Examining Dietary Clusters in Candidates for Metabolic-Bariatric Surgery and their Association to Metabolic Status

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Abstract

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Jessica Burdick

Candidates for metabolic-bariatric surgery (MBS) have a unique nutritional status profile; clustering their macronutrients and micronutrients dietary intakes may present inter-individual differences. This study aimed to: (1) describe the macro- and micro- nutrient intake patterns in candidates for a MBS; and (2) assess the associations between these patterns and metabolic status (body fat %, HbA1c, lipid profile, granulocytes (GR), international normalised ratio, C-Reactive Proteins). Three-day dietary data from a mobile application and metabolic markers from a blood draw were collected 3 months pre-MBS from a study conducted in Quebec, Canada. Participants' (N=30) mean age was 45.50 ± 9.83 years and BMI was 46.03 ± 7.61 kg/m². Using the FASTCLUS procedure, a high sugar/high caloric diet (Cluster 1), high protein/high cholesterol diet (Cluster 2), and a low fiber/low saturated fat diet (Cluster 3) were observed. Analyses demonstrated significantly greater low-density lipoproteins (LDL) (5.28 \pm 0.71 mmol/L) and GR (5.64 \pm 0.21 10⁹/L) in Cluster 1 relative to Clusters 2 (LDL: 2.38 \pm 0.28 mmol/L; p= 0.0130), (GR: $4.71 \pm 0.09 \ 10^9$ /L; p= 0.003) and 3 (LDL: $1.76 \pm 0.44 \ \text{mmol/L}$; p = 0.0097), (GR: $5.01 \pm 0.15 \ 10^9$ /L; p= 0.015). Findings can inform variability in nutrient distribution in candidates for MBS. Future studies should compare these clusters to a control group or post-surgery dietary clusters and metabolic status.

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Background Information

Obesity and Metabolic-Bariatric Surgery

Obesity is defined as a non-communicable disease (NCD) and is characterised as living with a body mass index (BMI) of 30 kg/m² and above⁽¹⁾. Although obesity has been commonly assessed using BMI cut-offs, studies are highlighting the complexity of this disease and the need to address further measures when diagnosing obesity. The Edmonton Obesity Staging System is a five-stage system that considers obesity-related subclinical risk factors, physical and psychological symptoms, and functional limitations to assess obesity and determine optimal treatments⁽²⁾. The European Association for the Study of Obesity (EASO) has similarly highlighted the importance of assessing medical, functional or psychological impairments or complications⁽³⁾. The EASO has also suggested considering the role of adipose tissue distribution and function and has classified obesity as a progressive disease with three states: (1) Asymptomatic state; (2) State where health impairments accompany abnormal and/or excessive fat accumulation; and (3) Life-threatening or disabling condition⁽³⁾. Furthermore, BMI cutoffs have been reported to have different implications in different populations. Individuals in Asian populations have a higher body fat percentage relative to individuals of the same age, sex, and BMI in European or white populations⁽⁴⁾. Additionally, Asian populations have a higher risk of developing type 2 diabetes and cardiovascular disease at a BMI lower than the World Health Organization cutoff for overweight (> 25 kg/m²)⁽⁴⁾. This highlights the inadequate assessment of risks related to overweight and obesity using BMI cut-offs in many Asian populations⁽⁴⁾. Despite these limitations, BMI measures and/or cut-offs are still used in current practice for policy purposes or clinically to screen for high-risk individuals, including in the decisions to offer MBS or $not^{(4,5)}$.

Obesity is quite prevalent, in 2020, it was reported that approximately 0.81 billion adults had obesity, and it is estimated that by 2035, 1.53 billion adults will be living with obesity, and 79% of adults with overweight and obesity will live in low- and middle-income countries ⁽¹⁾. The prevalence of obesity rates vary amongst low- and high- income populations; these rates have stabilised in high-income populations after the decade 2000-2010, but there remains a steady rise in low-income nations⁽⁶⁾. Obesity is further divided into subgroups: Class I: BMI 30-34.9 kg/m²; class II: BMI 35-39.9 kg/m²; and class III: BMI > 40 kg/m²⁽⁷⁾. It is predicted that the prevalence of class II and III obesity in high- and middle- income countries will double from 10% to 20% between 2020 and 2035⁽⁶⁾. In Canada, there was a 225% prevalence increase of class II and III obesity between 1990 and 2003⁽⁸⁾. Further, individuals with a high BMI (\geq 25 kg/m²) have an increased risk of cardiovascular disease, Type 2 diabetes, cancer, and mortality^(9,10). The antecedents of obesity are complex and multifactorial, including physiological factors such as energy intake and physical activity imbalance, genetics, hormonal imbalances, and energy homeostasis disruptions ^(11,12).

Metabolic-bariatric surgery (MBS) is considered the most effective treatment for class II & III obesity when other non-surgical interventions (e.g., changes in dietary and exercise patterns, medications) do not induce sustained or significant weight $loss^{(13)}$. Candidates for MBS typically have a body mass index (BMI) \geq 35 kg/m² or a BMI of 30-34.9 kg/m² paired with metabolic disease⁽¹³⁾. Although there are a variety of MBS procedures, sleeve gastrectomy and Roux-en-Y gastric bypass are the two most common. Sleeve gastrectomy is restrictive in nature as the functional portion of the stomach is reduced to approximately 15-25% of its original size⁽¹⁴⁾. Although the stomach size is reduced during sleeve gastrectomy, its function remains the

same⁽¹⁵⁾. After sleeve gastrectomy surgery, increased satiety (i.e., feelings of fullness) can occur as the removed region of the stomach contains production sites of hunger stimulating hormones (e.g., ghrelin)⁽¹⁵⁾. The Roux-en-Y gastric bypass procedure consists of the formation of a small pouch located at the upper portion of the stomach, the lower portion of the small intestine is then severed and reattached to the pouch. Food intake therefore bypasses the lower portion of the stomach and upper portion of the small intestine, highlighting the restrictive and malabsorptive properties of the Roux-en-Y gastric bypass. Typically, the Roux-en-Y bypass, relative to the sleeve gastrectomy procedure, is associated with more nutritional deficiencies as sections of the intestine are bypassed ⁽¹⁴⁾. Excess weight loss, which is a measure of post-operational weight loss over pre-surgical excess weight, is a consistent measure of MBS success, with an excess percent weight loss (%EWL) of more than 50% being considered clinically significant⁽¹⁴⁾. Short- and long-term weight loss has been documented following MBS. An average %EWL of 59% has been observed in participants who have undergone sleeve gastrectomy 1 year postoperationally⁽¹⁶⁾. Patients having undergone Roux-en-Y bypass had an %EWL of 69%-82% 2 years following surgery⁽¹⁶⁾. The success of MBS is measured by three primary outcomes: sustained weight loss; improvement in comorbid conditions; and patient's improved quality of life following surgery⁽¹⁴⁾. Weight loss following MBS has been associated with a multitude of factors, including changes in the quantity and quality of dietary intake^(15,17,18,19,20).

Nutritional status in candidates for MBS

Although MBS procedures have advantages, several post-surgical complications, such as micronutrient deficiencies, can arise and are commonly observed following malabsorptive procedures such as RYGB^(21, 22). The most common micronutrient deficiencies following malabsorptive MBS procedures include deficiencies in vitamin D, iron, vitamin B12, folate,

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thiamine (B1), and vitamin A⁽²³⁾. These deficiencies post-MBS can contribute to further complications such as protein-energy malnutrition, metabolic bone disease^(21,23), neuropathy, and iron-deficiency anemia⁽²⁴⁾.

Management of post-MBS micronutrient deficiencies is complex, as individuals commonly have deficiencies pre-MBS^(21,22). The development of micronutrient deficiencies in candidates for MBS is multifactorial and may be due to increased intake of calorically dense foods with low nutritional value⁽²⁵⁾. Variability in micronutrient deficiencies pre-MBS has been observed between sexes, ethnicities, and across baseline BMI levels. Many studies have found a greater risk of pre-MBS deficiencies in females relative to males^(26,27,28), other studies found increased risk in patients with greater baseline BMI values^(28,29) and specific ethnic groups⁽²⁷⁾. Some studies have also found vitamin D deficiencies to be associated with reduced levels of physical activity in individuals with obesity⁽³⁰⁾. These pre-MBS nutritional deficiencies have been found to be significantly associated with postoperative deficiencies⁽²⁵⁾. Therefore, nutritional status, defined as an individual's health status based on the intake and utilisation of dietary nutrients⁽³¹⁾, is a common assessment pre- and post- MBS^(23,32). Recent studies have demonstrated the importance of assessing micronutrient deficiencies and potentially intervening prior to surgery to ensure optimal nutritional status outcomes postoperatively^(21,22).

Nutritional status guideline assessments

Most available MBS nutritional status guidelines point out the need to identify and correct pre-MBS nutritional deficiencies as part of the comprehensive preoperative evaluation^(32,33,34,35,36,37). The American Society for Metabolic and Bariatric Surgery (ASMBS) has made

recommendations for pre-MBS micronutrient screening in their clinical practice guidelines, highlighting the importance of extensive pre-MBS screening for malabsorptive procedures⁽³²⁾. The American Society for Parenteral and Enteral Nutrition has also recommended a comprehensive presurgical screening for malnutrition to correct deficiencies pre-surgery⁽³⁴⁾. The Canadian Adult Obesity Clinical Practice Guidelines have recommended pre-MBS evaluation and collaborative support from a registered dietitian⁽³⁵⁾. Furthermore, preoperative recommendations were highlighted by the Guidelines for Perioperative Care in Bariatric Surgery: Enhanced Recovery After Surgery (ERAS) Society Recommendations endorsed by the International Association for Surgical Metabolism and Nutrition⁽³⁶⁾. ERAS strongly recommends preoperative counselling, smoking and alcohol cessation, preoperative weight loss, administration of glucocorticoids, carbohydrate loading, and preoperative fasting in non-diabetic patients⁽³⁶⁾. ERAS also recommends that prior to MBS, patients should undergo nutritional evaluation such as micronutrient measurements, with more extensive evaluations for malabsorptive procedures⁽³⁶⁾. Finally, the European Society for Clinical Nutrition and Metabolism (ESPEN) guideline covers both nutritional aspects of the ERAS concept and the special nutritional needs of patients undergoing other major surgeries (i.e., for cancer) and for those developing severe complications⁽³⁷⁾. ESPEN also highlights the need to assess for micronutrient deficiencies prior to MBS⁽³⁷⁾ (Table 1).

