with greater mortality risk in younger than older individuals, but also that there may be a sex difference in that older men may also have a greater obesity-related mortality risk than older women. Thus, these differences should be considered when designing obesity management strategies, as they highlight the need for more aggressive approaches for these populations.

Manuscript 2:

**The Association Between Weight Management Goals, Approach Selection,
and Weight Outcomes**

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Key Words (MeSH): Obesity, Motivation/Goals, Weight Loss, Body Weight Changes, Diet, Exercise

Running Title: Weight Management Approach.

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Abstract:

Objective: To investigate differences in the weight loss by weight management goal, approach employed, and the amount of desired weight loss.

Methods: Data from 5,352 adults attempting weight loss or preventing weight gain from NHANES (2007 to 2012) were analyzed using generalized linear models with least squared adjusted means and Bonferroni post hoc tests.

Results: Participants wanting to lose weight or prevent weight gain, wanted a 28.1-36.7% lower body weight. The approaches used for weight loss and weight gain prevention were similar, with dietary modification being the most common approach for both men and women (85.0-91.6%), followed by exercise (45.0-62.8%). Less than 5% of the participants were able to lose at least 5% of their body weight, while over 60% were able to prevent weight gain of over 2%. On average, both men and women tended to gain weight (1.7-3.3 kg) regardless of whether individuals were attempting to lose weight or prevent weight gain and the approaches they employed.

Discussion: In a nationally representative sample, weight management approaches showed limited success in preventing weight gain or achieving the desired weight loss. Both men and women tended to gain weight despite wanting to lose a significant amount of weight and employing several weight management approaches.

Introduction

With the rising prevalence of obesity, there are a significant number of adults attempting to lose weight. About 90% of the US adults who attempt to lose weight use dietary strategies, such as consuming fewer calories and reducing fat intake.⁷⁷ On the other hand, engaging in physical activity (46.0% men, 35.6% women) or using a combination of diet modification and exercise (28.6% men, 26.6% women) for weight loss are less common.⁷⁷ Additionally, there are sex-differences in the weight loss approaches used with women being more likely to use dietary strategies to lose weight, whereas men are more likely to use physical activity for weight loss.^{77,79}

Setting a goal for weight loss could be an important initial step, potentially motivating individuals through their weight loss journey. Some studies have shown that setting higher weight loss goals are associated with more weight loss.^{68,72–75,112} Meanwhile, others found no such association.^{68,71,72,75} Individuals who set greater weight loss goals may recognize the need to be more invested or make larger behavioural changes^{68,74}, or may be more likely to use specific strategies such as engaging in physical activity, consuming a well-balanced diet or having smaller portions.⁶⁸ It is accepted that weight losses of 5-10% of body weight are associated with significant improvements in physical and psychological health.⁶⁸ In contrast, individuals with obesity are reported to have weight loss goals of 22 to 35% of their body weight.

While there are some studies that have investigated the relationship between weight loss goals, strategies, and outcomes, there has been little research into how the magnitude of weight loss desired is related with the weight loss-specific practices used. Thus, the objective of this

study is to investigate whether desiring greater weight loss is associated with differences in the number and type of weight loss strategies used and ultimately greater weight loss achieved in a nationally representative sample of women and men.

Methods:

Publicly available anonymized data was obtained from individuals in the United States who participated in the National Health and Nutrition Examination Survey (NHANES) Continuous (years 2007 to 2012, n=30,442) on Sept 22, 2023. Surveys used were limited to years that asked participants about their desired weight (“How much would you like to weigh?”). Individuals who did not try to lose weight or prevent weight gain (n=5,821), as well as those under 20 years of age (n= 12,729) were excluded from the analysis. Those who were missing current self-reported weight or self-reported weight a year ago (n = 539), Body Mass Index (BMI; n=456) or desired weight (n = 5539) were also excluded. Outliers with extreme values for any variable of interest were also excluded (n=6). This resulted in 5,352 participants being included in the final analysis. Informed written consent was obtained from all participants before the examination, and the study protocol was approved by the National Center for Health Statistics. Because the current analysis only included publicly available data, the current study did not require ethical approval from our institution.

A detailed explanation of the data collection methods has been previously reported.^{93,94} A trained technician conducted measurements of height and weight during the physical examination.⁹⁴ Standing height was measured using a fixed stadiometer, and body weight was measured using an electronic load-cell scale while wearing underwear, a paper gown and paper pants.⁹⁴ Questionnaires were used to assess age, sex, education level, ethnicity, self-reported weight (current and 1 year ago), and weight loss/weight gain prevention history.⁹⁴ Educational level was reported as: Less than 9th grade; 9-11th grade; High school graduate/GED or equivalent; Some college or Associate of Arts degree; and College graduate or above. Education was re-classified as the presence or absence of postsecondary education (i.e., more than high

school). Ethnicity reported as: Mexican American, Other Hispanic, non-Hispanic white, non-Hispanic black, and other. Ethnicity was reclassified into the categories of "White," and "non-white."

Current self-reported weight was assessed by the question: "How much do you weigh without clothes or shoes?" Desired weight was assessed by: "How much would you like to weigh?" Desired weight change was defined as the difference between current self-reported weight and desired weight. Self-reported weight 1 year ago was assessed by: "How much did you weigh a year ago?" Weight change was defined as the difference between the current self-reported weight and self-reported weight 1 year ago. Clinically significant weight loss (CSWL) was defined as achieving a weight loss of 5% or more of one's self-reported weight 1 year ago.¹¹³

The participants were asked if they tried to lose weight or prevent weight gain in the past 12 months, and what methods they used to lose weight. Methods were reclassified into four groups:

- Dietary approaches:
 - Ate less food; switched to foods with lower calories; ate less fat; skipped meals; drank a lot of water; followed a special diet; ate fewer carbohydrates; ate more fruits, vegetables, salads; changed eating habits; ate less sugar, candy, sweets.
- Exercise approaches:
 - Exercised.
- Product approaches:
 - Ate diet foods or products; used a liquid diet formula.

- Other approaches:
 - Took non-prescription supplements to lose weight; took laxatives or vomited; started to smoke or began smoking again; joined a weight loss program; joined program to not gain weight; took non-prescription diet pills; took prescription diet pills; other.

Prescription diet pill use was not examined as its own category because of the low sample size. We also did not include “Ate less junk food or fast food” in our analysis because it was not included as an option in all survey years. The participants could choose any of methods listed above for weight loss and weight gain prevention. Those who attempted to lose weight were also asked whether they sought help from a health professional to lose weight in the past 12 months. The participants could choose any of the following options: “personal trainer”, “dietitian”, “nutritionist”, “doctor” or “other health professional”.

Statistical Analysis:

Participant characteristics are presented as means with standard errors (SE) and prevalence with SE. General linear models adjusted for age, ethnicity, BMI, and education level were used to calculate least squared adjusted means. Bonferroni post hoc tests were used to examine the differences in: 1) the adjusted prevalence of weight management approaches among those who tried to lose weight or prevent weight gain (Bonferroni adjustment = 0.05/2); 2) the adjusted prevalence of approaches and desired weight loss by whether or not they achieved a CSWL among those who tried to lose weight (Bonferroni adjustment = 0.05/2); and 3) adjusted mean differences in desired weight change and weight change based on the number of

approaches used (1, 2 or 3+ approaches: diet, exercise, products or other approaches) among those who tried to lose weight or prevent weight gain (Bonferroni adjustment = 0.05/6).

General linear models were used to examine the adjusted prevalence of different weight management combinations (i.e., diet-no exercise, exercise-no diet, a combination of diet and exercise, and all approaches combined), among those who tried to lose weight and those who tried to prevent weight gain (Bonferroni adjustment = 0.05/6). Due to the limited number of participants who used only Products or Other Approaches they were excluded from this sub-analysis (n=975).

All analyses were stratified by sex. All statistical analyses were weighted to be nationally representative of the U.S. population, performed using SAS software version 9.4, with a significance threshold of $P < 0.05$.

Results:

The characteristics of the participants are shown in **Table 2**. More participants tried to lose weight in the past year than tried to prevent weight gain (men: 32.0% versus 9.5%, women: 44.2% versus 8.8%, $P<0.05$). Those who tried to lose weight tend to be younger, with higher BMIs and desired weight loss, than those who tried to prevent weight gain. The majority of individuals attempting to lose weight or prevent weight gain were women, white, and had higher education. Despite men having higher BMIs than women (women: 30.8 kg/m², men: 32.1 kg/m²), women tended to have higher desired weight loss (women: 15.2 kg, men: 14.2 kg). Regardless of the weight management goal, participants tended to gain weight, with those who tried to lose weight gaining more weight, compared to those who tried to prevent weight gain (women: 2.6 versus 1.0 kg, men: 2.0 versus 1.7 kg). A small proportion of those who tried to lose weight sought help from a professional, with women seeking help more than men (7.5% of men and 12.6% of women, $P<0.05$). Only 2.4% of men and 4.9% of women who tried to lose weight successfully lost at least 5% of their body weight. Among those that tried to prevent weight gain, 3.1% of men and 7.6% of women achieved a 5% reduction in body weight. Sixty-three percent of men and 54.2% of women who tried to lose weight, and 67.5% of men and 64.0% of women who tried to prevent weight gain were able to prevent weight gain of over 2% of their starting weight. Majority of individuals used one or two approaches to lose weight or prevent weight gain. The weighted prevalence of the number of individual methods employed for weight loss and weight gain prevention is reported in Supplementary Table 1. Among those who tried to lose weight, men and women were most likely to use two approaches, while those who tried to prevent weight gain were most likely to use only one approach.

Table 2: Characteristics of individuals trying to lose weight or prevent weight gain stratified by sex.

	Tried to lose weight		Tried to prevent weight gain	
	Men	Women	Men	Women
N (n, %)	1581 (32.0)	2757 (44.2)	467 (9.5)	547 (8.8)
Age (Years)	46.0 $\pm$ 0.4	45.7 $\pm$ 0.4	49.0 $\pm$ 0.9 [†]	49.6 $\pm$ 0.9 [†]
BMI (kg/m²)	32.1 $\pm$ 0.2	30.8 $\pm$ 0.2 *	29.8 $\pm$ 0.3 [†]	28.7 $\pm$ 0.4 ^{*†}
White Ethnicity (%)	72.1 $\pm$ 2.2	70.3 $\pm$ 2.1	76.0 $\pm$ 2.3	72.6 $\pm$ 2.9
Higher Education (%)	67.5 $\pm$ 1.9	64.6 $\pm$ 1.6	72.8 $\pm$ 2.3 [†]	67.0 $\pm$ 2.9 *
Desired Weight Loss (kg)	14.2 $\pm$ 0.5	15.1 $\pm$ 0.3 *	9.3 $\pm$ 0.7 [†]	11.2 $\pm$ 0.6 ^{*†}
Weight Change (kg)	2.0 $\pm$ 0.2	2.6 $\pm$ 0.1 *	1.7 $\pm$ 0.5	1.0 $\pm$ 0.2 [†]
Sought help from a professional (%)	7.5 $\pm$ 1.1	12.6 $\pm$ 0.8 *	--	--
Lost at least 5% of body weight (%)	2.4 $\pm$ 0.4	4.9 $\pm$ 0.5 *	3.1 $\pm$ 0.7	7.6 $\pm$ 1.2 ^{*†}
Weight change < +2% (%)	63.0 $\pm$ 1.6	54.2 $\pm$ 1.2 *	67.5 $\pm$ 2.9	64.0 $\pm$ 3.0 [†]
Number of approaches (%):				
1 Approach	40.0 $\pm$ 1.8	35.6 $\pm$ 1.3 *	61.2 $\pm$ 3.1	59.0 $\pm$ 2.4
2 Approaches	49.1 $\pm$ 1.8	47.2 $\pm$ 1.3	35.8 $\pm$ 3.1	36.6 $\pm$ 3.0
3+ Approaches	10.8 $\pm$ 1.8	17.2 $\pm$ 1.0 *	3.0 $\pm$ 1.0	4.4 $\pm$ 1.1

BMI = Body Mass Index. Values reported are means $\pm$ standard error or prevalence (%) $\pm$ standard error.

* Significantly different from men (P<0.05). [†] Significantly different from Tired to lose weight (P<0.05). --

Question not asked in participants who tried to prevent weight gain.

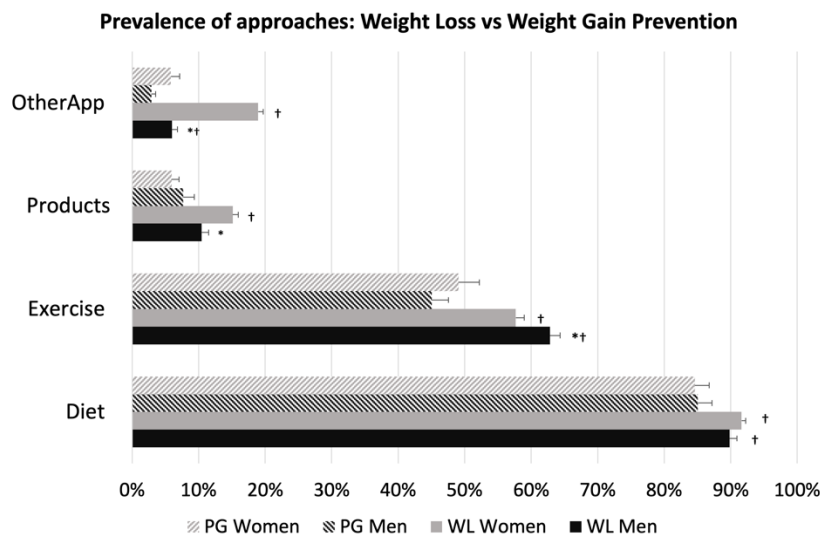


Figure 4 Legend. Differences in the prevalence of different approaches among those to tried to lose weight and those to tried to prevent weight gain. Values represent least squared adjusted prevalence adjusted for age, BMI, ethnicity, and education. PG= tried to prevent weight gain. WL= tried to lose weight. *= significant difference from women within weight management goal. †= Significantly different from PG within sex.

Figure 4 shows the prevalence of weight management approaches stratified by sex. Diet was the most prevalent weight management approach with 85.0 to 91.6% of the men or women who attempted weight loss or weight gain prevention reporting some dietary modification. Exercise was the second most prevalent approach (ranging from 45.0% to 62.8%), while a smaller portion of participants reported using weight management products (5.9% to 15.1%) or Other (2.9% to 18.9%) approaches for weight loss or weight gain prevention in the past year. When adjusted for age, BMI, ethnicity, and education, men and women who wanted to lose weight were more likely to use diet and exercise than those who wanted to prevent weight gain

($P < 0.05$). Men attempting to lose weight had a higher prevalence of using exercise, and a lower prevalence of using Products and Other approaches than women ($P < 0.05$).

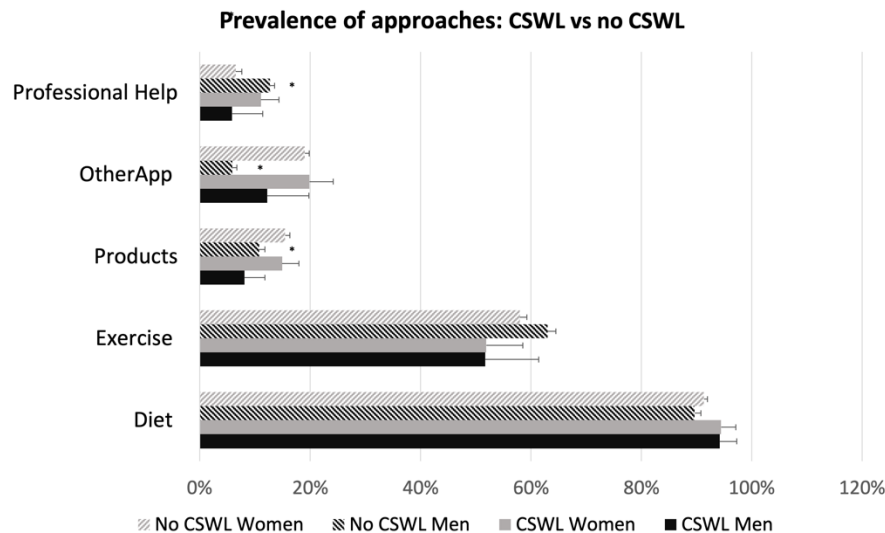


Figure 5 Legend. Differences in prevalence of different approaches among those to tried to lose weight and achieved a clinically significant weight loss and those who did not. Values represent least squared adjusted prevalence adjusted for age, BMI, ethnicity, and education. CSWL= clinically significant weight loss. *= significant sex difference within CSWL group. There were no significant differences between those who did and did not have a CSWL within each sex.