The process of nutrition screening and the identification of micronutrient deficiencies can help identify the MBS procedure most suitable for an individual patient⁽³³⁾. Currently, improvements are needed in the standardisation of the nutrition screening as well as micronutrient cutoffs for deficiency and insufficiency in candidates for MBS^(22,33). Some guidelines have suggested

multivitamin and mineral supplementation pre-MBS due to non-nutritionally balanced diets⁽³³⁾; however, there is still a lack of comprehensive pre-MBS dietary recommendations⁽²⁵⁾. Nutritional screening can improve the evaluation of dietary patterns by assessing nutrient intake in addition to whole foods, as dietary patterns are related to nutritional status. Studies have suggested the need to establish more precise dietary recommendations according to the individual characteristics of patients⁽³⁸⁾. Therefore, identifying specific dietary patterns in terms of nutrient intake in candidates for MBS can allow for a better understanding of inter-individual dietary intake profiles. This can potentially aid in developing comprehensive and possibly individualised pre-MBS recommendations.

| Guidelines | Nutritional Screening | Nutrients and Clinical Markers Assessed | Dietary Recommendations |
|---|--|---|--|
| American Society for Metabolic and Bariatric Surgery ^(32,23) | Medical nutrition therapy administered by a registered dietitian following a four step process (1) nutrition assessment, (2) nutrition diagnosis, (3) nutrition intervention and (4) monitoring and evaluation | Vitamin B1, vitamin B12, folate, iron, vitamins A, E, K, calcium, vitamin D, copper, thiamin, and zinc | N/A |
| American Society for Parenteral and Enteral Nutrition ⁽³⁴⁾ | Comprehensive preoperative screening by an experienced dietitian to identify psychosocial and economic factors contributing to abnormal eating patterns and to modify dietary beliefs and behaviours preoperative | Micronutrient deficiency evaluation | Nutrition therapy paired with very-low energy diet, 2-4 weeks before surgery |
| Canadian Nutritional Recommendations Pre-Surgery ⁽³⁵⁾ | Preoperative evaluation and collaborative support from a registered dietitian. Blood draws | Complete blood count, creatinine, iron panel, vitamin D, calcium, albumin and vitamin B12. Fasting plasma glucose, hemoglobin A1C, lipid | Preoperative optimization of micronutrient levels prior to surgery, specifically levels of vitamin D, vitamin B12 and iron, is recommended |

 Table 1. Pre-MBS Nutritional Status Screening Guidelines

| | | panel and liver enzymes. More selectively: Vitamin A, parathormone, phosphate, zinc, selenium and copper levels | Preoperative multivitamin complex with vitamin B1 started at least 1 month pre- surgery |
|--|---|---|--|
| Guidelines for Perioperative Care in Bariatric Surgery: ERAS Society Recommendations ⁽³⁶⁾ | Preoperative nutritional evaluation | Micronutrient evaluation | N/A |
| The European Society for Clinical Nutrition and Metabolism ⁽³⁷⁾ | Preoperative assessment should include screening for malnutrition and deficiency in vitamins and trace elements | Micronutrient deficiency evaluation in vitamins and trace elements | N/A |

Types of dietary patterns identified in obesity

In recent years, there has been a shift in evaluating associations between diet and specific health outcomes. Traditionally, diet was assessed using a single nutrient perspective; however, the focus has now shifted to dietary patterns⁽³⁹⁾. Dietary patterns are defined as the quantities, proportions, variety, or combination of different foods, drinks, and nutrients in diets, and the frequency with which they are habitually consumed⁽⁴⁰⁾. The reasoning behind this shift is that dietary patterns are more representative of what is actually being consumed as it accounts for a combination of foods and nutrients rather than one single nutrient or food^(39,40). Dietary patterns can be derived through an a priori approach using a set of predetermined criteria (e.g., Health Eating Index (HEI) or the Mediterranean Diet Score (MDS)) to characterise dietary intake or through an a posteriori approach using factor analysis of dietary intake data to summarise the nutritional characteristics of a population⁽⁴¹⁾.

Previous studies assessing dietary patterns in individuals with obesity have commonly used an a posteriori approach, and have generally identified two dietary patterns^(42,43). The prudent or Mediterranean diet, which is characterised by increased intake of fruits, vegetables, poultry, fish, low-fat dairy and whole grains, is associated with decreased rates of overweight and obesity^(42,43). Conversely, the Western diet, consisting of high fat, processed food, sugar-sweetened beverage consumption and red meat, is associated with increases in rates of obesity^(42,43). Variability in the reporting of diets labeled as western or prudent is observed as there may be differences in the food groups reported in each diet⁽⁴⁰⁾.

Characterisation of the Western Diet

The average American and Canadian diets, commonly referred to as the Western diet, have been identified and characterised. In 2005, the US diet was represented by macronutrient content as a percentage of energy intake, where 51.8% of energy intake came from carbohydrates, 32.8% from fats, and 15.4% from protein⁽⁴⁴⁾. Similarly, using data from the publicly available 2015 Canadian Community Health Survey, Ahmed et al⁽⁴⁵⁾ found the Canadian macronutrient percentage of energy intake was distributed as 49.3% from carbohydrates, 33.8% from total fat and 16.4% from protein⁽⁴⁵⁾. The estimated mean energy intake for Canadian males above 19 years was 2154 ± 40 kcal/day and for females was 1626 ± 16 kcal/day⁽⁴⁵⁾. The estimated mean calorie intake in US adults (aged above 19 years) is between 1 785 and 2 640 calories per day⁽⁴⁰⁾. The authors note that these numbers may be underestimated, as other studies have suggested an increased energy intake value⁽⁴⁰⁾.

In a typical US diet, vegetable oils and refined sugars contribute to 36.2% or more of total energy intake⁽⁴⁴⁾. This is relatively elevated as the 2010 Dietary Guidelines Advisory Committee recommends that no more than 5-15% of total calories should be derived from added sugars⁽⁴⁰⁾. The consumption of vegetable oils and refined sugars is suboptimal as it can displace the consumption of more nutrient-dense foods such as fruit, vegetables, lean meats, and seafood⁽⁴⁴⁾. The Institute of Medicine Dietary Reference Intakes (DRIs) suggests that added sugars should be less than 25% of calories per day to reduce the displacement of micronutrients in the diet⁽⁴⁶⁾. It has been reported that the general population of Canadian adults consume below the requirements for certain micronutrients⁽⁴⁵⁾. More than 40% of males and 60% of females had inadequate calcium intakes, and more than half the sample of both males and females had inadequate intakes of magnesium, increasing with older age⁽⁴⁵⁾. Further the majority of Canadians had inadequate intakes of vitamin B-12 (21%), thiamin (24.4%), B-6 (23-54%) and trace elements and of vitamin A (> 45%), vitamin D (94-98%), and vitamin C (38-64%)⁽⁴⁵⁾.

The fiber content (15.1 g/d) of the typical US diet is lower than the recommended values (25-30 g/day)⁽⁴⁶⁾. Further, the mean fiber intake for all Canadian adults aged \geq 19 years fell below their respective adequate intakes, with men averaging 18.4 ± 0.2 g/day and females 16.2 ± 0.3 g/day⁽⁴⁵⁾. The Western diet is composed of excessive saturated and trans fatty acids and has decreased n-3 poly-unsaturated fatty acids (PUFA) content relative to n-6 PUFAs with a ratio of 10:1⁽⁴⁴⁾. In Canadian adults, saturated fat contributed to 10.7% ± 0.18 of total energy and only 38% of individuals met the World Health Organization recommendation of less than 10% energy from saturated fat⁽⁴⁵⁾. Mono-unsaturated fatty acids (MUFA) and PUFAs contributed 12.7% ± 0.19 and 7.5% ± 0.13 respectively⁽⁴⁵⁾. Over the last 40 years, sodium intake in the US has

increased across both age and gender groups, averaging 3 400 mg/day⁽⁴⁶⁾. This exceeds the Upper Intake levels of the Institute of Medicine and the 2010 Dietary Guidelines Advisory Committee: <2 300 mg/day in the general population and <1 500 mg/day in higher-risk subpopulations⁽⁴⁰⁾. The mean sodium intakes for all Canadian adults exceeded the chronic disease risk reduction intake (2300 mg/d) where 75% of adult males consumed 3133 mg/d of sodium and 48% of females consumed 2325 mg/d⁽⁴⁵⁾.

Overall, the typical Western diet is calorically dense, high in sugar and refined oils, low in micronutrients (calcium, magnesium, B vitamins, vitamin A, D, C), low in fiber, high in saturated fat and high in sodium. The Western diet is commonly reported in studies assessing dietary intake and the risk of developing obesity^(42,43). More specifically, reported dietary intakes in candidates for MBS align with characteristics of the Western diet. The general diet is reported as being low in micronutrient content (i.e., below the dietary reference intake for iron, calcium, folic acid, vitamin B12, and vitamin B1, vitamin D), low in dietary fibre (23.0 g/day), and follows a similar macronutrient distribution: 13-17% protein, 32-36% fat, 47-55% carbohydrate and mean energy intake (2711-2801 kcal/day) of the general Western diet^(22,47).

Dietary intervention approaches for managing obesity

Studies have suggested that medical nutrition therapy, in conjunction with interventions (psychological, pharmacologic, surgical), should be tailored to meet an individual's health-related outcomes^(48,49). Some RCTs are looking at leveraging machine learning algorithms to use dietary intake, nutritional status and other markers to tailor dietary interventions⁽⁵⁰⁾. Precision nutrition considers individual-level and environmental characteristics, including pre-existing

dietary intake, to inform personalised dietary plans and has been suggested as an intervention in managing obesity and metabolic syndrome⁽⁵⁰⁾. This approach may also be suitable in addressing micronutrient deficiencies pre-MBS. However, accurate machine learning algorithms require high-quality data to be able to provide appropriate predictions.

Diet and metabolic status

Obesity has been associated with many metabolic perturbations including diabetes mellitus, dyslipidemia, and chronic low grade inflammation⁽⁵¹⁾. Clinically, diabetes risk, dyslipidemia, and inflammation have been measured with HbA1c levels, lipid profiles, and inflammatory markers respectively. There are clear associations between diet and macronutrient intake and these metabolic perturbations. For example, different whole food dietary patterns have been associated with measures of HbA1c, where western style diets were associated with a lack of metabolic control (HbA1c $\geq 7\%$)^(52,53). Furthermore, one meta-analysis found that a larger carbohydrate restriction was positively correlated with HbA1c reductions in individuals with Type-2 diabetes⁽⁵⁴⁾.

Dyslipidemia is characterised by decreased high density-lipoproteins (HDL) and increased lowdensity-lipoproteins (LDL), triglycerides, and free fatty acids⁽⁵⁵⁾. Lipid profiles have also been shown to be influenced by diet^(55,56). One study found that a diet high in MUFA and low on carbohydrates and saturated fatty acids resulted in a 27%-46% reduction in postprandial triglyceride levels in patients with obesity⁽⁵⁷⁾. Additionally, two systematic reviews and metaanalyses found that low-carbohydrate diets are effective at improving high density lipoprotein (HDL) and triglyceride (TG) profiles in comparison to low-fat diets^(,59) Further, the American Scientific Report of the 2020 Dietary Guidelines Advisory Committee⁽³⁹⁾, reported on the associations between dietary patterns and cardiovascular risk factors (e.g., dyslipidemia) in the general adult population. Previous research assessing nutrient specific dietary patterns indicate that patterns lower in saturated fat, cholesterol, and sodium and richer in fiber, potassium, and unsaturated fats are beneficial for reducing cardiovascular disease risk in the general adult population⁽³⁹⁾.

Dietary carbohydrates high in glycemic load and glycemic index values have been associated with increased c-reactive protein levels and low plasma levels of adiponectin; two blood markers that are characterised as chronic low grade inflammation status related to obesity^(60,61,62).

Although there is a clear link between diet and metabolic status in individuals with obesity, and the general population, there is limited data on nutrient level dietary patterns and their implications on metabolic status in candidates for MBS.

Objectives

To summarise, the prevalence of class II and III obesity has been increasing in Canada. Obesity is a major risk factor for other chronic diseases and reduces an individual's quality of life and overall life expectancy. MBS is one of the most effective interventions to treat or manage class II and III obesity. Although advantageous, MBS does have post-surgical complications such as nutritional deficiencies that contribute to adverse health outcomes. Candidates for MBS commonly have micronutrient deficiencies pre-MBS that can contribute to post-MBS complications. Nutritional guidelines for MBS highlight the importance of assessing nutritional status pre-surgery and possibly intervening to reduce post-surgical complications. These nutritional guidelines still need improvements in nutritional screening and dietary recommendations pre-MBS. Further, previous studies have assessed whole food dietary patterns in individuals with obesity, not accounting for nutrient composition. Some studies have also found associations between diet and clinical markers for metabolic perturbations associated with obesity, such as diabetes mellitus (i.e., HbA1c), dyslipidemia (i.e., lipid profiles) and chronic low grade inflammation (i.e., inflammatory markers). By assessing nutrient intake of candidates for MBS and their associations to clinical metabolic factors, we can gain a better understanding of inter-individual dietary intakes which can potentially improve nutritional screening and dietary recommendations pre-MBS.

Therefore, the objectives of this study are:

 To describe dietary patterns in candidates for a primary MBS, using dietary clusters formed from macronutrient and micronutrient intake; and

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(2) To assess how these dietary clusters are associated with metabolic status (body fat %, HbA1c, Lipid profile, Granulocytes (GR), International Normalised Ratio (INR), C-Reactive Proteins (CRP))

Hypotheses

- (1) Based on previous literature, the dietary clusters will follow a trend similar to the Western diet, that has been described as being high in sugar, fat, low in dietary fiber, and calorically dense. Seeing that patients with similar body composition profiles will be assessed, it is expected that there will be 2-4 different clusters.
- (2) The diets that are relatively greater in sugar, saturated fat, cholesterol and sodium will be associated with greater values in HbA1c, LDL, GR, INR, and CRP and lower values in HDL.

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Examining Dietary Clusters in Candidates for Metabolic-Bariatric Surgery and their Association to Metabolic Status

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Abstract

Candidates for metabolic-bariatric surgery (MBS) have a unique nutritional status profile; clustering their macronutrients and micronutrients dietary intakes may present inter-individual differences. This study aimed to: (1) describe the macro- and micro- nutrient intake patterns in candidates for a MBS; and (2) assess the associations between these patterns and metabolic status (body fat %, HbA1c, lipid profile, granulocytes (GR), international normalised ratio, C-Reactive Proteins). Three-day dietary data from a mobile application and metabolic markers from a blood draw were collected 3 months pre-MBS from a study conducted in Quebec, Canada. Participants' (N=30) mean age was 45.50 ± 9.83 years and BMI was 46.03 ± 7.61 kg/m². Using the FASTCLUS procedure, a high sugar/high caloric diet (Cluster 1), high protein/high cholesterol diet (Cluster 2), and a low fiber/low saturated fat diet (Cluster 3) were observed. Analyses demonstrated significantly greater low-density lipoproteins (LDL) (5.28 \pm 0.71 mmol/L) and GR (5.64 \pm 0.21 10⁹/L) in Cluster 1 relative to Clusters 2 (LDL: 2.38 \pm 0.28 mmol/L; p= 0.0130), (GR: $4.71 \pm 0.09 \ 10^9$ /L; p= 0.003) and 3 (LDL: $1.76 \pm 0.44 \ \text{mmol/L}$; p = 0.0097), (GR: $5.01 \pm 0.15 \ 10^9$ /L; p= 0.015). Findings can inform variability in nutrient distribution in candidates for MBS. Future studies should compare these clusters to a control group or post-surgery dietary clusters and metabolic status.

Keywords: Metabolic-bariatric surgery, nutritional deficiencies, dietary patterns, dietary clusters, metabolic status

1. Introduction

1.1 Obesity & Metabolic-Bariatric Surgery

Obesity (body mass index (BMI) \geq 30 kg/m²) is prevalent worldwide; in 2020 approximately 0.81 billion adults were living with obesity and it is projected that by 2035, 1.53 billion adults and two in every five children will be living with obesity⁽¹⁾. In Canada, there has been a 225% prevalence increase of class II (BMI > 35 kg/m²) and III (BMI \geq 40 kg/m²) obesity between 1990 and 2003⁽²⁾. Furthermore, a high BMI (\geq 25 kg/m²) contributes to five million deaths out of the 41 million adult deaths each year globally⁽¹⁾.

Metabolic-bariatric surgery (MBS) is considered the most effective treatment for classes II & III obesity when other non-surgical interventions do not induce sustained or significant weight $loss^{(3)}$. Canadian guidelines for MBS indicate that individuals with a BMI ≥ 40 kg/m², a BMI ≥ 35 kg/m² paired with one or more obesity-related comorbidities, or with poorly controlled Type 2 diabetes and a BMI of 30-35 kg/m² can be considered for MBS⁽⁴⁾.

1.2 Nutritional Status, Diet, and MBS

Following MBS, many complications such as nutritional deficiencies may arise, due to the drastic reduction of food intake and decreases in nutrient absorption. These nutritional deficiencies may result in serious health conditions such as anemia, neuropathy, and osteoporosis⁽⁵⁾, reducing the patients' quality of life. As such, nutritional status, defined as an individual's health status based on the intake and utilization of dietary nutrients⁽⁶⁾, is one of the key outcome measures following MBS⁽⁷⁾. Nutritional management of patients undergoing MBS is complex, as patients are commonly deficient in micronutrients such as iron, ferritin, vitamin

B12, folate and vitamin D pre-surgery⁽⁸⁾. Pre-surgical nutritional status has been found to be associated with post-surgical nutritional status⁽⁹⁾ and related complications. As such, there is a growing need for better and consistent nutritional status assessments pre-surgery⁽¹⁰⁾. Furthermore, the development of obesity-related nutritional deficiencies pre-MBS is multifactorial and may be due to the dietary intake of calorically dense foods with low nutritional quality⁽⁸⁾ demonstrating a link between diet and nutritional status. Therefore, assessing pre-surgical dietary intake can further our understanding and development of interventions (e.g., dietary screening process, recommendations) to manage nutritional deficiencies which may ultimately aid in mitigating possible post-surgical complications.

Previous studies have identified dietary patterns associated with risks of obesity, such as the Western, Mediterranean, and Prudent diets and have characterized these patterns in terms of whole foods (e.g., meat, refined grains, dairy products)^(11,12,13). Although whole food dietary patterns have been established in patients with obesity, there is a lack of studies assessing macroand micro-nutrient level patterns among candidates for MBS. Previous studies assessing nutrient intakes have generally taken a reductionist approach by assessing the relationship(s) between single nutrients and measures of obesity^(14,15,16). Although there are advantages to these dietary assessment approaches, whole food dietary patterns may not provide the specific nutrient compositions⁽¹⁷⁾ and single nutrient assessment excludes nutrient synergies, underrepresenting the combination of foods consumed⁽¹⁸⁾. Candidates for MBS have a unique nutritional status (i.e., are at a greater risk of developing nutritional deficiencies), indicating the need for a more precise understanding of their dietary intake at the nutrient level. Therefore, assessing dietary patterns by clustering macro- and micro- nutrients is ideal in this population to provide a better

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understanding of inter-individual differences which can potentially aid in developing precise pre-MBS screening tools and recommendations.