Figure 5 shows the prevalence of weight loss approaches used stratified by weight loss outcomes ($>5\%$ WL) and sex. When adjusted for age, BMI, ethnicity, and education, no differences in the prevalence of any of the weight loss approaches were observed by weight loss outcome, in either men or women ($P > 0.05$). Men who did not achieve a CSWL had a higher prevalence of using exercise and seeking professional help, and a lower prevalence of using

products and other approaches to lose weight, than women who did not achieve a CSWL ($P<0.05$).

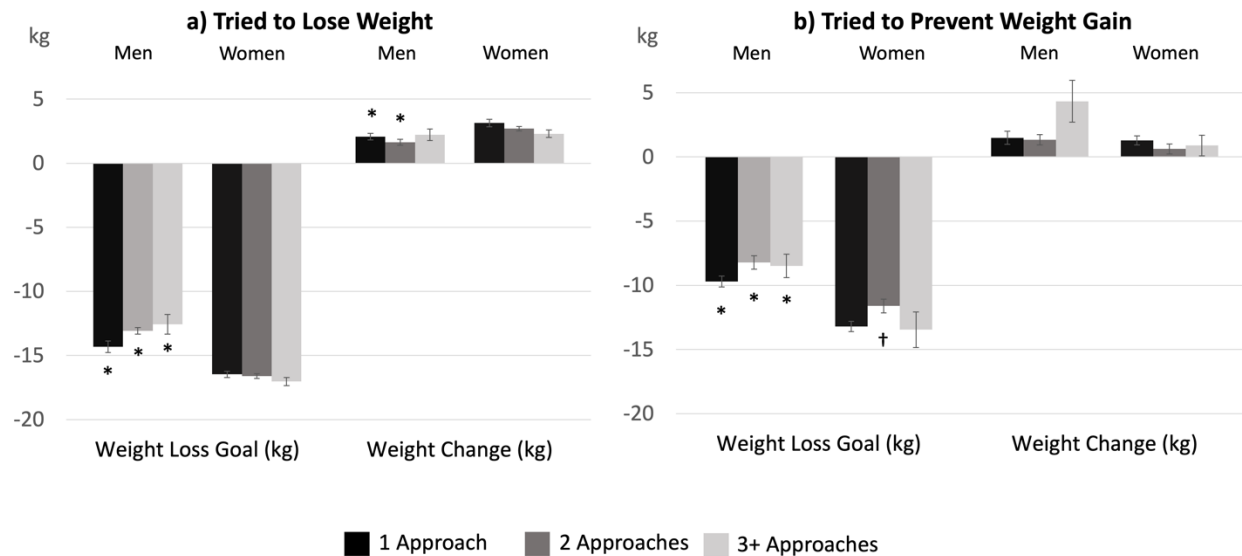


Figure 6 Legend. Differences in the average desired weight loss and weight change by the number of approaches used among those who wanted to lose weight (a), and those who wanted to prevent weight gain (b). Values represent least squared adjusted means adjusted for age, BMI, ethnicity, and education. *= significant difference from women for a given number of approaches. †= significantly different from using 1 Approach within sex.

The average desired weight loss did not differ between those who did and did not achieve a CSWL within each sex (12.7 to 16.7 kg, $P>0.05$). **Figure 6** shows the desired weight loss and weight change, based on the number of approaches used in men and women. The number of approaches used was not associated with the magnitude of the desired weight loss or the weight change attained ($P>0.05$).

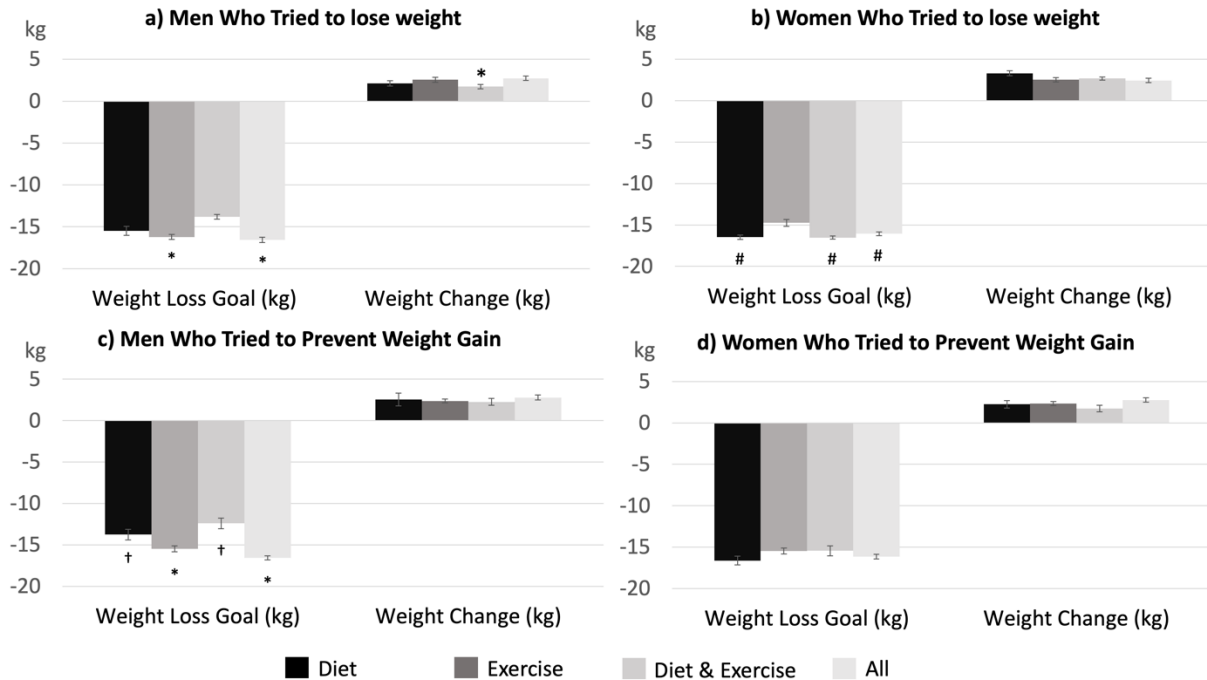


Figure 7 Legend. Differences in the average desired weight loss, and weight change by the combination of approaches used among men (a) and women (b) who wanted to lose weight, and men (c) and women (d) who wanted to prevent weight gain. Values represent least squared adjusted means adjusted for age, BMI, ethnicity, and education. *= significantly different from Diet & Exercise. # = significantly different from Exercise. † = significantly different from All.

Figure 7 shows the desired weight loss and weight change based on the specific weight management combination of approaches used. There were only small differences between groups, with no consistent differences between the type of weight management approach used and the magnitude of the desired weight loss (12.4 to 16.6 kg) or weight change observed (1.7 to 3.3 kg weight gain).

Discussion:

This study examines the relationship between weight management goals with the approaches used to achieve the desired weight. Regardless of the weight management goal, participants tended to gain weight. The number of strategies and type of strategy used was not related with the amount of weight loss achieved. The type of strategies used for weight gain prevention were similar to what was used for weight loss, but in general, individuals used fewer strategies for weight gain prevention as compared to weight loss.