1.3 Metabolic status and diet in MBS

In addition to being a disease itself, obesity is a major risk factor for many metabolic perturbations, such as diabetes mellitus, dyslipidemia, and inflammation⁽¹⁹⁾. Clinically, diabetes risk, dyslipidemia and inflammation have been measured with HbA1c levels, lipid profiles, and inflammatory markers respectively. There are clear links between diet and macronutrient intake, and these perturbations. For example, different whole food dietary patterns have been associated with measures of HbA1c, where western style diets (i.e., high sugar, dairy products) were associated with a lack of metabolic control (HbA1c \geq 7%)^(20,21). Furthermore, one meta-analysis found that a larger carbohydrate restriction was positively correlated with HbA1c reductions in individuals with Type-2 diabetes⁽²²⁾. Lipid profiles have also been shown to be influenced by diet^(23,24). In fact, two systematic reviews and meta-analyses found that low-carbohydrate diets are effective at improving high density lipoprotein (HDL) and triglyceride (TG) profiles in comparison to low-fat diets^(17,25). Dietary carbohydrates high in glycemic index and glycemic load values have been positively associated with c-reactive proteins^(16,26,27). However, there is limited data on nutrient level dietary patterns and their implications on metabolic status in candidates for MBS.

The objectives of this study were to: (1) Describe dietary clusters, in terms of macronutrient and micronutrient intake, in candidates for a primary MBS; and (2) assess how these dietary clusters were associated with metabolic status (body fat %, HbA1c, Lipid profile, Granulocytes, International Normalised Ratio, C-reactive proteins).

2. Methods

2.1. Study Design and Selection of Participants

This was a cross-sectional sub-study, of an ongoing prospective observational study: "Evaluation of the impact of radical nutrition and microbiome changes on brain function and structure [EMBRACE] study" (trial registration NCT05318781) conducted at the Centre intégré Universitaire de santé et de services sociaux du Nord de l'île de Montréal (CIUSSS-NIM), Quebec, Canada. The primary aim of the parent study is to evaluate the effects of MBS-induced changes in gut microbiota and dietary patterns on post-surgical cognition. The self-report questionnaires, dietary intake, blood samples, and weight data were collected from the parent study at 3 months pre-surgery. The EMBRACE study was given primary ethical approval by the Research Ethics Board (REB) at the coordinating study site (REB#: MP-32-2022- 2412) and the full protocol has already been published⁽²⁸⁾. All procedures involving human participants were in accordance with the ethical standards of the institutional and national research committee and with the 1964 Helsinki Declaration and its later amendments or comparable ethical standards.

2.1.a. Description of Participants

Candidates for a primary MBS were recruited from the metabolic-bariatric outpatient clinic at the CIUSSS-NIM, which has one of the largest outpatient MBS clinics in Canada. *Inclusion criteria:* Participants were included if they were aged 30 years or older, were available for two years of follow-up, and could read and speak French or English.

Exclusion criteria: Participants were excluded if they had previously undergone MBS, were using long-term antibiotics, had used commercially available prebiotic/probiotic in the past 3 months, had a history of significant intestinal disease/disorder that influenced the gut microbiota (e.g., Crohn's disease); had a non-MBS in the last 6 months; had a diagnosed neurologic

disorder/deficit (e.g., dementia, stroke, or seizures), a severe Axis 1 psychotic disorder (e.g., schizophrenia), or bipolar disorder, had a current bacterial, fungal, or viral infection or a diagnosed infectious disease, were pregnant or breastfeeding, had active cancer, advanced kidney or liver disease, or had undergone organ transplantation.

2.2 Data Collection and Measurements

2.2.a. Recruitment

Participants who had been recruited from an ongoing MBS study (The Research on Bariatric Care for Obesity Treatment [REBORN] study)⁽²⁹⁾ and had previously provided consent to be contacted for other studies were recruited by research assistants. After being provided with a full description of the study and having their eligibility checked, all eligible participants received an electronic informed consent form along with a verbal explanation of the form.

2.2.b. Laboratory Visits

All assessments were administered to the participants 3 months pre-surgery. Prior to the scheduled laboratory visits, participants completed self-report questionnaires and were asked to avoid non-steroidal anti-inflammatory medications within 5 days of the visit; alcohol, drugs, analgesic medication, or exercise within 24 hours of the visit; and food, caffeinated drinks, and smoking within 12 hours of the visit. Laboratory visits were performed in the morning in a silent, temperature-regulated environment. Each assessment consisted of anthropometric measurements (i.e., weight, height, waist circumference), a blood draw, and participants were given verbal instructions on how to capture food diaries.

2.2.c. Instruments and Procedure

Self-report variables:

Demographics: Participants' age, sex, ethnicity, marital status, and socioeconomic status (years of education, income, and residential deprivation^(30,31) were captured.

Physical Activity: Physical activity information was collected using the adapted Godin Leisure-Time Exercise Questionnaire⁽³²⁾.

Medical History: The current and lifetime history of comorbidities such as respiratory diseases, cardiovascular disease, cardiovascular disease risk factors, cancers, mental health status, previous emergency hospital visits within the last 12 months, surgery history, and currently prescribed medication were obtained (Appendix A)⁽²⁹⁾.

Diet intake food diary: We administered Keenoa, a mobile application, that was used as a 3-day food diary to collect dietary data^(33,34). Participants were instructed to record all food and beverages they consumed via photo capture^(33,34) (Appendix B)⁽²⁸⁾. The mobile app uses artificial intelligence to recognise food items, reducing the amount of itemizing that the user needs to do^(33,34). Participants estimated portion sizes using reference photographs (validated 2-dimensional food portion visual) (Appendix C)⁽³⁵⁾. A registered dietitian and trained research assistant reviewed the data entered in Keenoa and contacted the participant to clarify entries at the end of the first and third days of the data entry⁽³⁶⁾. As with previous studies, macronutrient, micronutrient, simple sugar, fatty acid, energy intake, cholesterol, and total dietary fiber were captured from the food diaries (Table 1) using the Canadian Nutrient File⁽³⁷⁾, a food composition database⁽³⁸⁾.

Measured variables:

Clinical Metabolic Factors: During the laboratory visits, blood samples were drawn in the morning following a 12-hour fast. No more than 150 ml of blood (i.e., 20 tubes) was drawn per visit for each participant. After blood was drawn, the samples remained undisturbed at room temperature to allow clotting to take place for 30 minutes. After 30 minutes had elapsed, two LBTT 2.7 cc tubes, four LTT 4 cc tubes, and two YTT 5 cc tubes of blood samples were transported in an ice-filled cooler to the biomedical lab of the Hôpital du Sacré-Cœur de Montréal (HSCM). The remaining tubes (i.e., 12 tubes) were stored and shipped for analyses pertaining to the parent study. Universal precautions and institutional requirements were followed, including the use of gloves and eye protection. The clinical markers assessed from the blood were HbA1c, C-reactive Proteins (CRP), Granulocytes (GR) and International Normalised Ratio (INR) and the lipid profiles assessed were total cholesterol, LDL, HDL, and triglycerides. Anthropometrics: Weight was measured on a digital medical scale, height was measured using a stadiometer, and BMI was calculated as standard^(39,40). Body composition was measured using the foot-to-foot Tanita TBF-310 standard single frequency (50kHz) bioelectrical impedance analysis (BIA; Tanita Corp., Tokyo, Japan)⁽⁴¹⁾. BIA estimates total body water from the opposition of flow to an electric current through body tissues, which can then be used to determine estimates of fat-free body mass and body fat.

| Macronutrients | Simple Sugars | Fatty acids | Energy Intake | Micronutrients | Additional |
|----------------------|-------------------------|-----------------|------------------|------------------|----------------------|
| Total Protein (g) | Total | Total saturated | Total Energy | Sodium (mg) | Total |
| Total fat lipids (g) | monosaccharides (g) | fatty acids (g) | Kilocalories | Magnesium (mg) | dietary fiber (g) |
| Total carbohydrate | Total disaccharides (g) | Total | (kcal) | Calcium (mg) | Cholesterol |
| (g) | | monounsaturated | | Phosphorus (mg) | (mg) |
| | | fatty acids (g) | | Vitamin B12 (ug) | |
| | | Total | | Vitamin B6 (mg) | |
| | | polyunsaturated | | Vitamin D (IU) | |
| | | fatty acids (g) | | Vitamin C (mg) | |
| | | | | Zinc (mg) | |
| | | | | Potassium (mg) | |

Table 1. Self-Report Dietary Intake Assessments

2.3 Statistics

2.3.a. Primary outcome

Cluster Analysis: The averages of the three-day dietary content (i.e., macronutrients, micronutrients, simple sugars, fatty acids, total dietary fiber, cholesterol, energy intake) from 3 months pre-surgery were standardized using PROC STDIZE and then were analysed using the FASTCLUS procedure in SAS to establish dietary pattern clusters. The FASTCLUS procedure generates mutually exclusive clusters by comparing Euclidean distances between each participant and each cluster center in an interactive process using a k-means method. We specified a minimum of 5 participants per cluster⁽⁴²⁾, to ensure the stability of each individual cluster. In addition, we used Pseudo F Statistics and Cubic Clustering Criterion (CCC> 3) in SAS to confirm the structures. The Kolmogorov-Smirnov test was used to assess the normality of each variable entered in the clusters. For data that was normally distributed, differences in the means of each variable found in each cluster was obtained using an independent or unpaired t-

test. For the non-normally distributed data, the Mann-Whitney U Test was used to assess differences in the medians of each variable found in each cluster. Two-sided p-values <0.05 were considered statistically significant. The assumptions were met for all models. All statistical analyses were performed using SAS 9.4.

2.3.b. Secondary outcome

Analysis of Covariance (ANCOVA): Nine ANCOVA models were used to analyse the associations between the dietary clusters and the metabolic status (one for each dependent variable). The dietary clusters were set as the independent variable in all nine models which were exclusive based on the dependent variables: body fat %; HbA1c; total cholesterol; LDL; HDL; triglycerides; GR; INR; and CRP. All nine models were adjusted for age, sex, ethnicity, marital status, years of studies, gross income, physical activity and baseline BMI. Normality checks and Levene's test were carried out and the assumptions were met. Post-hoc comparisons using the Scheffe test were then performed to assess where the differences were found in each model. Two-sided p-values <0.05 were considered statistically significant. All statistical analyses were performed using SAS 9.4.

3. Results

3.1. Study Participants

From the parent study, out of the 51 participants tested at the lab at baseline, 21 participants were excluded for the following reasons: not meeting the Keenoa criteria (29%), non-respondent (19%), on the very low-calorie diet (24%), drop out (19%), underwent MBS (9%) (Figure 1), The mean age of the participants (N=30) was 45.50 ± 9.83 years and mean BMI was 46.03 ± 7.61 kg/m². A total of 20 (69%) of the participants were female. The total cholesterol (4.81 \pm 0.98 mmol/L) and LDL (2.80 \pm 0.75 mmol/L) mean values were within range of the HSCM biomedical lab reference values. The HbA1c (5.8 \pm 0.5 %), triglyceride (1.84 \pm 1.04 mmol/L), and CRP (10.00 [4.00, 13.00] mg/L) mean values were above the reference values. The baseline characteristics of the participants are shown in Tables 2 and 3.

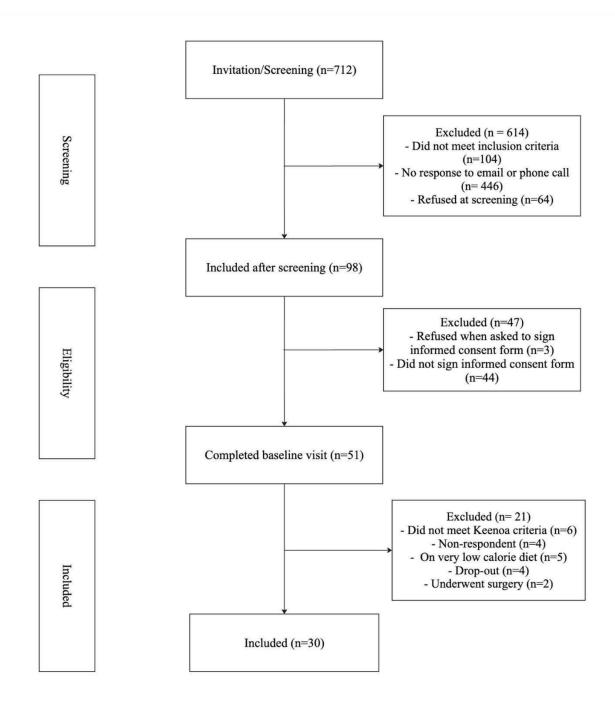


Figure 1. Flowchart

| Demographics and A | Participants (N= 30) | |
|---------------------------|----------------------|----------------------|
| Age (years) | | 45.50 ± 9.83 |
| BMI (kg/m ²) | | 46.03 ± 7.61 |
| Fat percentage (%) | | 50.80 [48.10, 54.50] |
| Sev. [0/ (NI)] | Female | 69% (20) |
| Sex [% (N)] | Male | 31% (9) |
| Ethnicity [% (N)] | White | 77% (23) |
| | Other | 23% (7) |
| Education Loval [94 (NI)] | High school or less | 57% (17) |
| Education Level [% (N)] | University | 43% (13) |
| | < 84 000\$ | 58% (15) |
| Income [% (N)] | > 84 000\$ | 42% (11) |
| Physical Activity (MET h | rs/week) | 18.97 ± 16.28 |

 Table 2. Anthropometric and Demographic Characteristics of Candidates for MBS

Values are expressed by mean \pm SD, unless stated otherwise. Data is presented in median [25th percentile, 75th percentile]

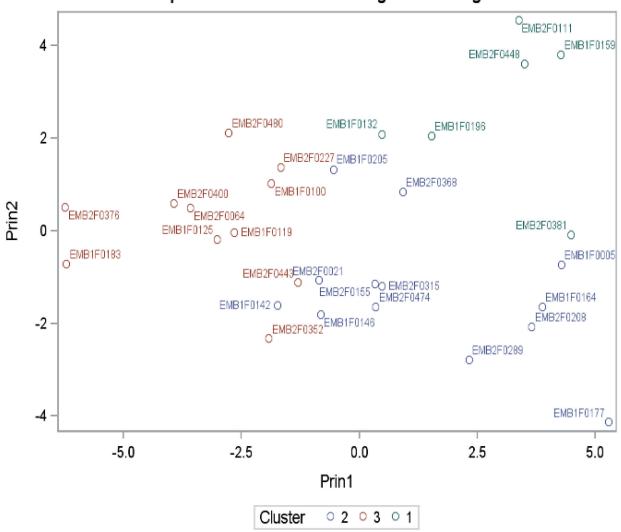
| Serum Clinical Markers | Reference Values | Total Participants (N=30) |
|----------------------------|-------------------------|---------------------------|
| HbA1c (%) | 4-5.7 | 5.80 ± 0.50 |
| Total Cholesterol (mmol/L) | < 5.2 | 4.81 ± 0.98 |
| LDL (mmol/L) | < 3.0 | 2.80 ± 0.75 |
| HDL (mmol/L) | - | 2.73 ± 1.44 |
| GR (10 ⁹ /L) | - | 4.79 ± 0.37 |
| INR | - | 0.94 [0.91, 0.98] |
| Triglycerides (mmol/L) | < 1.7 | 1.84 ± 1.04 |
| CRP (mg/L) | < 10 | 10.00 [4.00, 13.00] |

Table 3. Serum Clinical Markers

Reference values were taken from the HSCM biomedical lab Data is presented in means \pm SD Data is presented in median [25th percentile, 75th percentile]

3.2. Dietary Clusters Descriptions

Using a structured k-means method, three dietary clusters were derived (Figure 2). Cluster 1 had six participants, cluster 2 had 13 participants and cluster 3 had 11 participants, the descriptive of each dietary cluster (i.e., average of three days) can be found in Table 4.



Graphic with three clusters using K-means algorithm

Figure 2. K-Means Cluster Analysis

| | Nutrient Status | Cluster 1 (N=6) | Cluster 2 (N=13) | Cluster 3 (N=11) |
|-------------|---|-----------------------|-----------------------|----------------------|
| Macro- | Total Protein (g/day) | 99.07 ± 8.15 | 118.22 ± 25.02 | 65.41 ± 21.67 |
| nutrients | Total Fat (g/day) | 99.07 ± 8.15 | 118.22 ± 25.02 | 65.41 ± 21.67 |
| | Total Carbohydrate (g/day) | 316.14 ± 55.11 | 219.17 ± 50.71 | 182.09 ± 51.59 |
| Micro- | Sodium (mg/day) | 3059.77 ± 1204.44 | 3536.66 ± 1336.14 | 3457.54 ± 2831.90 |
| nutrients | Magnesium (mg/day) | 384.24 ± 112.94 | 300.84 ± 66.88 | 225.32 ± 83.98 |
| | Calcium (mg/day) | 1114.20 ± 204.59 | 877.28 ± 275.53 | 597.50 ± 311.53 |
| | Phosphorus (mg/day) | 1491.33 ± 257.51 | 1529.35 ± 380.61 | 887.71 ± 272.76 |
| | Vitamin B12 (ug/day) | 4.07 ± 0.93 | 6.26 ± 2.36 | 2.90 ± 1.56 |
| | Vitamin B6 (mg/day) | 2.01 ± 0.36 | 2.61 ± 1.86 | 1.45 ± 1.06 |
| | Vitamin D (IU/day) | 168.54 ± 99.57 | 239.48 ± 149.64 | 120.23 ± 140.44 |
| | Vitamin C (mg/day) | 139.22 ± 80.35 | 93.54 ± 45.90 | 78.12 ± 57.67 |
| | Zinc (mg/day) | 13.02 ± 2.95 | 12.49 ± 3.11 | 7.24 ± 2.17 |
| | Potassium (mg/day) | 3808.69 ± 850.83 | 3033.06 ± 701.99 | 1880.09 ± 516.79 |
| Simple | Total other monosaccharides (g/day) | 8.02 ± 5.0 | 3.94 ± 3.44 | 1.81 ± 2.50 |
| Sugars | Total other disaccharides (g/day) | 5.32 ± 3.78 | 4.62 ± 3.31 | 2.60 ± 3.26 |
| | Glucose (g/day) | 23.13 ± 9.94 | 9.62 ± 5.42 | 8.32 ± 4.77 |
| | Fructose (g/day) | 25.98 ± 8.41 | 9.62 ± 5.45 | 10.33 ± 6.51 |
| | Sucrose (g/day) | 34.54 ± 9.70 | 12.93 ± 7.75 | 9.19 ± 6.87 |
| | Galactose (g/day) | 2.34 ± 4.06 | 0.68 ± 0.93 | 0.17 ± 0.22 |
| | Lactose (g/day) | 4.55 ± 3.37 | 8.13 ± 7.34 | 4.50 ± 5.96 |
| | Maltose (g/day) | 2.75 ± 0.87 | 4.61 ± 3.78 | 1.72 ± 1.40 |
| Fatty Acids | Total saturated fatty acids (g/day) | 32.89 ± 15.89 | 31.90 ± 11.45 | 18.96 ± 7.41 |
| | Total monounsaturated fatty acids (g/day) | 42.36 ± 20.80 | 38.62 ± 14.45 | 22.24 ± 8.18 |
| | Total polyunsaturated fatty acids (g/day) | 19.12 ± 6.74 | 19.78 ± 9.02 | 12.12 ± 4.08 |
| Additional | Total dietary fibre (g/day) | 25.21 ± 8.90 | 16.99 ± 4.79 | 12.46 ± 4.79 |
| | Cholesterol (mg/day) | 309.61 ± 131.75 | 534.06 ± 281.20 | 214.97 ± 132.28 |
| Energy | Total energy in kilocalories (kcal/day) | 2620.89 ± 690.37 | 2254.50 ± 527.50 | 1533.15 ± 355.86 |

Table 4. Description of Dietary Clusters Derived from Three-Day Food Diary Averages

Data is presented in means \pm SD

3.2.a. Cluster 1: High sugar / high caloric diet

Cluster 1 had the greatest amount of total carbohydrate relative to the other clusters. It also had the greatest amount of simple sugars: glucose; fructose; and sucrose. It had the greatest amount of magnesium, calcium, vitamin C, potassium, total monounsaturated fatty acids, total saturated fatty acids, total dietary fiber and was the most energy-dense.