Similar to other studies, the desired weight loss observed in this study ranged from 28.1% to 36.7%,^{72,114–116} with women generally have higher desired weight loss than men. However, such high desired weight loss is unlikely to be attainable as it far exceeds the average 3–5% typically observed with most lifestyle interventions.^{1,69,70} Dietary approaches for weight loss were extremely common in this study (89.8% for men and 91.6% for women) and others.^{77,117,118} In this study, we did not examine the difference between the various types of diets, however, other research suggests minimal differences in the long term achieved weight loss between them.^{119–121} It is well established that calorie-reducing diets are more effective than exercise as a primary driver of weight loss.^{122,123} This difference likely contributes to the greater popularity of dietary approaches than exercise for weight loss. Other factors, such as limited time, physical limitations, fear of injury, lack of knowledge, insufficient professional guidance, absence of social support, and various environmental and institutional barriers, may also contribute to the lower participation in exercise.^{124–127} Thus, there may a large disconnect between desired weight loss and what can realistically be achieved through lifestyle interventions.¹²⁸ Despite this, we observe that only a small percentage of those trying to lose weight, seek help from a professional. Limited access, lack of trust, cost, emotional and other factors, maybe act barriers

to seeking professional help.^{128–130} Thus, public health policies, and public education could play a powerful role in addressing this issue.¹²⁸

Our study demonstrates that individuals who want to lose more weight do not differ in the amount of weight they lose, regardless of the type or number of weight management approaches used. Despite attempting to lose weight or prevent weight gain, both men and women tended to gain weight. This suggests that the general effectiveness of self-directed lifestyle interventions may be poor, even if individuals utilizing multiple different weight management methods and strategies. While combining diet and exercise under controlled randomized controlled trial settings has been shown to be a more efficacious long-term weight loss strategy, than diet or exercise alone.¹²³ However, the effectiveness of weight loss products and other approaches such as laxatives, non-prescription weight loss pills or joining a commercial weight loss program, whether used alone or in combination with diet and exercise is typically examined under less stringent settings, and studies have been less conclusive as to their efficacy.^{131–134} The findings of this study suggest that, in uncontrolled settings within the general population, there may be no clear association between the number or different combination of approaches participants used and their weight-related goals or outcomes. In fact, the average 1-year weight gain in our sample (0.62 to 3.13 kg) was higher than the United States' average weight gain of 0.42 kg per year seen in the general population, despite having a similar BMI.¹³⁵ Considering that our sample consists of individuals struggling with weight management, it is likely that without their efforts, the weight gain could have been even more significant. Therefore, these findings may highlight the need and importance of developing more effective weight management strategies for populations at high risk for weight gain and may support the need for greater use of effective weight loss medications, such as semaglutide and tirzepatide.

Only 2.4% of men and 4.9% of women who attempted to lose weight achieved a CSWL (reduction of at least 5% of their body weight). As a reference, ~30% of patients attending a clinical weight management clinic were able to attain a CSWL using largely lifestyle approaches.^{136,137} This enforces the importance of having support and accountability in achieving weight loss.¹³⁸ Interestingly, we observe men who did not achieve a CSWL were more likely to exercise and seek professional help, but also had a lower desired weight loss. This may suggest that support may be less effective for men, or that men may be more willing to exercise and seek professional help only when facing weight management challenges. Women did not achieve a CSWL were more likely to use Products and Other approaches for weight management. This may indicate differences in the effectiveness of weight loss approaches or that these women who attempted using weight loss products or other less common approaches, may be trying them as a ‘last resort’ due to past weight struggles. In a clinical weight management sample, it is reported that only 5% of women and 12% of men have never attempted to lose weight.¹³⁹ More research is needed to fully understand this difference in approaches between men and women. Together, these results may suggest that other associated factors, such as adherence, environment, physiological and psychological factors, may be important considerations for weight loss, beyond simply the specific weight loss approaches taken.^{89,120–122,140}

Strengths and limitations

One notable strength of this study is the use of a large nationally representative sample of the United States population. Although there may be a high correlation between self-reported and measured weight,¹⁴¹ a key limitation is the use of questionnaires and self-reported data, which are subject to response and recall biases. Approximately 75% of people discontinue weight management approaches within six months,¹²⁸ which may reduce the effectiveness of such

approaches, but reflects the differences often seen between efficacy and effectiveness studies. Given that adherence is a predictor of weight loss outcome,⁸⁹ the inability to examine adherence and compliance with the various weight management methods is another limitation of the current study. Further, these individuals may have begun their weight effort at any point within the 12 months before the assessment, or even earlier. Thus, the lack of differences between groups may also reflect the variability in the length or time course of weight management intervention. Nevertheless, these results may indicate the true differences of lifestyle interventions in laboratory versus real-life settings. The data used in this study were collected (2007-2012), prior to the approval of the most effective current weight loss medications. Consequently, further research is necessary to assess the evolving prevalence of weight loss medication use, as well as their effects, in recent years and moving forward.

Implications for Practice

Traditionally, lifestyle management has been the first line treatment for obesity, wherein pharmaceuticals and surgical options are only considered after the individual has demonstrated that lifestyle options are not sufficient. Our results indicate that regardless of how many and the type of behaviours chosen, individuals tend to gain weight. This supports newer clinical obesity guidelines¹ that propose that positive diet and physical activity behaviours should be encouraged regardless of body size or composition, but that reliance on other obesity interventions is required.

This study highlights the complex and multifactorial nature of weight management. There is a disconnect between an individual's desired weight loss and what realistically is achievable through lifestyle interventions. These interventions showed limited success in preventing weight

gain or achieving weight loss, and both men and women tend to gain weight despite their efforts.

Therefore, the number and type of strategies used may not be associated with weight management outcome.

Manuscript 3:

The Association of Motivational Factors with Weight Loss and Treatment Time in a Publicly Funded Weight Management Clinic

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Running Title: Weight Loss Motivation.

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Author Contributions: The authors had full access to all the data in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. AY wrote the manuscript and analyzed the data. JK revised the manuscript for important intellectual content. All authors contributed to the concept and design of the study, interpretation of the data, and had approval of the final submitted version of the manuscript.

A form of this manuscript has been published.

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Abstract:

Objective: To explore differences in weight loss (WL) and treatment time with having health, mobility, and/or esthetics motivations for attempting WL.

Methods: Data from 7,540 adults with overweight or obesity who participated in a publicly funded weight management program at the Wharton Medical Clinic were analyzed. Patients' weight loss motivations were categorized into six groups: Health only; Health & Esthetics; Health & Mobility; Health, Mobility & Esthetics; No Health; and None.

Results: Women with Health, Mobility & Esthetics or No Health motivations had marginally higher WL goals compared to other groups, with no differences in men. Men with Health & Esthetics, or Health & Mobility motivations showed marginally higher 6-month attendance rates. Men who discontinued after one visit were 40% less likely to have a Health & Esthetics motivation as opposed to Health only, compared to those who continued. No differences were observed in WL between motivation groups in either sex. No correlation was found between WL goals and WL attained. Only weak correlations between treatment time and WL were observed across most motivation groups.

Discussion: Despite small differences in treatment time and WL goals, motivations for attempting weight loss were not significantly associated with differences in the WL achieved.

Introduction:

The rising prevalence of obesity and its complications underscores the importance of obesity and weight management in the face of this global epidemic. The most commonly cited primary motivations for weight loss are improving one's health followed by improving one's appearance.^{67,83–86} Other motives for losing weight include social pressure, improved energy, improved social life, improved performance, improved self-esteem and special events.⁸⁷ Numerous studies have shown differences in the amount of weight loss attained depending on the primary motivations for losing weight.^{67,84–86}

Health, as the primary motivation, has been associated with favourable weight loss outcomes,^{67,84,86} while appearance has been associated with negative outcomes,^{67,84,87} and the effect of having other weight loss motivations is not clear. Women are more likely to have an aesthetic motivation than men,^{67,85,88} and having an aesthetic motivation has been associated with greater discontinuation of treatment.^{67,89,90} This may be important as the length of the treatment has been identified as a key factor influencing weight loss success.⁸⁹ Sasdelli and colleagues⁶⁷ found that those with aesthetic motivation were 4.18 times more likely to discontinue at 6 months as compared to those who did not have an aesthetic motivation. Conversely, having a health motivation was associated with a 51% lower likelihood of discontinuing at 6 months.⁶⁷ Although there is some evidence suggesting that these primary motivations such as health or esthetics can impact weight loss results, the majority of these studies focused on one primary motivation. Therefore, there is limited data on how having multiple motivations may be associated with differences in weight loss outcomes and treatment time.