3.2.b. Cluster 2: High protein / high cholesterol diet

Cluster 2 had the greatest amount of total protein and fat in comparison to the other clusters. It was high in phosphorus, vitamin B12, vitamin B6, vitamin D, cholesterol, sodium, and total polyunsaturated fatty acids.

3.2.c. Cluster **3**: Low fiber / low saturated fat diet

Cluster 3 had the least amount of total dietary fiber, total protein, fat, and carbohydrate relative to the other clusters. It was also high in sodium and was the least energy-dense.

3.3 Dietary Clusters and Metabolic Status

There was a significant difference in mean LDL values across clusters (F=8.54, p = 0.0244). LDL ($5.28 \pm 0.71 \text{ mmol/L}$) was significantly higher in Cluster 1 than in Clusters 2 ($2.38 \pm 0.28 \text{ mmol/L}$; p= 0.0130) and 3 ($1.76 \pm 0.44 \text{ mmol/L}$; p = 0.0097) (Table 5). There was also a significant difference in mean GR values across clusters (F=9.14, p= 0.01). GR ($5.64 \pm 0.21 \text{ 10}^{9}$ /L) was significantly higher in Cluster 1 than that of clusters 2 ($4.71 \pm 0.09 \text{ 10}^{9}$ /L; p= 0.003) and 3 ($5.01 \pm 0.15 \text{ 10}^{9}$ /L; p= 0.015). There were no significant differences in body fat%, HbA1c, cholesterol, triglyceride levels, HDL, INR, and CRP levels across clusters.

| | Mean Estimate \pm SD | | | | P-value | | | |
|--------------------------|------------------------------|---------------------|------------------|-------------------|-------------------------------|-------------------------------|-------------------------------|--|
| | F-Statistic (p-value) | Cluster 1 | Cluster 2 | Cluster 3 | Cluster 1 vs. Cluster 2 | Cluster 1 vs. Cluster 3 | Cluster 2 vs. Cluster 3 | |
| Body Fat % | 0.63 (0.55) | 50.31 ± 4.03 | 52.07 ± 2.36 | 54.99 ± 3.66 | 0.70 | 0.31 | 0.46 | |
| HbA1c (%) | 0.56 (0.60) | 6.33 ± 0.48 | 5.86 ± 0.22 | 6.05 ± 0.32 | 0.33 | 0.54 | 0.57 | |
| Cholesterol (mmol/L) | 1.96 (0.18) | 414.41 ± 142.69 | 661.85 ± 87.28 | 401.84 ± 133.63 | 0.13 | 0.93 | 0.09 | |
| Triglyceride (mmol/L) | 0.21 (0.81) | 2.68 ± 1.86 | 1.44 ± 0.59 | 1.64 ± 1.16 | 0.55 | 0.66 | 0.88 | |
| LDL (mmol/L) | ¹ *8.54 (0.02) | 5.28 ± 0.71 | 2.38 ± 0.28 | 1.76 ± 0.44 | *0.01 | *0.01 | 0.26 | |
| HDL (mmol/L) | 1.13 (0.37) | 1.70 ± 1.59 | 2.64 ± 0.71 | 3.74 ± 1.17 | 0.60 | 0.20 | 0.43 | |
| GR (10 ⁹ /L) | *9.14 (0.01) | 5.64 ± 0.21 | 4.71 ± 0.09 | 5.01 ± 0.15 | *0.003 | *0.015 | 0.095 | |
| INR | 0.18 (0.84) | 1.03 ± 0.37 | 1.15 ± 0.17 | 0.98 ± 0.28 | 0.77 | 0.91 | 0.56 | |
| CRP (mg/L) | 1.85 (0.24) | 21.64 ± 7.34 | 11.04 ± 3.45 | 22.65 ± 5.29 | 0.25 | 0.88 | 0.10 | |

Table 5. Dietary Clusters vs. Metabolic Status ANCOVA Analyses and Post-Hoc Test

¹ *Statistically significant (p<0.05)

4. Discussion

4.1 Dietary Clusters

This cross-sectional study was conducted in candidates for a MBS. Three dietary clusters using the average intakes of macro- and micro- nutrients over three days, were identified, and defined as follows: high sugar/high caloric diet; high protein/high cholesterol diet; and low fiber/low saturated fat diet.

Relative to the other clusters, the high sugar/high caloric diet cluster was high in magnesium, calcium, vitamin C, potassium, monounsaturated fatty acids, saturated fatty acids and dietary fiber. This provides insight into the types of nutrients that are closely related to this cluster. Dagan et al⁽⁴³⁾ conducted a study in which participants with similar sample characteristics had a similar distribution of macronutrient content and energy intake as the distribution found in the high sugar/high caloric dietary cluster. They found that patients pre-MBS (N=100) with a mean BMI of 42.3 ± 4.7 kg/m³ and age of 41.9 ± 9.8 years had a mean energy intake of 2710.7 ± 1275.7 kcal/day, and a mean protein, fat and carbohydrate intake of 114.2 ± 48.5 g/day, 110.6 ± 54.5 g/day, and 321.6 ± 176.1 g/day, respectively⁽⁴³⁾. Sanchez et al⁽⁴⁴⁾ performed a similar analysis on the diets of women eligible for MBS (N=103) and found a similar distribution of mean energy intake (2801 ± 970 kcal/d), protein (93.5 ± 28.6 g/d), fat (101.8 ± 49.7 g/d) and carbohydrates (386.4 ± 144.7 g/d). This suggests that diets that are calorically dense and high in carbohydrate content have been commonly observed amongst candidates for MBS.

The high protein/high cholesterol diet cluster was relatively high in fat, phosphorus, vitamin B12, vitamin B6, vitamin D, and total polyunsaturated fatty acids. There is evidence that the consumption of dietary protein contributes to the intake of micronutrients such as vitamin D,

potassium, and calcium, and of saturated fat and solid fats⁽⁴⁵⁾. Protein intake has been observed to contribute to the severity of obesity with varying degrees based on protein source. Higher intakes of plant-based proteins have been associated with protective effects on obesity, whereas higher animal-based protein intakes (i.e., red meat, processed meat) have been associated with weight gain^(46,46). A systematic review and meta-analysis also found that although there was heterogeneity across studies, red and processed meat intake was positively associated with the risk of obesity, BMI and waist circumference⁽⁴⁷⁾. Although protein was not separated by source, the cluster high in protein was also high in fat and cholesterol, which may suggest consumption of animal-sourced protein, as aligned with previous studies^(46,48).

The low fiber/low saturated fat diet cluster was also relatively high in sodium, but low in energy intake and in fat, carbohydrate, and protein content. Key nutrient characteristics in this cluster have been previously assessed with risks and measures of obesity. One meta-analysis and systematic review found a positive association between the risk of obesity and sodium intake⁽⁴⁹⁾. One review found that consumption of dietary fibers varying in solubility, viscosity and source (i.e., fruits, vegetables, grains and fungi) were positively associated with improved body weight, adiposity and overall inflammation⁽⁵⁰⁾. In addition to being low in dietary fiber, this cluster was also low in magnesium, calcium, phosphorus, vitamin B12, vitamin B6, vitamin D, vitamin C, zinc, and potassium relative to the other two clusters. This suggests the types and amounts of nutrients that are closely related to each other in this cluster and suggests that this diet may have consisted of a low intake of fruits and vegetables.

Although all participants were candidates for MBS and shared similar age and body composition profiles, these clusters describe specified variability in dietary intake. While previous studies

have made general descriptions of a singular diet (i.e., Western diet) being positively associated with obesity $risk^{(11,12,13)}$. The Western diet has been generally described at the food group level: high in red meat and processed/high sugary foods; and low in fruits and vegetables, and at the nutrient level: calorically dense (1626 – 2154 kcal/day); high in saturated fats (10.7% of total energy); sucrose (> 36% of total energy), sodium (2325-3133 mg/day); and low in fiber (16.2-18.4 g/day)⁽⁵¹⁾. The macronutrient distribution as a percentage of energy intake in the Western diet has been reported as follows: 49.3% of carbohydrates; 33.8 % of fats; and 16.4% of protein⁽⁵¹⁾. Some key nutrient characteristics found within all three diet clusters observed in this study do align with the typical Western dietary nutrient trends. For example, individuals in all three diet clusters had an average sodium intake ranging between 3060 - 3537 mg/day, and diet clusters 2 and 3 were low in dietary fibre ranging between 12.5 - 17.0 g/day. Although the key characteristics across clusters follow the Western diet trend, we were able to identify and describe specific differences within the diet consumed by candidates for MBS. This is novel, as it provides preliminary insights into the different diets at the nutrient level found within candidates for MBS, rather than categorizing foods consumed into a single, general diet. Identifying one general diet in this population can lead to a general dietary intervention, limiting the potential for personalised interventions. For example, individuals in cluster 1 had the greatest simple sugar (around 106.6 g/day), carbohydrate (316.1 g/day) and the greatest fibre content (25.2 g/day), and although still high relative to the upper limit intakes, cluster 1 had the lowest sodium content (3060 mg/day), relative to individuals in clusters 2 and 3. As such, individuals in this cluster may need different dietary recommendations relative to the other clusters in terms of the amounts of certain nutrients.