While there is some evidence showing that an individual's primary motive may influence weight loss outcomes, the association between weight loss motives, weight loss outcomes, and their connection with treatment time is not fully understood. Thus, a better understanding of how having one or multiple primary motives for weight loss may influence weight loss outcomes could provide some insight needed for improving the efficacy of lifestyle interventions.

Methods:

The data was obtained from electronic medical files of 14,300 adult patients (age > 18 years) with overweight or obesity (baseline BMI ≥ 25 kg/m²) who attended the Wharton Medical Clinic (WMC) weight management program between September 1, 2016, and December 2019. Patients who enrolled in the program within six months of December 2019 were excluded from the study in order to accurately assess six-month patient completion and weight loss. Outliers with extreme weight, height, or weight loss, as well as those who are missing sex, age, education, weight loss data, weight loss goal or weight loss motivation, or had errors in data entry, were excluded from the analysis, leaving 7540 patients to be included in the analysis.

As previously reported, the WMC is a medical weight management centre, with a team of physicians, behavioural therapists, dietitians, and nutritionists.^{142,143} They offer dietary, physical activity, behavioural, pharmaceutical, and medical interventions for weight loss.¹⁴² WMC operates under the Ontario Health Insurance Plan and offers additional complimentary services, such as educational sessions and drop-in visits.¹⁴² All patients are referred by their primary care physician or another specialist and can remain in the program for as long as they choose.^{136,142} The care is given in accordance with the Canadian Obesity Guidelines.¹

At their initial visit, patients completed questionnaires about their demographics, behavioural goals and medical, physical activity, nutrition, and weight loss history.¹⁴² Patients self-reported their ethnicity as: "White/Caucasian," "South Asian," "East Asian," "Black," "Aboriginal," or "Other". Ethnicity was re-classified as White or None-White for the analyses. Patients also self-reported having completed "less than high school," "high school or GED," "college," or "university" as their educational level. Educational level was re-classified as the presence or absence of postsecondary education (college and university). Additionally, patients

self-reported that their main motivations for losing weight were “to improve health,” “mobility,” “esthetics,” and/or “other.” Patients' weight loss motivation was categorized into six groups: Health (H), Health and Esthetics (HE), Health and Mobility (HM), Health, Mobility, and Esthetics (HME), No Health (NoH) motivation and None. Due to a limited number of patients who reported having only Esthetics or Mobility as their motivation, these patients were combined with those who reported Esthetic and Mobility as their motivation into the No Health motivation group.

Standard assessments include anthropometrics, electrocardiography, calorimetry, and blood work performed at baseline and as needed.¹⁴² Standard techniques and a high-capacity platform scale operated by trained personnel were used to weigh patients in lightweight clothes without shoes.¹⁴² The duration of treatment was calculated from the date of the first and the last visit.

Patients also self-reported their ultimate weight goal. The patient's weight loss goal was calculated as a percentage of body weight to lose $((\text{initial weight} - \text{goal weight}) / \text{initial weight}) \times 100\%$. The percentage of body weight lost was also calculated $((\text{initial weight} - \text{final weight}) / \text{initial weight}) \times 100\%$. Clinically significant weight loss was defined as losing 5% or more of one's starting weight.¹¹³

A 20-minute session on nutrition and program expectations was also provided to patients.¹⁴² A physician and bariatric educator help patients create realistic goals and select the optimal therapy combination after identifying the causative factors, complications, and comorbidities linked with obesity.¹⁴² Patients are also recommended to attend educational workshops over the course of the program.¹⁴² They may also receive weight management education, as well as tailored weight loss strategies, dietary plans and physical activity

recommendations under the supervision of the physician.^{136,142} Patients were asked to provide written informed consent for the use of their medical data for research purposes and were advised that their decision to participate would have no impact on their medical care at WMC.¹⁴² Patients received no incentives for participation.¹⁴² The York University Research Ethics Board has approved all methods (Ethics Certificate #: e2023-204).

Statistical analysis

For all baseline characteristics, means with standard deviations (SD) and prevalence were calculated. ANOVA with Fisher's Least Significant Differences post hoc tests and Chi-Square tests were used to assess the baseline differences between weight loss motivation groups. ANCOVA was used to examine differences in weight loss goal, and 6-month attendance, between the weight loss motivation groups adjusted for age, baseline BMI, ethnicity, and education level. To assess the odds of achieving a clinically significant weight loss, not achieving clinical weight loss, and discontinuing after the initial visit by motivation groups, a multinomial logistic regression, adjusted for age, baseline BMI, ethnicity, and education level was used. After excluding those who discontinued the program after their initial visit, ANCOVA was used as a sub-analysis to further investigate the differences in weight loss, and achieving a clinically significant weight loss between the motivation groups for those who continued the program after the initial visit, adjusted for age, baseline BMI, ethnicity, education level and treatment time. A correlation between weight loss goals and treatment time with weight loss, stratified by motivation groups, was also performed for those who continued the program after the initial visit. All results were stratified by sex. All statistical analyses were performed using SAS software version 9.4 and a significance threshold of $P < 0.05$.

Results:

The characteristics of the patients are shown in **Table 3**. The analysis comprised of 7540 patients. The majority of patients were women, white, and had higher education. Among both women and men, HME was the most prevalent motivation combination (women: 37.6%, men: 33.1%) while NoH was the least prevalent (women: 2.0%, men: 1.4%). Women and men with HE motivation tend to be younger and have a lower BMI compared to most other motivation groups, while those with HM tend to be older and have a higher BMI ($P<0.05$).

Table 3. Patients' characteristics stratified by motivation and sex.

Women (N = 5589)						
Motivation	H	HE	HM	HME	NoH	None
N (n, %)	1392 (24.9)	1033 (18.5)	687 (12.3)	2103 (37.6)	114 (2.0)	260 (4.7)
Age, years	47.7 ± 12.8 ^{bc}	41.2 ± 12.7 ^{acdef}	51.9 ± 12.8 ^{abdef}	47.5 ± 12.9 ^{bc}	48.8 ± 16.1 ^{bc}	48.3 ± 13.1 ^{bc}
BMI, kg/m²	37.5 ± 6.8 ^{bcd}	36.9 ± 6.0 ^{acdf}	41.2 ± 8.9 ^{abdef}	40.1 ± 7.5 ^{abcef}	37.7 ± 7.6 ^{cd}	38.7 ± 8.2 ^{abcd}
Treatment time, months	4.0 ± 5.9 ^{cd}	3.9 ± 6.0 ^{cd}	4.8 ± 6.4 ^{ab}	4.5 ± 6.4 ^{abf}	4.0 ± 5.7 ^f	5.5 ± 7.5 ^{abde}
Weight change, kg	-1.8 ± 4.6 ^{cd}	-1.8 ± 4.8 ^{cd}	-2.7 ± 7.9 ^{ab}	-2.3 ± 5.8 ^{ab}	-1.6 ± 4.7	-2.3 ± 5.7
White Ethnicity (n, %)	901 (64.7) ^{bcd}	747 (72.3) ^{acdf}	549 (79.9) ^{abef}	1676 (79.7) ^{abef}	81 (71.1) ^{cd}	164 (63.1) ^{bcd}
Higher Education (n, %)	997 (71.6) ^{bcd}	860 (83.3) ^{acdf}	454 (66.1) ^{abd}	1637 (77.8) ^{abcf}	80 (70.2) ^b	179 (68.9) ^{bd}
Men (N = 1951)						
Motivation	H	HE	HM	HME	NoH	None
N (n, %)	604 (31.0)	290 (14.9)	270 (13.8)	646 (33.1)	27 (1.4)	114 (5.8)
Age, years	50.7 ± 13.4 ^{bcd}	44.4 ± 13.1 ^{acdef}	53.3 ± 13.8 ^{abdf}	48.3 ± 13.4 ^{abc}	50.4 ± 15.5 ^b	49.2 ± 14.1 ^{bc}
BMI, kg/m²	37.9 ± 6.7 ^{cde}	37.7 ± 6.4 ^{cde}	41.6 ± 7.7 ^{abf}	41.3 ± 7.2 ^{abf}	42.6 ± 10.2 ^{abf}	39.0 ± 7.0 ^{cde}
Treatment time, months	4.3 ± 6.2	4.7 ± 5.9	5.2 ± 6.5	4.4 ± 6.3	4.0 ± 6.7	4.8 ± 7.5
Weight change, kg	-2.4 ± 6.1	-2.5 ± 5.1	-2.8 ± 6.1	-3.0 ± 7.0	-2.2 ± 4.6	-2.1 ± 5.1
White Ethnicity (n, %)	455 (75.3)	217 (74.8)	216 (80.0) ^f	507 (78.5)	23 (85.2)	80 (70.2) ^c
Higher Education (n, %)	428 (70.9) ^{bc}	235 (81.0) ^{acdf}	167 (61.9) ^{abd}	471 (72.9) ^{bc}	18 (66.7)	78 (68.4) ^b

N= Number of patients. BMI= Body Mass Index. H= Health. HE= Health and Esthetics. HM= Health and Mobility. HME= Health, Mobility, and Esthetics. NoH= No Health. Values reported are means (M) + standard deviations (SD) or prevalence (%).

a = significantly different from H (P<0.05). b = significantly different from HE (P<0.05). c = significantly different from HM (P<0.05). d = significantly different from HME (P<0.05). e = significantly different from NoH (P<0.05). f = significantly different from None (P<0.05). H: health motivation. HE: health and esthetic motivation. HM: health and mobility motivation. HME: health, mobility and esthetic motivation. NoH: no health motivation. None: no motivation.

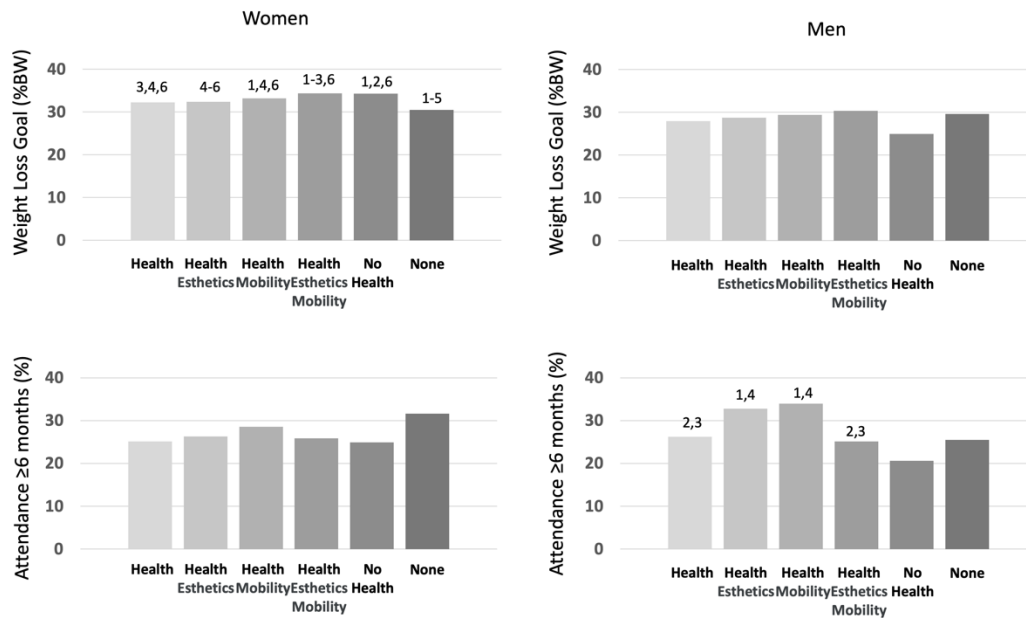


Figure 8 Legend. Differences in weight loss goals and 6 months attendance stratified by motivation and sex. Values represent least squared adjusted means adjusted for age, BMI, ethnicity and education. 1 = significantly different from Health ($P<0.05$). 2 = significantly different from Health and Esthetic ($P<0.05$). 3 = significantly different from Health and Mobility ($P<0.05$). 4 = significantly different from Health, Esthetic, and Mobility ($P<0.05$). 5 = significantly different from No Health ($P<0.05$). 6 = significantly different from None ($P<0.05$). None: no motivation.

Figure 8 shows the weight loss goal and 6-month attendance results by motivation groups in men and women. When adjusted for age, baseline BMI, ethnicity, and education, women with HME and NoH motivations tend to have higher weight loss goals compared to most other groups (HME: 34.3%, NoH: 34.3%, versus range of 30.5% to 33.2%, $P<0.05$), while those with no motivations had the lowest weight loss goal (30.5%). No significant differences in weight loss goals were observed between motivation groups in men.

While no significant differences in 6-month attendance were observed between the motivation groups in women, a higher percentage of men with HE and HM attended the clinic for more than 6 months compared to H and HME motivations (**Figure 1**: HE: 32.8%, HM: 34.0% vs H: 26.2%, HME: 25.1%, $P<0.05$).

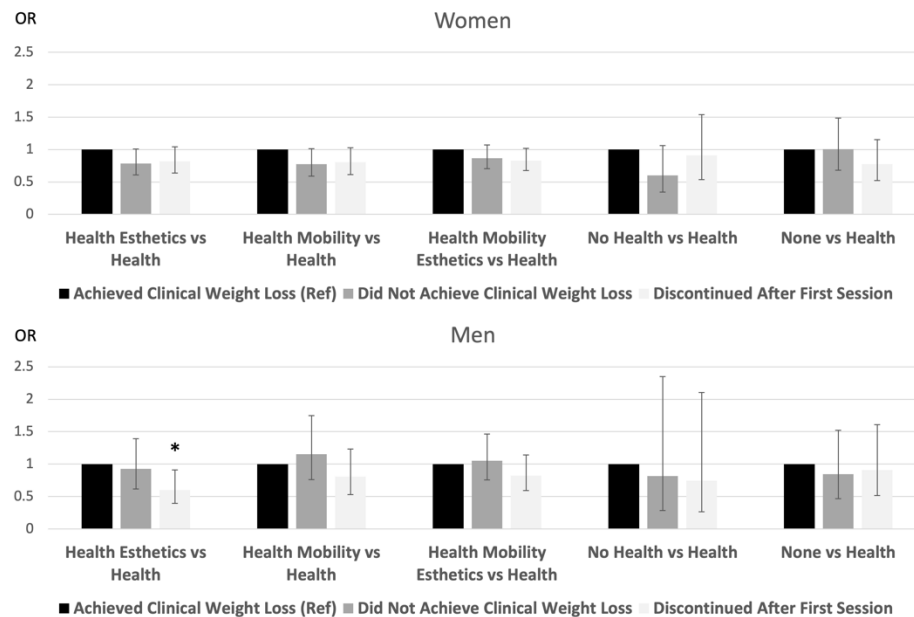


Figure 9 Legend. Odds of not achieving a clinically significant weight loss and discontinuing after the first session versus achieving a clinically significant weight loss by motivation group compared to the health only motivation group. Error bars represent 95% confidence intervals. Odd ratios are adjusted for age, BMI, ethnicity, and education.

* Significantly different from those who achieved clinical weight loss. ($P<0.05$). Reference group: those who achieved clinically significant weight loss.

The results of the multinomial logistic regression are shown in **Figure 9**. In women, motivation was not significantly associated with differences in the odds of achieving a clinically significant weight loss, not achieving a clinically significant weight loss or discontinuing after a

single visit. Men who discontinued after one visit were 40% less likely to have a HE motivation as opposed to H only, compared to those who stayed at the clinic ($P<0.05$).