Currently, according to the Canadian Nutritional Recommendations Guidelines⁽⁵²⁾, there is a general pre-MBS evaluation, consisting of blood draws; however, the pre-MBS dietary intake screening process is unclear. Therefore, the variability in dietary intake observed in this study can inform pre-MBS screening to consider assessing dietary micro- and macro-nutrient intake distribution, complementary to the nutritional status assessed by the blood draws. This will not only provide some structure and methodology for pre-MBS dietary screening, but it can account for the inter-individual dietary differences and can aid in developing personalised dietary interventions to address possible malnutrition or micronutrient deficiencies. The dietary interventions can differ across each identified dietary cluster in terms of the type and amount of nutrients recommended, and additional dietary supplementation (if necessary) tailored to the specific nutrient profile of each cluster. However, other factors would have to be considered when developing personalised dietary interventions, such as the individuals' nutritional and metabolic status, as well as the individuals' nutrient and respective whole food dietary intake. Future studies can also assess the relationships between nutrient and respective whole food clusters with nutritional status pre- and post- MBS. This can further our understanding and development of dietary interventions to improve pre-MBS nutritional status to reduce postsurgical complications.

4.2 Dietary Clusters on Lipid profile and inflammation

LDL and GR were found to be significantly higher in the high sugar/high caloric diet group (clusters) relative to the high protein/high cholesterol and low fiber/low saturated fat diet clusters. This is consistent with literature that found that in the general population, carbohydrates with a high glycemic index, and sugar and fructose tended to be associated with increases in LDL concentrations⁽⁵³⁾.

Although there were no significant differences in CRP values between clusters, the CRP values were greater in the high sugar/high caloric diet and low fiber/low saturated fat diet. The lack of statistical significance may be due to the small sample size, and limited statistical power. Previous studies have reported that dietary carbohydrates high in glycemic load and glycemic index values are associated with increased CRP levels^(16,26,27). Further, Lin et al ⁽⁵⁴⁾ found that sugar sweetened beverages were positively associated with CRP values in US adults with obesity. The CRP values found within the two dietary clusters were a little over double the reference values. This may suggest that individuals in these clusters have an increased risk for post-MBS complications due to the inflammatory burden (i.e., impaired healing, increased risk of infection)⁽⁵⁵⁾. Future studies with larger sample sizes can evaluate the associations between dietary clusters with additional inflammatory markers such as pro-inflammatory cytokines and adipokines pre-MBS. This evaluation can lead to a better understanding of diet on inflammation, which can be another factor to consider when developing dietary interventions/recommendations pre-MBS to reduce post-MBS complications.

These findings suggest that the variability in dietary clusters amongst candidates for MBS have different implications on metabolic status. Although all participants had similar body composition profiles, the high sugar/high caloric diet cluster had greater LDL and GR values, relative to the other diet clusters. This suggests the need for dietary interventions for this cluster pre-MBS tailored to improve LDL and GR status, which are risk factors for dyslipidemia, cardiovascular disease, and chronic low-grade inflammation respectively. In addition to assessing dietary nutrient intake, pre-MBS screening can also consider dietary habits, physical activity levels and psychosocial factors when tailoring dietary interventions^(56,57), as these factors

can also contribute to metabolic status. Currently, there is a growing need for precision nutrition, which considers individual-level and environmental characteristics, to inform personalised dietary plans and has been suggested as an intervention in managing obesity and metabolic syndrome⁽⁵⁸⁾. This provides preliminary insights on what can be considered in the future for personalised nutrition in candidates for MBS.

4.3 Strengths and Limitations

There were some limitations to this study which need to be considered when interpreting the results. There was a small sample size, limiting the power and generalizability of the findings. Also, this was a cross-sectional study, limiting the potential findings of causal relationships; however, it did provide preliminary insights into the dietary patterns at the nutrient level found in candidates for MBS. We did not adjust for nutrient supplementation, which may have influenced the nutrient dietary intakes. Although we adjusted for physical activity levels, we did not adjust for medication use, which could have affected the secondary analyses assessing the clinical metabolic markers. For example, certain medication use could have played a role in altering the clinical marker values so that they could fall within optimal ranges. We also did not adjust for psychological measures such as depression, anxiety and eating behaviours, which could have impacted the clinical metabolic metabolic measures and nutrient dietary intakes.

Limitations were also observed when capturing food data using Keenoa. Participants may have experienced reactivity, where their behaviour may have changed due to the awareness that they are being monitored. For example, participants may have underreported their dietary intake which may not accurately reflect what is consumed daily. When recording food diaries in Keenoa, although participants were provided with a guide to serving sizes, some individuals did

not accurately report their portion sizes based on the image provided by the participant in the mobile application. The possible underreporting of dietary intake may have contributed to the decreased value in total energy intake observed in cluster 3 (1533 kcal/day) relative to cluster 1 (2621 kcal/day) and 2 (2255 kcal/day). Further, TANITA was used for assessing body composition when DEXA is the gold standard for measuring body composition. We used the TBF-310 TANITA single-frequency foot-to-foot BIA device (SF-BIA) with four electrodes (i.e., two anterior and two posterior). Mulasi et al⁽⁴¹⁾ has reported that the SF-BIA device makes assumptions which decrease the likelihood that it can accurately differentiate between intracellular water (ICW; within cells) and extracellular water (ECW; blood plasma and interstitial) in the body, ultimately limiting the accuracy of the estimated fat mass and fat free mass. Firstly, the SF-BIA assumes that the human body is a single, symmetrical cylinder, rather than making a more accurate depiction of the human body having five distinct cylinders accounting for the limbs and trunk⁽⁴¹⁾. Further, SF-BIA assumes that the ICW/ECW ratio is constant suggesting that the bioelectrical current is conducted uniformly across all tissues of the body⁽⁴¹⁾. It also assumes that the hydration of body tissues remains constant, that a single frequency of 50kHz will penetrate all cells uniformly, and that the impedance is equal to the resistance, assuming that the reactance is negligible⁽⁴¹⁾. Previous studies have shown that fat-free mass has been overestimated in a cardiac and renal setting between an SF-BIA device and DEXA⁽⁵⁹⁾. BIA results are valid in individuals that have a BMI up to 34 kg/m², but must be interpreted with caution in individuals with a BMI greater than 34 kg/m² and require further validation in these individuals⁽⁵⁹⁾. However, different BIA modalities such as multifrequency devices in individuals within a normal body fat range have been highly correlated to DEXA

measures^(60, 61, 62). Therefore, results regarding body fat percentage from the secondary analysis in our study can be interpreted with caution.

In spite of these limitations, to the best of our knowledge this is one of the first studies to use the approach of assessing dietary patterns by clustering the macro- and micro- nutrients in candidates for MBS. This study demonstrates the dietary inter-individual differences amongst candidates for MBS, highlighting the importance of assessing dietary intake nutritional status in patients prior to surgery as there may be variability in nutrient profiles, and implications on metabolic status. There are strengths to using the mobile app Keenoa to capture food data. Firstly, the foods were captured in real-time, which lessened the risk of omitting dietary intake (forgotten foods) and increased the accuracy of reporting portion sizes. The accuracy of the dietary assessment was further enhanced as registered dietitians and research assistants verified the quality of the data entry. Furthermore, collecting data over three non-consecutive days may have increased the accuracy of the individual's diet (i.e., consecutive days of diet may be related), and may have lessened respondent fatigue. We assessed various macro- and micronutrient parameters and identified dietary patterns through cluster analysis, which served as a strength as interactions between the dietary content were considered and more accurately represented an individual's daily meal, in comparison to assessing a single nutrient or food.

4.4 Conclusion

Three dietary patterns in candidates for a MBS were identified: high sugar/ high caloric diet; high protein/high cholesterol diet; and low fiber/low saturated fat diet – all of which could be defined with a standard Western diet paradigm. The group high in sugar/calories was significantly associated with increased LDL and GR concentrations in comparison to the other

two groups. These preliminary findings demonstrate variability and inter-individual differences in macro- and micro- nutrient clusters in candidates for MBS. It also demonstrates that these variabilities have different associations with measures of metabolic status such as LDL and GR concentrations. Future studies should assess the dietary clusters using a larger sample size to potentially fine tune the clusters in this population. Future studies should also compare pre-MBS dietary clusters to a control group and post-MBS outcomes such as nutritional status, metabolic status, and weight outcomes. This can potentially aid in developing individual-based recommendations pre-MBS based on the individual's profile, which may mitigate post-MBS complications.