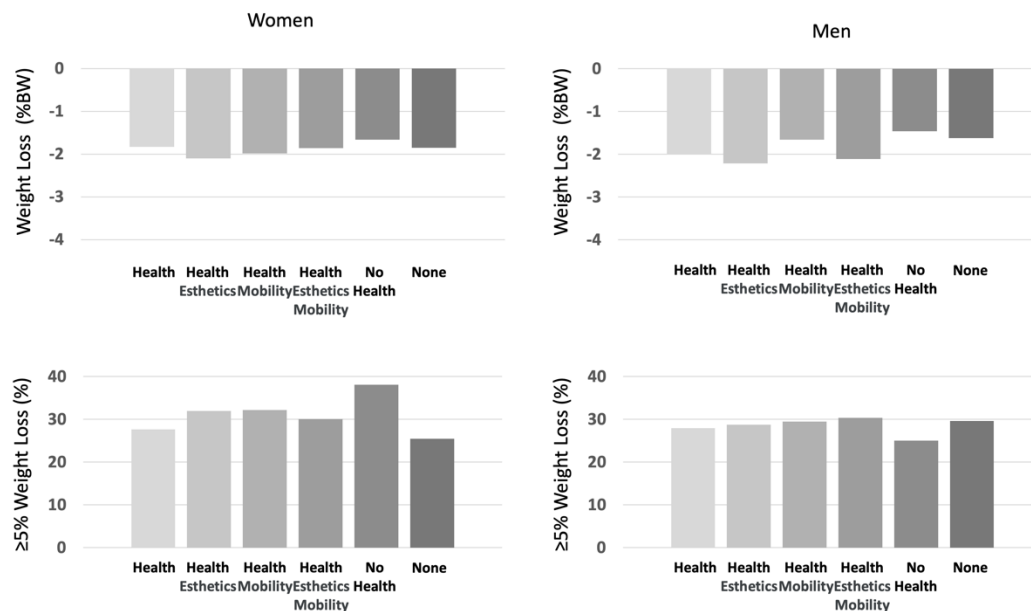


Figure 10 Legend. Weight loss and the proportions of individuals who attained a clinically significant weight loss, stratified by motivation and sex. Values represent least squared adjusted means adjusted for age, BMI, ethnicity, education and treatment time. No differences between the groups ($P>0.05$). $N=4271$. The sample only includes those who attended more than once.

Weight loss results for those who continued the program after their initial visit are shown in **Figure 10**. In both men and women who continued with the program, no significant differences were observed in the proportion of patients who achieved a clinically significant weight loss or in the percentage of weight loss between the motivation groups ($P<0.05$).

Table 4. Correlation between weight loss goal and treatment time with weight loss stratified by motivation group and sex.

Women				
Motivation	Weight Loss Goal r	P Value	Treatment Time r	P Value
H	0.06	0.08	0.16*	<.0001
HE	0.01	0.76	0.20*	<.0001
HM	0.06	0.23	0.18*	0.0002
HME	0.08*	0.01	0.14*	<.0001
NoH	0.12	0.40	0.19	0.16
None	0.08	0.32	0.23*	0.003
All	0.07	0.0003	0.17*	<.0001
Men				
Motivation	Weight Loss Goal r	P Value	Treatment Time r	P Value
H	0.004	0.95	0.22*	<.0001
HE	-0.01	0.93	0.17*	0.02
HM	0.02	0.77	0.12	0.13
HME	-0.003	0.95	0.23*	<.0001
NoH	0.27	0.32	-0.16	0.55
None	0.25	0.05	-0.05	0.72
All	0.02	0.50	0.18*	<.0001

* Significant r

H: health motivation. HE: health and esthetic motivation. HM: health and mobility motivation. HME: health, mobility and esthetic motivation. NoH: no health motivation. None: no motivation.

The results of the correlation analysis between weight loss goals and treatment time with weight loss by motivation groups are shown in **Table 4**. There was a weak association between weight loss goals and weight loss for only the HME motivation group in women, with no association in the group overall. No significant association was observed between weight loss and weight loss goals in men. Weak associations were found between weight loss and treatment time for most motivation groups in women and half of the motivation groups in men.

Discussion:

This study provides insight into the association between weight loss motivations with weight loss goals and the weight loss achieved in patients referred to an obesity management clinic. No differences in weight loss or the odds of achieving a clinically significant weight loss were found between the motivation groups. However, there were modest differences in weight loss goals and the treatment time by motivation group that differed by sex. Although there were very weak associations between treatment time and weight loss that may not translate into meaningful differences in weight loss.

The length of the treatment has been shown to be associated with greater weight loss success.⁸⁹ Health, as the primary motivation, has been associated with favourable weight loss outcomes,^{67,84,86} and lower discontinuation rates.^{67,144} On the other hand, esthetics has been associated with less weight loss,^{67,84,87} and greater discontinuation of the treatment.^{67,89,90,144} In the current study, while some small differences in 6-month attendance were observed among men, these differences may not necessarily translate into additional weight loss. Indeed, the observed differences in weight loss between motivation groups were less than 0.7%, with no significant differences in the proportion of those who achieved a clinically significant weight loss between the motivation groups in either men or women. This is in line with our observation that the association between treatment time and weight loss while statistically significant, is quite weak in men and women. There is a large variation in how long individuals may need to attend the program in order to attain a meaningful or clinically significant weight loss that may not be related to their motivational reasons for attending the clinic.

People are motivated by a variety of reasons to lose weight. In this study, the majority of the patients had health motivation either alone or in combination with esthetic and/or mobility

goals for losing weight, with most patients having more than one motivation. This may be due to the fact that patients are referred to the clinic by their primary physician or another health professional; therefore, improving health may be expected to be a more common motivation in this sample. Our sample had very few patients who reported having only esthetics or mobility motivations, thus, we were unable to examine the Esthetics and Mobility motivations separately. It has been shown that some motivations, such as health and esthetic, may not be truly independent of each other.⁸⁴ It has also been suggested that the effect of esthetic motivation may diminish the effect of health motivation on weight loss.⁸⁴ However, in this study, such diminishing effect of esthetic motivation was not observed. In fact, no differences in any of the variables between motivation groups were found. More studies on the relationship between attrition and motivations (both alone and in combination) with weight loss are needed to understand their association.

The magnitude of the weight loss goals observed in this study ranged between 25.4% and 38.1%, among motivation groups and is similar to findings in other studies (21.6 - 40.3%).^{72,114–116} It has been demonstrated that weight loss goals for those primarily motivated by esthetic reasons are similar to those motivated to lose weight for health reasons.^{114,144} Some studies have shown that setting higher weight loss goals is associated with more weight loss in the short term.^{72,74,75,144} Meanwhile, others found no such association.^{68,71} In the current study, no differences in average weight loss goals were observed across different motivation groups among men. Among women, some small differences ($\leq 3.8\%$) in average weight loss goals exist between the motivation groups. Further, this study demonstrates that no association exists between weight loss goals and weight loss in men or women. The observed disconnect between weight loss goals and weight loss might stem from the demanding nature of achieving higher goals. In fact, given the magnitude of the weight loss goals, it is unlikely that this could be achievable through diet and lifestyle modification

alone. In fact, such high weight loss goals a weight loss that far exceeds the 3-5% weight loss that is typically achieved by lifestyle interventions and is more consistent with what is observed through bariatric surgery.⁶⁸⁻⁷²

About one third the participants lost more than 5% of their body, while two thirds did not, despite their motivation for weight loss. This highlights the complex and multifaceted nature of obesity and weight loss, which can be influenced by variety of physiological, environmental and sociological factors that extend beyond person level behavioral or motivational factors. For example, in the pathophysiology of obesity there are abnormalities in food intake regulation and energy expenditure that have been linked to genetics.^{59,145} Further, the set point theory suggests that the body may respond to weight loss with compensatory mechanisms that would impair weight loss, such as increased appetite and adaptive thermogenesis.^{58,59} These responses can hinder further weight loss and potentially lead to weight regain. Therefore, such physiological factors may overshadow the effects of motivation alone. However, more studies on the relationship between weight loss goals and different motivations for weight loss, while considering potential physiological effects, are needed to fully understand their association.

Strengths and limitations

A notable strength lies in the use of a large sample size, primarily comprising individuals with high levels of obesity, a demographic that often seeks weight loss interventions. However, with such a large sample size, even minor differences can be statistically significant, despite lacking clinical relevance. Despite the large sample size, there were a small number of patients who chose only esthetics or mobility as their motivation. Additionally, patients did not rate their motivations for weight loss. Consequently, for those with multiple motivations, it remains unclear

which one was the primary motivation for weight loss. The patients were individuals attending a publicly funded weight loss program, which may enhance the potential generalizability of the findings to those seeking similar treatments. However, the predominantly white and female sample population and the retrospective nature of the analysis may constrain the broader applicability of the results. Future research should include more ethnically diverse populations to evaluate broader applicability of these findings. Further, these results highlight the heterogeneous responses to lifestyle interventions and reinforce the need for future research to clarify the predictors of lifestyle obesity management. A small subset of patients in the study may have used weight loss medications. However, during most of the study period, only orlistat was available, and given the generally low interest in medications at the clinic, in conjunction with the high cost and low long term adherence rates for weight loss medications,¹⁴⁶ it is unlikely that medications would have influenced our results. In fact, the minimal weight loss observed would have only been overestimated if there had been prevalent medication use. Furthermore, other influential factors such as adherence to dietary and physical activity plans were not controlled or adjusted for in the study. However, the influence of such factors may better reflect the complexities of weight loss interventions for individuals as they occur in real-world contexts.

In summary, in a sample of patients attending a weight management centre, no significant differences in weight loss were observed based on motivational reasons driving this weight loss attempt or their weight loss goal. Further research is needed to explore the connection between weight loss, weight loss goals, attrition, and motivations for weight loss, both independently and in combination.

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General discussion:

Obesity is a complex, multifactorial and chronic disease that is associated with many health risks that has been on the rise over the past decades.^{1,44} Under the previous obesity management pyramid hierarchical system,⁴⁴ patients would start with lifestyle interventions; if insufficient weight loss was achieved, then pharmacotherapy would be recommended, and finally or bariatric surgery, depending on their eligibility.⁴⁴ However, as also observed in our results, lifestyle interventions often show very limited success rates.^{61,64} Although the majority of people in the general population used self-directed approaches, only a small percentage achieved a meaningful weight loss. Further, motivational reasons for weight management, do not appear to have a significant effect on the weight management outcome. This may highlight the importance of considering the individual's biology in defending body weight and the set point theory.^{58,59} This also raises concerns about the appropriateness of positioning lifestyle interventions as the initial step, given it is not likely to lead to meaningful weight outcomes. The new Canadian clinical obesity guidelines recommend the use of nutrition therapy and exercise for everyone for health benefits, regardless of their BMI, and not for weight loss specifically.¹ In addition to nutrition and exercise, the current obesity guidelines also recommend the use of psychological, medical and surgical interventions alone, or in combination with each other, depending on the patients' preferences and individual conditions.¹ The new guidelines recommend pharmacotherapy for those with BMI of above 30 kg/m² or 27 kg/m² with obesity related complications, while recommend bariatric surgery for those with BMI of above 40 kg/m² or 35 kg/m² with obesity related complications.¹ Our results also support the limited effectiveness of lifestyle interventions on their own, the need for more aggressive approaches, such as bariatric surgery and pharmacotherapy, particularly for those with severe obesity, especially adults

younger than 65 years of age, while those with lower levels of obesity may not necessarily require medical intervention. Currently, use of pharmacotherapies tends to be low,¹⁴⁷ however, with the advances in pharmacotherapy and the emergence of newer weight loss medications, such as semaglutide and tirzepatide, that have improved weight loss outcomes may improve the use of more comprehensive support systems in obesity management. In our third study, a higher proportion of those who receive treatments under the supervision of health care professionals achieved a meaningful weight loss than what is typically observed in the general public.¹³⁷ This may suggest having a stronger clinical support systems may lead to better weight outcomes, better adherence, and ultimately be more beneficial for those receiving treatments for obesity management. However, more research is necessary to refine and optimize clinical and individualized obesity management systems.

In short, obesity management is complex and likely will require a multi-pronged approach. Obesity class III is generally associated with the highest mortality risk, while there were minimal differences between obesity class I and II, it is unclear whether current guidelines for initiating treatment outcomes should be re-considered, especially among adults younger than 65 years of age. Further, given the age differences in mortality risk, and the concerns with muscle loss with weight loss,¹⁴⁸ the benefits of obesity reduction for older adults are unclear. More research is necessary to fully understand the optimal obesity management strategies that should be used and the prioritization of those at greatest health risk.

Future directions:

Our research suggests that a stronger clinical support systems may be needed in order to achieve better weight outcomes and better adherence with self-directed obesity lifestyle

interventions. Future research may focus more on role of clinical support in weight management, and combination of different elements that may optimize and improve the efficacy of clinical weight management intervention, as well as role of newly approved weight loss medications. Further identification of which obesity populations would best benefit from intervention should be clarified in order to optimize clinical care and patient burden to those at greatest risk for negative outcomes. Currently, there are many barriers to effective obesity interventions ranging from health insurance coverage for pharmacological interventions,^{62,63} discrimination in clinical care,⁶³ and built environments that favor excess dietary consumption and sedentary behaviors.¹ Research is needed to develop public health policies and clinical care infrastructure that can better support individuals attempting obesity reduction.

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Abbreviations:

ACC: Accidents

AD: Alzheimer's disease

AOC: All other causes

ANCOVA: Analysis of covariance

ANOVA: Analysis of variance

BIA: Bioelectrical impedance analysis

BMI: Body Mass Index

CDC: Centers for Disease Control and Prevention

CeVD: Cerebrovascular diseases

CLRD: Chronic lower respiratory diseases

CSWL: Clinically significant weight loss

DM: Diabetes mellitus

DXA: Dual-energy X-ray absorptiometry

F: Females younger than 65 years of age

GED: General Educational Development

H: Health motivation

HD: Diseases of the heart

HE: Health and Esthetics motivation

HM: Health and Mobility motivation

HME: Health, Mobility, and Esthetics motivation

HR: Hazard ratio

IP: Influenza and pneumonia

kg: Kilogram

kg/m²: Kilograms per square meter

M: Males younger than 65 years of age

MN: Malignant neoplasms

NHANES: National Health and Nutrition Examination Survey

NNN: Nephritis, nephrotic syndrome, and nephrosis

NoH: No Health motivation

NW: Normal weight

OB I: Obesity class I
OB II: Obesity class II
OB III: Obesity class III
OF: Older females
OM: Older males
OW: Overweight
PG: Prevent weight gain
SD: Standard deviation
SAS: Statistical Analysis System
TTM: Transtheoretical Model
WMC: Wharton Medical Clinic
WL: Weight loss

Appendices:

Appendix A.

S1 Table. Number of individual weight management methods employed among those trying to lose weight or prevent weight gain stratified by sex.

Number of methods (%)	Tried to lose weight		Number of methods (%)	Tried to prevent weight gain	
	Men	Women		Men	Women
1	21.5 $\pm$ 1.2	17.5 $\pm$ 1.1	1	36.0 $\pm$ 3.0	30.9 $\pm$ 2.7
2	21.4 $\pm$ 1.5	19.9 $\pm$ 0.9	2	17.9 $\pm$ 1.8	21.3 $\pm$ 2.4
3	16.3 $\pm$ 1.1	16.8 $\pm$ 0.8	3	22.6 $\pm$ 2.4	21.4 $\pm$ 2.5
4	13.6 $\pm$ 1.5	13.5 $\pm$ 0.7	4	9.4 $\pm$ 1.4	12.2 $\pm$ 1.8
5	9.3 $\pm$ 1.0	10.9 $\pm$ 0.6	5	6.2 $\pm$ 1.6	8.4 $\pm$ 1.9
6	8.0 $\pm$ 1.0	6.8 $\pm$ 0.6	6	4.2 $\pm$ 1.2	2.7 $\pm$ 0.7
7	3.9 $\pm$ 0.5	5.4 $\pm$ 0.6	7+	3.6 $\pm$ 1.0	3.2 $\pm$ 0.8
8	2.8 $\pm$ 0.5	4.1 $\pm$ 0.4			
9	1.2 $\pm$ 0.3	2.9 $\pm$ 0.4			
10+	1.9 $\pm$ 0.4	2.3 $\pm$ 0.3			

Values reported are prevalence (%) $\pm$ standard error.