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Appendix A: Demographics and Medical History Questionnaire⁽²⁹⁾

Demographics

_____)

Please answer the questions below (Check the box or write the appropriate answer):

1. Date of birth (dd-mm-yyyy): _____

- 2. Age __
- 3. Sex:
 - 🗌 Man
 - Woman
- 4. Are you pregnant or are you planning to be pregnant in the next 12 months?
 - Yes
 - 🗌 No
 - I don't know
- 5. Are you currently participating to another research project?
 - Yes (which one: _____
 - 🗌 No
 - I don't know
- 6. What is your marital status?
 - □ Single
 - Common law partner
 - Married
 - Divorced / Separated
 - Widowed
- 7. How many people live with you? ______(Please describe in the table below)

| Person | Number of people (write a number) |
|----------------------|-----------------------------------|
| Mother | |
| Father | |
| Brother | |
| Sister | |
| Child | |
| Spouse | |
| Friend | |
| Other | |
| Prefer not to answer | |

8. Are any of those people overweight?

| Person living with you (according to the categories above, if more than 1 sister for example, write sister 1, sister 2, etc.) | Weight status |
|---|-----------------------|
| Is your overweight, or has he ever been? | Yes No I don't know |
| Is your overweight, or has he ever been? | Yes No I don't know |
| Is your overweight, or has he ever been? | Yes No I don't know |
| Is your overweight, or has he ever been? | Yes No I don't know |
| Is your overweight, or has he ever been? | Yes No I don't know |
| Is your overweight, or has he ever been? | Yes No I don't know |
| Is your overweight, or has he ever been? | Yes No I don't know |
| Is your overweight, or has he ever been? | Yes No I don't know |
| Is your overweight, or has he ever been? | Yes No I don't know |
| Is your overweight, or has he ever been? | Yes No I don't know I |

- 9. What is your highest level of education?
 - No level attained
 - Primary (6th grade)
 - Secondary 3 (9th or 10th grade)
 - Secondary 5 (12th grade (including SSD, DVS, AVS and other equivalent diploma)
 - College (CEGEP or classical course)
 - University Undergraduate degree
 - University Graduate degree

| 10. What is your current employment status? | | | | | | |
|---|--|-------------------------------|--|--|--|--|
| Full-time work | | Retired | | | | |
| Part-time work | | Unemployed | | | | |
| At home, worked in the past | | Sick leave or maternity leave | | | | |
| At home, has never worked | | Social welfare | | | | |
| Disability | | Unemployment insurance | | | | |
| | | Student | | | | |

11. What was the total gross income of your family, before taxes and other deductions, in the last year? (Revenu Québec quintile)?

| Less than 23 000 \$ | | | | | |
|------------------------|--|--|--|--|--|
| 23 001 \$ to 37 000 \$ | | | | | |
| 37 001 \$ to 57 000 \$ | | | | | |
| 57 001 \$ to 84 000 \$ | | | | | |

More than 84 000 \$ Doesn't know

Prefer not to answer

- 12. Aboriginal persons First Nations Metis Inuk/Inuit
 - A. Are you an Aboriginal person, that is, First Nations, Métis or Inuk/Inuit? First Nations includes status and Non-Status Indians.
 - Yes (Please answer question 12. B)
 - 🗌 No
 - Don't know
 - Prefer not to answer
 - B. (If you answered yes to the question A) Are you a First Nations, Métis or Inuk/Inuit??
 - First Nations (North American Indian)
 - Metis
 - 🗌 Inuk / Inuit
 - Don't know
 - Prefer not to answer
- 13. You may belong to one or more racial or cultural groups on the following list. Are you....?
 - White
 - South Asian (e.g. East Indian, Pakistani, Sri Lankan)
 - Chinese
 - Black
 - 🛛 Filipino
 - Latin American
 - Arab
 - Southeast Asian (e.g. Vietnamese, Cambodian, Malaysian, Laotian)
 - U West Asian (e.g., Iranian, Afghan)
 - C Korean
 - Japanese
 - Other (Specify)

14. What is your height? _____(cm) or _____ (feet & inches)

15. What is your weight? _____(kg) or _____(pounds)

16. What is your waist circumference? _____(cm) or _____ (feet & inches)

17. How old were you when you started to have excess weight? _____ years old

| Medical condition | Yes | No | l don't know | If so, since when |
|--|-----|----|-----------------|----------------------|
| Cancer (in the past 5 years) | | | | Age: |
| If so, specify: | | | | |
| Sleep apnea | | | | Age: |
| Snoring | | | | Age: |
| Arthro-skeletal disorders (e.g., arthritis, arthrosis) If so, specify: | | | | Age: Age: |
| Chronic obstructive pulmonary disease (COPD) | | | | Age: |
| Chronic bronchitis | | | | |
| Emphysema | | | | |
| Asthma | | | | Age: |
| Anxiety Disorder (Generalized Anxiety Disorder, Panic Disorder, Social Anxiety) | | | | Age: |
| Mood Disorder (Major Depressive Disorder) | | | | Age: |
| Obsessive Compulsive Disorder (OCD) | | | | Age: |
| Bipolar disorder | | | | Age: |
| Schizophrenia | | | | Age: |
| Alzheimer | | | | Age: |
| Other (s) If so, specify: | | | | Age: Age: Age: |
| Surgeries (Other (s) than bariatric surgery)? If so, specify: | | | | Age: Age: Age: |

Do you suffer from or have you ever had one of the following diseases or medical conditions?:

Medical History

Do you suffer from or have you ever had one of the following diseases or medical conditions?:

| Medical condition | Yes | No | l don't know | If so, since when… |
|---|-----|----|-----------------|--------------------|
| Stroke/ Transient ischemic attack (TIA) | | | | Age : |
| Heart attack | | | | Age: |
| Other hearth diseases (example: Coronary Artery Disease, atherosclerosis) | | | | Age: |
| Glucose intolerance (pre-diabetes) | | | | Age: |
| Type 1 diabetes (juvenile) | | | | Age: |
| Type 2 diabetes (non-insulin dependant) If so, how is it treated? Insulin Oral hypoglycemic Diet | | | | Age: |
| Hypertension (high pressure) | | | | Age: |
| If so, do you take a medication for it? | | | | |
| High cholesterol (dyslipidemia) | | | | Age: |
| If so, do you take a medication for it? | | | | A |
| Gastroesophageal reflux disease | | _ | | Age: Age: |
| Non-alcoholic fatty liver disease (NAFLD) | | | | Age |
| Gallbladder disease or Gallstones | | | | Age: |
| Other gastrointestinal disease(s) | | | | |
| If so, specify: | | | | Age: |
| Chronic renal disorder | | | | Age: |
| Polycystic Ovary Syndrome | | | | Age: |
| Liver Cirrhosis | | | | Age: |

Bariatric Surgery

 When did you first start the process of bariatric surgery? (The beginning of the process of bariatric surgery is defined as the date you first register on http://www.chirurgiebariatrique.com or the date your doctor submitted a referral to the surgeons office.)______(DD/MM/YYYY)

2. What are your expectations regarding bariatric surgery?

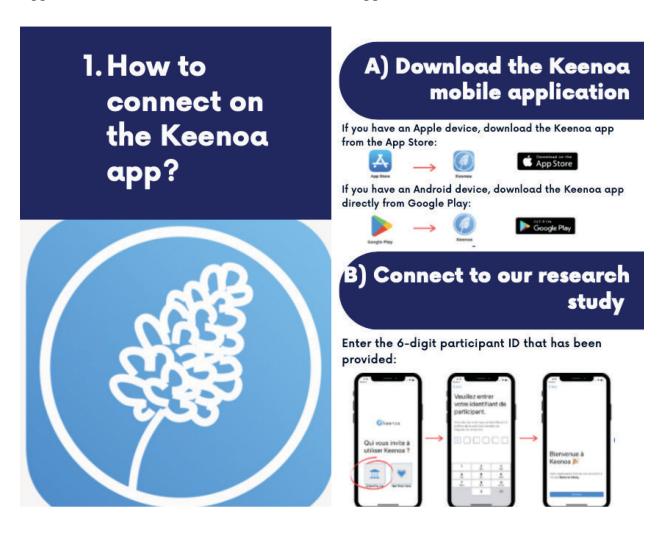
3. Have you undergone any bariatric surgical procedure (surgery for weight loss) in the past?

- Yes
- □ No (if no, move on to the next section: "Mental health treatment")
- 4. If yes, how many bariatric surgeries have you undergone? _____

| Tick the box if applicable | Surgery type | Number of this surgery type undergone | Surgery dates (DD/MM/YYYY) |
|----------------------------------|--|---|-------------------------------|
| | Gastric bypass (Roux-en Y gastric bypass) | | |
| | Sleeve gastrectomy | | |
| | OAGB (One anastomosis gastric bypass, mini gastric bypass surgery) | | |
| | Adjustable band | | |
| | BPD/DS (biliopancreatic diversion with or without duodenal switch) | | |
| | Other – Please specify : | | |
| | l don't know | | |

5. Please indicate and specify the number of all the previous bariatric procedures you have ever had:

Appendix B: Instructions on How to Use Mobile Application Keenoa⁽²⁸⁾



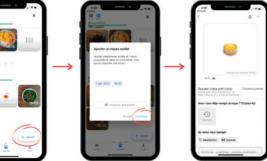


3.How to log forgotten or missed meals?

A) Press on the "+" button located on the bottom right corner of your food diary.

B) Select the time and day of the meal consumed.

C) Upload a photo or log your meal manually. If logged manually, an emoji will replace the photo of the meal.





Appendix C: Serving Sizes⁽³⁵⁾

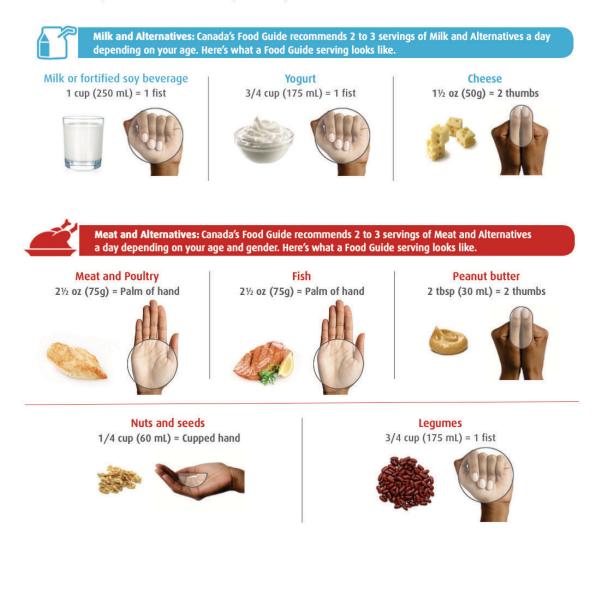
Handy Guide to Serving Sizes

Learn how to use your hand to estimate Canada's Food Guide serving sizes and compare them to the food portions you eat.



Handy Guide to Serving Sizes

Learn how to use your hand to estimate Canada's Food Guide serving sizes and compare them to the food portions you eat.





Visit www.unlockfood.ca/handyguide to use the interactive version of the Handy Guide to Serving Sizes and watch videos to help you manage your food portions.

Dietitians look beyond fads and gimmicks to delivery reliable life-changing advice. Find a dietitian at www.dietitians.ca/find.

Handy Guide to Serving Sizes

Find out how to manage your portions of these foods:

