IFSO-WGO GUIDELINES ON OBESITY

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Commonly-used abbreviations

General	
IFSO	International Federation for the Surgery of Obesity and Metabolic Disorders
WGO	World Gastroenterology Organisation
IBW	Ideal body weight
EWL	Excess weight loss
TWL	Total weight loss
FDA	Federal Drug Administration (USA)
CE	Conformitè Europëenne
NIH	National Institutes of Health (USA)
BMI	Body mass index
EGD	Upper gastrointestinal endoscopy
GI	Gastrointestinal
MDT	Multidisciplinary team
N/A	Data not available
QALY	Quality-adjusted life year
QALYs	Quality-adjusted life years
RCT	Randomized clinical trial
SAE	Serious adverse event
UGI	Upper gastrointestinal
UK	United Kingdom
US/USA	United States of America
Co-morbid conditions	
BP	Blood pressure
COVID-19	Coronavirus disease of 2019
CVD	Cardiovascular disease
ESRD	End-stage renal disease
GERD	Gastroesophageal reflux disease
HTN	Hypertension
MAFLD	Metabolic-associated fatty liver disease (same as NAFLD, see below)
NAFLD	Non-alcoholic fatty liver disease
NASH	Non-alcoholic steatohepatitis
T2DM	Type 2 diabetes mellitus
Endoscopic metabolic & bariatric therapy	
EMBT	Endoscopic metabolic & bariatric therapy
BPD	Biliopancreatic diversion
DJBL	Duodenojejunal bypass liner

DMR	Duodenal mucosal resurfacing
ESG	Endoscopic sleeve gastroplasty
GAT	Gastric aspiration therapy
IGB	Intragastric balloon
POSE	Primary Obesity Surgery - Endoluminal
Metabolic & bariatric surgery	
MBS	Metabolic & bariatric surgery
AGB	Adjustable gastric banding
BPD	Biliopancreatic diversion
BPD-DS	Biliopancreatic diversion with duodenal switch
DS	Duodenal switch
GB	Gastric bypass
LRYGB	Laparoscopic Roux-en-Y gastric bypass
LSG	Laparoscopic sleeve gastrectomy
MGB	Mini gastric bypass (same as OAGB, see below)
OAGB	One-anastomosis gastric bypass
RYGP	Roux-en-Y gastric bypass
SADI	Single-anastomosis duodenal-ileal bypass
SG	Sleeve gastrectomy

I. INTRODUCTION

Worldwide, an estimated 2.2 billion people are living with overweight, among whom approximately 1.5 billion live with obesity, both numbers continuing to increase(2, 3, 4). Its rising incidence affects all age groups, even children and adolescents(5). Its presence further increases a person's risk of developing numerous other life-altering and oftentimes life-threatening complications, most notably type 2 diabetes mellitus(6, 7, 8), cardiovascular disease(8, 9, 10, 11), sleep apnea(12, 13), chronic kidney diease(14, 15), and at least thirteen different types of cancer, which include breast, colorectal, endometrial, esophageal, gallbladder, gastric cardia, hepatocellular, ovarian, pancreatic, renal, and thyroid cancer, in addition to meningioma and multiple myeloma(16, 17). Worldwide, the percentage of cancer considered attributable to obesity, expressed as its *population attributable fraction*, has been estimated as 11.9% in men and 13.1% in women(16). As such, it has been linked to a significantly increased risk of premature mortality(18), including 15-20% of all cancer-related mortality(19), as well as to an overall decrease in quality of life(4). These associations between obesity and severe morbidity and premature mortality have repeatedly been shown to extend even to childhood obesity(20, 21, 22, 23, 24).

Management is difficult, with weight loss typically followed by weight regain. For this reason and for the various associated metabolic changes that co-occur, it has been termed a "chronic relapsing progressive disease"(25). Healthcare providers who merely instruct their patients to "eat less and exercise more" rarely attain long-term outcome success. That said, relatively recent changes in its management include pharmacological, endoscopic and surgical interventions, alongside dietary changes, other lifestyle changes like exercise, and counselling. And, among these, procedural interventions – like bariatric surgery and endoscopic therapy – especially appear to be significantly more effective than dietary and lifestyle changes alone, in terms of inducing weight loss, reducing comorbidities, and improving patients' overall quality of life(26, 27, 28, 29). Numerous such operative interventions exist, however, and which are used and how often vary between practices and regions(30). These procedures also carry risks of their own, including a low, but non-negligible (0.15% to 0.35%) risk of intra-operative mortality(31, 32); numerous common and potentially fatal nutritional difficiencies(33, 34, 35, 36); other short-term and long-term complications, including various post-operative bleeding and various gastrointestinal syndromes(31); and the potential emergence of new post-operative addictive behaviours like substance abuse(37). Consequently, these procedures should not be used to replace, but rather to supplement other, non-operative approaches to obesity management, including dietary and lifestyle changes, the identification and treatment of psychopathology, psychosocial counselling, and pharmacotherapy(37). However, as with the choice of operative procedures, considerable variability also exists in how and to what extent such services are co-administered(38).

Variability also exists in which patients are considered for endoscopic and bariatric procedures, and numerous questions relating to indications and contraindications remain(39). Who is too young(40)? Who is too old(41)? When is someone psychologically at too great a risk(42)? Are alcohol use and cigarette, e-cigarette, and/or marijuana smoking absolute contraindications(43, 44, 45, 46)? Questions also persist as to what constitutes treatment success and failure(29, 47), how much weight regain is acceptable(48), which metric to use when measuring weight regain (e.g., weight in kilograms, body mass index [BMI], percentage of presurgery weight, percentage of nadir weight, percentage of maximum weight lost)(49), and when and how to manage such patients(50, 51)... among many others.

It was such variability in, and uncertainty about so many obesity management practices that led the World Gastroenterology Organisation (WGO)(52) and the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) to join forces in the spring of 2021 to take steps towards the drafting of international guidelines for the assessment, treatment, and monitoring of obesity, beginning by enlisting the services of an international, MD-PhD level expert (KPW) in the design and orchestration of health and healthcare surveys. This soon resulted in the design, development, and orchestration of a two-stage online Delphi consensus survey of 94 international experts in obesity management, spanning all six major continents, including experts in bariatric surgery and endoscopic bariatric procedures, as well as internists and hepatologists, specialists in behavioural health (e.g., psychologists, psychiatrists), and nutritionists/dietitians specializing in obesity management. The survey focussed on six main areas: (1) obesity epidemiology and risk factors; (47) patient selection for endoscopic and surgical bariatric procedures; (3) pre-opereative and post-operative psychological issues; (4) patient preparation for endoscopic and surgical bariatric interventions; (5) bariatric interventions;

and (6) post-procedural outcomes and follow-up. The survey asked experts to vote on up to 180 statements, depending on their area of expertise in each of the six above-listed areas. Consensus – defined as at least 70% inter-voter agreement – was reached on 152 (87.8%) of these statements, with consensus only considered valid when at least 80% of field-eligible experets voted on a given statement.

The current guidelines are, therefore, an assimilation of these consensus survey results – which are being published eslewhere en masse – combined with an exhaustive review of the published obesity literature spanning all the issues of concern. The document ends with an overall summary and a review of areas for which either no consensus was reached or currently-published evidence remains inadequate.

The discussion and guidelines are presented in the following order:

Introduction
Obesity, definition, epidemiology, and risk factors
Obesity-associated co-morbid conditions
Psychological impact of obesity and its management
Lifestyle factors and other non-operative management
Pre-operative patient assessment and preparation
Endoscopic metabolic and bariatric therapy (EMBT)
Metabolic and bariatric surgery (MBS)
Post-operative outcomes and follow-up
Conclusions

Common abbreviations used throughout these guidelines are listed in Table 1-1, below.

II. Obesity definition, physiology, epidemiology, and risk factors

1. DEFINITION AND SUBTYPES OF OBESITY

a. Definition

Obesity is a disease characterized by the accumulation of subcutaneous and/or visceral fat to a degree that can lead to organ dysfunction and other forms of pathology. It is typically associated with weight that exceeds a level considered within normal limits for a person of given stature. However, as explained below, it also can occur in individuals whose body mass index (BMI) falls within the normal range. With limited frequency, it is associated with osteopenia and sarcopenia.

Obesity is a multifactorial disease, though excess weight in childhood predisposes individuals to a greater risk of obesity in adulthood(25, 53, 54). To understand obesity, three essential concepts must be appreciated.

First, primary obesity is distinct from the rare monogenic forms of obesity that are caused by some mutation of a key gene in weight regulation.

Second, in its primary form, obesity is caused by several factors, the main ones being the excessive intake of calories and unhealthy foods, "poor nutrition", lack of physical activity, dysfunction or imbalance of the gut microbiome, congenital alterations, genetic susceptibility, and epigenetic alterations.

Third, primary obesity must also be considered a social disease. This implies that those who live with obesity must not only overcome the physical limitations associated with it, but considerable stigma and discrimination(55, 56, 57, 58, 59, 60, 61, 62, 63). As practitioners, we also are required to identify food addiction and the social burdens of obesity. The obesogenic environment, above all represented by advertising and poor nutrition, leads to a modified taste and reward system, up to the development of food addiction(64).

The metric that is most commonly used to identify and rate the severity of overweight and obesity is the BMI, which is calculated using a patient's height (in meters) and weight (in kilograms). The BMI is independent of age and gender. However, different inter-category delineation thresholds have been introduced for different ethnic groups to highlight increased metabolic risk in lower BMI levels(65). In population-based studies, a strong correlation between BMI and body fat content has been reported. However, different individuals with equal BMIs can have markedly different percentages of body fat(66). The BMI also does not provide any information on fat distribution (e.g., visceral fat; fatty infiltration in individual organs, etc.), which is considered an important determinant of metabolic and cardiovascular risk(67).

Visceral fat and, therefore, metabolic and cardiovascular risk, can be measured using various imaging tools — including computed tomography (CT), magnetic resonance imaging (MRI), and abdominal ultrasound — or simply by measuring a person's waist circumference. Waist circumference can, in turn, be viewed relative to a patient's height or hip circumference. It must be considered, however, that different measurement points and threshold levels have been employed in the literature(68).

Diagnosing obesity and accurately evaluating its severity is required for appropriate treatment, and this involves two levels of evaluation:

<u>Level 1</u>: Body mass index (BMI): a person's weight (in kilograms) divided by the square of that individual's height (in meters). Internationally-shared definitions for adults are: ≥25 kg/m^2 for excess weight and ≥30 kg/m^2 for obesity. Obesity is further subdivided into three levels, class I-III, based upon the BMI, with BMI from 30.0-34.9 kg/m^2 considered class I obesity, BMI 35.0-39.9 kg/m^2 considered class II obesity, and BMI ≥ 40 kg/m^2 considered class III obesity.
<u>Level 2</u>: Fat mass percentage (FM%), which is measured using various imaging tools. The gold standard for body composition is dual X-Ray absorptiometry (DXA), for which established

thresholds for FM% are 25% for adult males and 32% for adult females. Bioimpedance analysis (BIA) is an alternative way to evaluate fat composition, given its simplicity and more widespread accessibility. However, it cannot assess the distribution and presence of visceral fat. Estimates of fat mass have an average error of ± 5%, which varies with a person's state of hydration(69).

b. Obesity subtypes and how to characterize them

The classification of obesity phenotypes is then obtained by combining BMI, FM%, and the presence or absence of metabolic syndrome(25, 70, 71), as indicated in the table and figure below. Recall that patients living with obesity do not necessarily have to be overweight, as indicated below as phenotypes #2 (normal weight obese) and #3 (metabolically obese with normal weight).

A **TOFI** (thin-on-the-outside fat-on-the-inside) body type has been observed in both female and male patients who have an increased individual risk of developing metabolic disease(66). The elevated visceral fat in these people is characterized by ectopic fat deposition in the liver, skeletal muscles, the pancreas, and other organs. Lipid accumulation in non-adipose cells impairs the normal function of several tissues (lipo-toxicity) and is one link between visceral fat and both metabolic disorders and cardiovascular disease(72).

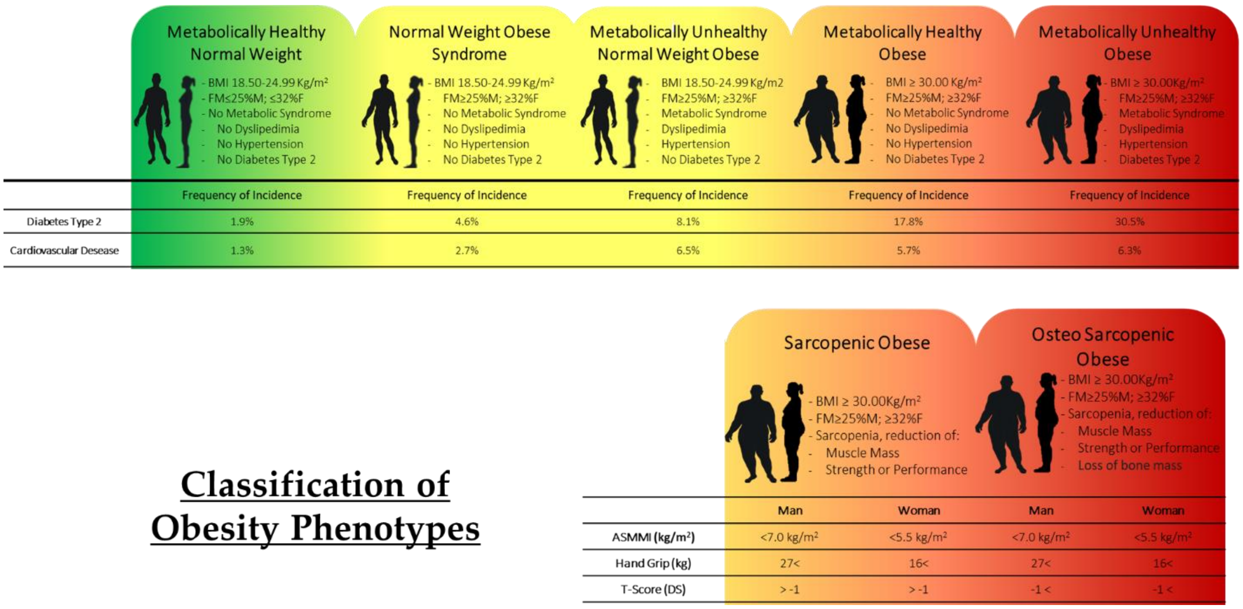
Some individuals with obesity may, counterintuitively, have reduced muscle and/or bone mass; and this, too, must be recognized by practitioners treating patients with obesity.

Table 2-1: The five phenotypes of obesity

Obesity Phenotypes	**BMI**		**FM%**		**MS**	
	-	**+**	**-**	**+**	**-**	**+**
1. Normal Weight Lean	✓		✓		✓	
2. Normal Weight Obese Syndrome	✓			✓	✓	
3. Metabolically Obese Normal Weight	✓			✓		✓
4. Metabolically Healthy Obese		✓		✓	✓	
5. Metabolically Unhealthy Obese		✓		✓		✓

BMI = body mass index; FM% = fat mass percentage; MS = metabolic syndrome

Figure 2-1: Classification of obesity phenotypes, including sarcopenic and osteo-sarcopenic obesity



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c. Obesity in children and adolescents

The pediatric application of BMI uses growth and range curves that consider growth phases and gender differences in fat expansion and distribution. The World Health Organization defines nutritional status for children and adolescents based on growth curves for age and sex(52), as follows:

BMI +1 standard deviation for age and sex = “Overweight”

BMI +2 standard deviations for age and sex = “Obese”

As in adults, since BMI does not directly measure body fat, research has shown that direct measurements — such as skin fold thickness, bioelectrical impedance, and dual energy X-ray absorptiometry — are needed to accurately classify obesity in non-adults(73). In youths, healthcare professionals must perform second-level assessments that measure fat and assess for the presence of metabolic alterations to identify children at increased cardiometabolic risk and/or those already showing signs of metabolic syndrome(74).

2. PHYSIOLOGY OF WEIGHT GAIN

The mechanisms that regulate weight, weight loss, obesity, the experiences of hunger and satiety, and other factors linked to weight are complex. They include, among other factors, several hormones and other incorporated factors The most relevant are described in the following paragraphs.

Adipocytokines are messengers of fatty tissue that play an essential role in people with obesity. Increased levels in pro-inflammatory adipocytokines lead to chronic general inflammation, atherosclerosis, thrombosis, T2DM, and arterial hypertension. Clinically-significant weight loss results in lower levels of pro-inflammatory adipocytokines, while anti-inflammatory adipocytokines increase (75).

Peptide YY (PYY) is produced by neuroendocrine cells in the terminal ileum and colon and plays an important role in the feeling of satiety. In persons with obesity, PYY is decreased, thereby causing patients to experience a permanent feeling of hunger (76).

Another important gastrointestinal hormone in patients with obesity is ***glucagon-like peptide (GLP-1*****),** which reduces appetite and stimulates insulin secretion while suppressing glucagon secretion and prolonging stomach emptying. These effects are used in GLP-1 agonists for the management of weight loss and treatment of T2DM(77).

Ghrelin, which is mainly produced in the stomach, leads to feelings of hunger and increased food intake. High levels of ghrelin increase cortisol, adrenaline, and growth hormone levels, while causing a simultaneous reduction in insulin secretion (78). Ghrelin and PYY act as short-term regulators of hunger and satiety, whereas long-term regulators — like **leptin** and insulin — affect energy storage and nutritional status.

In addition, the entire gastrointestinal microbiome and bile acids play important roles in the development of obesity. These systems are currently under intensive research and may play a future role in therapy to achieve more conservative weight loss and treat AHCs (79).

3. PREVALENCE OF OBESITY WORLDWIDE

Obesity has been termed a 21st century global epidemic(80). Worldwide, 2.2 billion people are living with overweight, with a body mass index (BMI) >25kg/m^2, or obesity, with a BMI

>30kg/m^2(81), with increasing rates of obesity covered extensively by the medical, scientific, and lay press in recent decades. One study of 1,698 population-based data sources, encompassing more than 19.2 million people in 186 countries, documented a linear increase in the average BMI from 1975 to 2014(82), the World Health Organization (WHO) documenting near tripling of the prevalence of obesity since 1975(83). Predictions are that, by 2025, the prevalence of obesity will reach between 1.0(84) and 1.5(81) billion people, with roughly 200 million meeting criteria for severe (Class II or III, see Table 2-2) obesity(84). This global increase in the prevalence of severe obesity is of particular concern, since those suffering from severe obesity (BMI greater or equal to 35 kg/m^2) have been identified as a subgroup with particularly high risk of comorbidities(83, 85, 86, 87) and reduced quality of life(88, 89). Worldwide, obesity has become one of the largest contributors to poor health and healthcare costs, with annual costs estimated as high as two trillion USD, equivalent to 2.8% of the world's gross domestic product (GDP) and equal to the costs attributed to smoking(90). According to the WHO, most of the world's population now lives in countries where overweight and obesity kill more people than being underweight(83).

Table 2-2: Classes of obesity in adults

Class I	BMI = 30-34.9 kg/m^2
Class II	BMI = 35-39.9 kg/m^2
Class III	BMI $\geq$ 40 kg/m^2

BMI = body mass index

4. TRENDS IN CHILDHOOD OBESITY

Perhaps even more concerning than the overall increased prevalence of obesity is the increased rate of childhood obesity, an increase that has paralleled the trend seen in adults. The global prevalence of overweight and obesity among children and adolescents ages 5-19 rose from 4% in 1975 to over 18% (or 340 million worldwide) in 2016(3). Concerning numbers also have been reported by the World Obesity Federation (2, 91), with an estimated 6.8% of children ages 5-19 affected with obesity and an estimated of 205.5 million children expected to be affected by 2025. In addition, the prevalence of obesity among boys, in particular those ages 12–17 years, was significantly higher than for adolescent girls (16.2% versus 9.3%). According to the WHO, over 340 million children and adolescents ages 5-19 were affected by overweight or obesity worldwide in 2016, while 39 million children under the age of five were affected in 2020(3).

Akin to what is seen in adults, childhood obesity is linked to numerous adverse physical and mental health outcomes, like steatohepatitis, type 2 diabetes, sleep apnea, cardiovascular diseases, and polycystic ovary syndrome(92, 93, 94). It is also linked to negative societal outcomes, including poor self-esteem, reduced academic performance, depression, and decreased quality of life(93, 94). In addition, the majority of adolescents with obesity will become adults with obesity(95), with severe obesity acquired at a young age of particular concern. In a survey conducted in the United States, young adults from 20 to 30 years of age who were affected by severe obesity (defined as a BMI $\geq 45 kg/m^2$) had a decreased life expectancy of five and eight years among black and white women, respectively, with 13 and 20 quality years of life lost for white and black men, respectively(96).

5. ETHNICITY AND GEOGRAPHIC ORIGINS OF OBESITY

The global and regional prevalence of obesity was evaluated in a large study using 1698 population-based data sources with more than 19.2 million adults participants from 186 countries(2). Over the past four decades, obesity has increased both globally and in all world regions, except certain parts of sub-Saharan Africa and Asia. Since 2000, the rate of increase in BMI has been slower than in the preceding decades in high-income countries and in some middle-income countries. However, because the rate of BMI increase has accelerated in other regions, the global increase in BMI has not slowed. This said, while obesity rates have increased in almost every region, the absolute prevalence of obesity differs significantly between regions of the world, the highest prevalence rates seen in the Middle Eastern and Western Pacific regions, where numbers of affected individuals in some areas exceed two out of every three people(97).

Other demographic factors have been identified – like age, sex, and ethnicity, as well as indigenous and immigration status – as predictors of obesity. Ethnicity appears to have a strong influence on the risk of developing obesity and some obesity-related diseases. In the United States, according to the Centers for Disease Control(98), non-Hispanic Black adults (49.6%) have the highest age-adjusted prevalence of obesity, followed by Hispanic adults (44.8%), non-Hispanic and White adults (42.2%), with Asian adults lagging considerably behind(17.4%). At the same time, the prevalence of type 2 diabetes in adults was the highest in Hispanics (12.5%) followed by non-Hispanic blacks (11.7%), Asians (9.2%) and non-Hispanic Whites (7.5%). A

WHO expert consensus panel concluded, in 2004, that Asians generally have a higher percentage of body fat than Caucasian people of the same age, sex, and BMI(99). The risk factors for type 2 diabetes and cardiovascular disease are, thus, substantial even below the standard BMI limit of 25 kg/m^2, varying from 21 to 26 kg/m^2 in different Asian populations. No attempt was made by the panel to redefine cut-off points for each population separately, however. The experts concluded that no single BMI threshold is adequate to universally justify taking action against risks related to overweight or obesity in many populations.

6. SOCIOECONOMIC FACTORS

On a regional level, obesity is no longer a concern of high-income countries only. Indeed, low- and middle-income countries have witnessed the highest rise in the prevalence of obesity over the last few decades. Many such countries now face the double burden of undernutrition and obesity in their population. In a survey of 685,616 individuals from 57 low and middle-income countries, the global prevalence of overweight was 27% and of obesity was 21%(100). A higher risk of type 2 diabetes also was observed at a BMI > 23kg/m^2, including a 43% greater risk of diabetes among men and 41% among women.

The costs of obesity and obesity-related disease are a significant threat to national and global healthcare systems. It is estimated that the direct cost of high BMI to health services globally is US$ 990 billion per year, which is over 13% of all healthcare expenditures(84). The exact cost is difficult to assess, however, when we consider the different components of cost specific to certain diseases and related diseases, costs to society in terms of lost productivity, costs to patients and their families, and costs to insurers and other payers. Several literature reviews have been published in an attempt to assess the global cost of obesity, but most authors consider obesity a single disease, not a risk factor. In a recent systematic review that analyzed 23 studies(101), every study revealed substantial economic burdens in both developed and developing countries. There was, however, a high level of heterogeneity in the studies' methodological approaches, in the populations studied and, in particular, in the obesity-related diseases and complications included in analysis. Among countries belonging to the Organization for Economic Co-operation and Development (102), combined direct and indirect healthcare costs have been estimated as approximately 3.3% of the total gross domestic product (GDP), a figure which is only expected to grow, impairing economic growth and national healthcare budgets(102). This accounts for 8.4% of total healthcare spending, or 425 billion per year for the 52 member countries within the OECD.

7. HEALTH RISKS OF OBESITY

a. Overview

The underlying causes of obesity are extremely complex. However, they ultimately lead to an energy imbalance between calories consumed and calories expended. Major societal and environmental changes cannot be ignored, leading to changes in dietary habits and physical activity. As stated above, other contributors to obesity include a person's sex and ethnicity, socioeconomic status, genetics, regional food, and built environments. A collaborative analysis of 57 prospective studies, including almost 894,576 patients, identified a direct correlation between baseline BMI and mortality. At 30-35 kg/m^2, median survival was reduced by 2-4 years and at 40-45 kg/m^2, by 8-10 years (comparable to the effects of cigarette smoking). Among multiple associated diseases, cardiovascular disease and cancer were among the two leading causes of premature death(103).

Obesity increases the risk of 13 different cancer types, including colon, kidney, esophageal and pancreatic cancers in both sexes and endometrial and post-menopausal breast cancers in women(104). It is estimated that 20% of all cancers can be attributed to obesity, independent of diet. Obesity also increases the risk of developing type 2 diabetes(6, 7, 8), cardiovascular disease(10, 11), the so-called metabolic syndrome(72, 105), liver disease(106, 107, 108), gallbladder disease(109, 110), pancreatitis(109, 110), sleep apnea(12, 13), and chronic kidney disease(14, 15), among other conditions. In addition, obesity is associated with functional limitations and psychological symptoms that adversely impact quality of life in both adults and non-adults(111, 112, 113, 114). It increases the risk of osteoarthritis nearly three-fold and negatively impacts mobility(115). It is also associated with increased risks of depression, anxiety, and reduced quality of life(111, 112, 113, 114, 116), among many other mental health conditions. For example, individuals living with obesity are twice as likely to be diagnosed with a mood disorder than individuals without obesity(116).

Excess body weight, defined using someone's BMI, is useful on a population level and has been shown to correlate with increased risk of mortality(117). As discussed above, mortality risk rates in Western European and North American populations appear to be lowest for men and women in the 22.5-25 kg/m^2 range, with each 5-point increase in BMI associated with a 30% increased risk in all-cause mortality(96). A similar relationship has been demonstrated in several large-scale studies independent of sex and ethnicity. In one meta-analysis of 239 studies that incorporated more than 10 million individuals across four continents, all classes (Class I-III) of overweight and obesity were associated with an increased risk of all-cause mortality in every region in the world, except for South Asia(118).

However, while useful at a population level, health professionals should not rely solely on a patient's BMI to predict their individual health risk. Rather, they should use it in conjunction with other existing assessment tools.

b. Mechanisms behind the increased health risk

The mechanisms behind the increased health risks associated with obesity appear to be multi-factorial. One mechanistic causative pathway that is well established is that the expansion of body fat results in both adipose tissue dysfunction and chronic inflammation; and that both of these, in turn, have consequences that adversely affect a person's metabolism, body mechanics, and social health(119).

The visceral expansion and spill-over of fat mass leads to altered homeostasis and organ dysfunction(25). However, overall, it is the distribution of visceral body fat, rather than fat quantity, which predominantly determines these metabolic and functional alterations(120).

The term *"adiposopathy"* refers to the concept of *"diseased fat"*, highlighting the pathogenic role that adipose tissue can have(121). Growth of visceral adipocytes exceeding the vascular support capacity of the adipose tissue, and the deposition of ectopic fat, are two anatomical manifestations of adiposopathy that have been linked to systemic responses that lead to metabolic disease(121, 122). Adiposopathy exerts numerous adverse effects on physical, metabolic, and psychological health, which include metabolic syndrome; respiratory disorders; joint pain; diabetic retinopathy; low self-esteem; cardiovascular, neurological, pulmonary, musculoskeletal, dermatological, gastrointestinal, genitourinary, and renal disease; various psychological disorders; and cancer(123).

In obesity, three progressive phases of metabolic disorder secondary to adiposopathy and inflammation have been recognized:

Prodromal phase: presence of peripheral fat expansion and low-grade inflammation, with some limitations of function, like joint stress and soft tissue compression(124, 125).
Intermediate phase: presence of adiposopathy and metabolic alterations due to lipotoxicity and the ectopic redistribution of fat in organs and muscles, causing dysfunctional alterations of adipose tissue and tissues affected by ectopy(126). At the same time, there is an increase in adipokines and inflammatory cytokines, accompanied by progressive metabolic inflexibility, insulin resistance, and increased oxidative stress. Possible manifestations in this phase are comorbidities linked to obesity — like type 2 diabetes, hypertension, and dyslipidaemia(127).
Final phase: presence of adiposopathy-related damage, moderate to severe inflammation, and the increased risk of cardiovascular events. Chronic expansion of visceral fat and ectopia cause severe inflammation and alterations in the cross-communication between adipose, muscle and bone tissue(127). Inflamed visceral fat also contributes to perpetuating intestinal dysbiosis, accompanied by alterations in intestinal microbiota(25).

Obesity is characterized by low-grade systemic inflammation, due to both the abnormal production of adipokines and the activation of pro-inflamed pathways. Indeed, levels of a broad range of inflammatory markers — such as C-reactive protein, IL-6, the IL-1 family [IL-1α, IL-1β and IL-1 receptor antagonist] and TNF- α — are increased in persons with obesity relative to lean individuals(128). The presence of inflammatory processes and the increased cytokine activity also increase the risk of chronic degenerative diseases and dementia(129). Furthermore, the presence of polymorphisms and allelic variants of cytokine genes are involved in obesity and related chronic degenerative diseases. Among the first genes activated with any harmful provocation are the genes for IL-6, IL-1, and TNF-α. These molecules activate each other, and both are fundamental components of the inflammatory process(60).

8. ECONOMIC IMPACT OF OBESITY

Obesity, defined as an abnormal or excessive accumulation of fat, has rapidly become a global health concern. This is largely because of its link to a number of comorbidities, including chronic diseases like type 2 diabetes mellitus, cardiovascular disease, and cancer(130). It also results in more frequent patient visits to general practitioners and hospitals(131). Since 1997, the worldwide prevalence of obesity has nearly tripled, with 39% of adults living with overweight and 13% living with obesity in 2016(132). If the incidence continues to increase at this rate, it is estimated that almost 50% of the world's population will be affected by overweight or obesity by 2030(133). The primary cause of obesity in the global community is increased energy-dense food consumption and reduced physical activity due to sedentary lifestyles(132).

Obesity places a large economic burden on individuals themselves, as well as on governments and healthcare systems. These costs may be direct or indirect. Direct costs include the costs of diagnosing and treating obesity, while indirect costs involve productivity losses due to morbidity and early mortality. At a personal level, obesity creates physical and social problems that reduce wellbeing and productivity. Accordingly, these costs reduce societies' economic growth through diminished productivity at work, lost work days, and increased disability(134).

The current literature contains several analyses of obesity's impact on the economy. A report by the McKinsey Global institute in 2014 estimated that the global economic impact imposed by obesity on the world economy was equivalent to $USD2 trillion, which is 2.8% of the world's gross domestic product (GDP)(133). Figure 1 depicts the total costs of obesity reported for different countries(135). Estimated direct and indirect costs to the United Kingdom's (UK) National Health Service (NHS) for treating overweight and obesity in 2007 were 4.2 billion and 15.8 billion pounds, respectively(136). Additionally, overweight and obesity accounted for 23% of all prescription costs in the UK, an excess of 2.94 billion pounds for medications, relative to what would be anticipated among individuals with a normal BMI(137). In two studies in Germany, the direct and indirect costs of obesity increased from €9.8 million in 2002 to €12.2 million in 2008(138, 139). In a separate study in Canada, obesity's impact on the economy amounted to $1 billion Canadian dollars(140). In Brazil, two other studies derived estimated costs of obesity to the economy as $1.1 trillion(141) and $269.6 billion USD(142). The differences between these studies may be partially due to the studies' heterogeneity in methodologies, cost analyses (including the types of cost that were estimated), and inclusion of comorbidities. Obesity costs consist of both direct medical costs for managing obesity and related comorbidities, and societal costs that impact the economy, due to increased unemployment and foregone productivity secondary to deteriorations in physical and psychological wellbeing(133, 134).

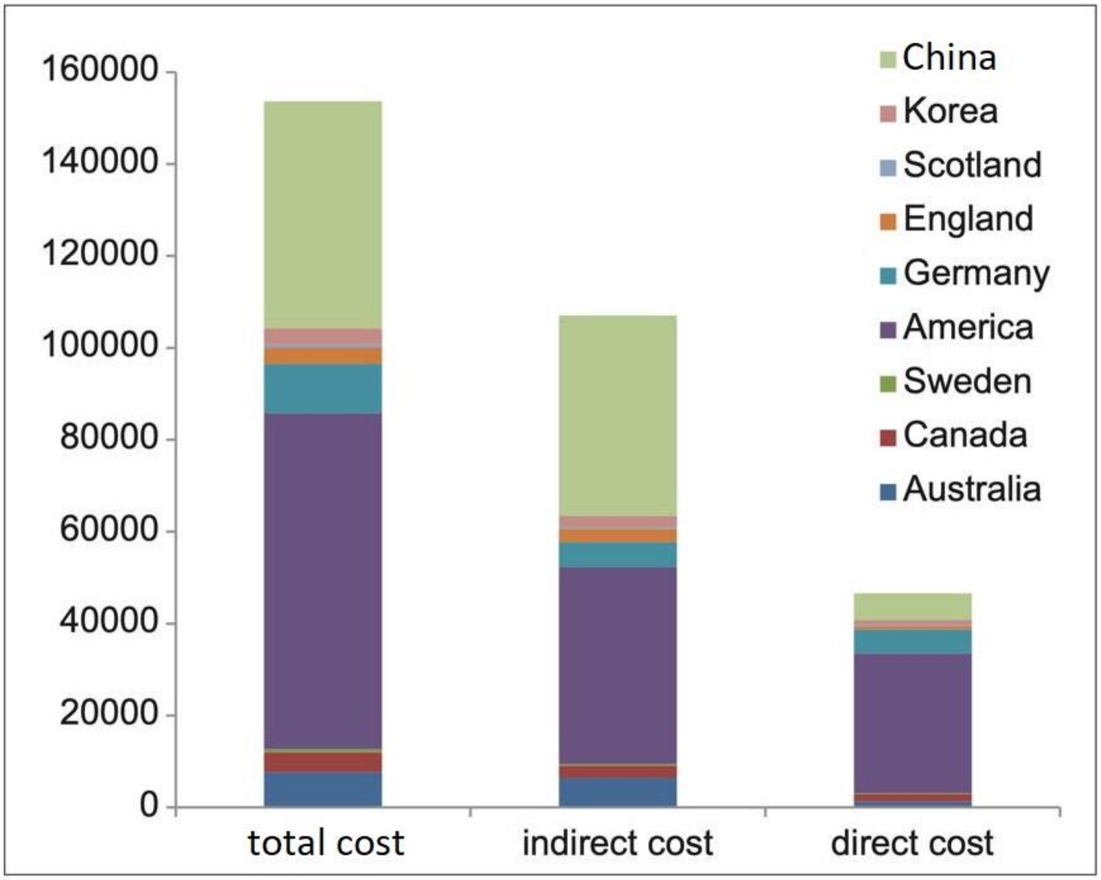


Figure 2-2: Total, direct, and indirect costs of obesity in different countries(135)

Despite these differences, it is unequivocal that obesity is responsible for a large percentage of the costs affecting national economies. A key principle of economic success is that decision making must include ensuring the efficient allocation of finite resources to maximise productivity. Such decisions involve minimizing opportunity costs and ensuring optimal cost effectiveness(143).

Bariatric surgery remains the gold standard treatment for severe obesity and has been consistently documented as efficacious and safe(144, 145). It also reduces the incidence of obesity-related comorbidities(146). However, bariatric procedures are not inexpensive. For example, the median cost of a sleeve gastrectomy, a popular bariatric procedure, was $10,531 USD in 2013(147). Despite these costs, in a 2019 meta-analysis, bariatric surgery was found to be a cost saving procedure over someone's lifespan, even when indirect costs are not considered, while also reducing annual direct costs(148). These results were consistent with a separate systematic review in 2018(149) and with five recently-published European modelling studies(150, 151, 152, 153), all of which documented bariatric surgery to be a cost effective and cost saving procedure relative to conventional (non-surgical) obesity management. Additionally, bariatric surgery was found to reduce the proportion of costs sustained for medications to treat comorbidities like diabetes and hypertension(148). A cost-utility analysis conducted in the United Kingdom revealed that bariatric surgery produced per-patient savings of €2742 (£1944) and provided an additional 0.8 life-years and 4.0 quality-adjusted life-years, the authors concluding that bariatric surgery can save the healthcare system significant funds in the long-term(150).

Of course, the global pandemic caused by SARS coronavirus-2 (COVID-19) has upended much of the success of obesity treatment, in multiple ways. First, it has diverted limited health resources away from "elective" treatments like bariatric endoscopy and surgery. Second, it has had major economic impacts on local, regional, and national economies, so that it may take considerable time for such diverted and, thereby, depleted resources to be restored. Globally, world output fell by 3.3% over the pandemic's first year, with advanced economies including the USA and Europe experiencing an average fall of 4.7% in their GDP(154). This said, less-economically-developed countries appear to have suffered the worst, as the budget allocated to the healthcare response to COVID-19 represents only 8% of pre-COVID-19 public spending on health in high-income countries, compared to 36% in low-income countries(155).Third, the need for social distancing, restricted services, and widespread lockdowns has prevented many persons with obesity from seeking treatment either to treat their obesity itself or related conditions, adversely affecting their health. Even routine healthcare services have been reduced(156, 157). This cost of such foregone care, especially for chronic diseases like hypertension and diabetes, is likely to increase long-term costs. Fourth, obesity has been shown to significantly increase an individual's risk of severe symptoms, hospitalization, and death related to COVID-19(158, 159, 160, 161).

At the start of the COVID-19 pandemic, the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) issued a series of recommendations. These recommendations included postponing all elective surgeries during the pandemic and rescheduling them for when the pandemic is over(162). Such postponements generate costs, however, including the costs of foregoing the treatment and management of obesity, the costs associated with managing obesity-related comorbidities, and the adverse psychological effects of treatment deferments on patients. Therefore, while the COVID-19 pandemic justly halted elective bariatric surgeries, efforts must now be made to prioritise bariatric surgeries in the post-COVID-19 era, especially since these surgeries are cost effective and save the healthcare system money in the long-term(150, 163).

In addition to reduced access to routine healthcare services for chronic diseases, strict social distancing regulations and lockdown laws combined with socioeconomic stressors and deteriorations in mental wellbeing may have other long-term consequences for obesity. Alongside several other societal obesogenic factors, increased socioeconomic stress and reduced mental wellbeing may lead to altered eating behaviours(164, 165, 166, 167), as well as to an increase in sedentary lifestyles. Thus, while COVID-19 regulations generally have been effective at reducing spread of the virus, they may be a risk factor for obesity and other associated metabolic diseases(168). This may further increase the demand for bariatric surgery and ultimately overwhelm financial resources as fiscal budgets struggle to accommodate this increased prevalence of obesity.

To summarize, overweight and obesity currently place a large economic burden on the global community, while bariatric surgery has repeatedly been shown to be a cost effective and cost saving treatment modality for obesity. Further studies are necessary to assess bariatric surgery as a cost avoidance measure to reduce the economic costs of obesity. This is especially true now, following a massive global pandemic, when the funds and resources needed to manage obesity-related comorbidities have been so severely restricted.

9. AREAS OF CONSENSUS

In the two-round Delphi survey conducted of 94 international, multi-disciplinary experts in obesity management, the following areas of strong consensus were reached pertaining to obesity definition, epidemiology, and risk factors (Table 2-3).

Table 2-3: Consensus reached on obesity's definition, epidemiology, and risk factors

Statement	Most common choice	% consensus
Since obesity is a major contributor to the global burden of chronic disease, disability, and healthcare costs, all medical societies should cooperate to address this problem systematically.	Agree	100.0%
Longitudinal national and regional surveillance of obesity, with measured data, should be conducted on a regular basis.	Agree	100.0%
Global rates of obesity are currently increasing in children and adolescents.	Agree	100.0%
Most children and adolescents with obesity grow up to have obesity in adulthood.	Agree	100.0%
Children and adolescents with severe obesity are at risk of significant obesity-related comorbidities, like type 2 diabetes mellitus, hypertension, etc.	Agree	100.0%
Obesity is a chronic disease, caused by abnormal or excess body fat accumulation that impairs health and increases the risk of premature morbidity and mortality.	Agree	97.9%
Ethnicity and geographical origins are important factors in the pathophysiology of obesity and metabolic diseases.	Agree	91.5%
	Agree	90.4%

Interventions for obesity and metabolic diseases should take the patient's ethnicity and geographic location into consideration.		

10. CONCLUSIONS AND RECOMMENDATIONS

Based upon our review of published scientific literature and the results of the IFSO/WGO Delphi survey, the following conclusions and recommendations pertaining to post-operative follow-up and outcomes are made:

Obesity is a chronic disease caused by abnormal or excess body fat accumulation that impairs health.

It is associated with increased risks of premature morbidity and mortality.

Rates of overweight and obesity continue to rise globally.

Obesity has become a leading cause of chronic disease, disability, and healthcare costs worldwide.

Even though the overall rates of overweight and obesity are rising globally, geographical origins and ethnicity are important factors to take into consideration.

Since ethnicity and geographical origins are important factors in the pathophysiology of obesity and associated diseases, interventions should take these specifics into consideration.

Longitudinal national and regional surveillance of obesity, using empirical data, should be done on a regular basis.

To stem the rising tide of obesity and its numerous complications and costs, healthcare providers, insurers, and public officials must work together to increase public awareness both about the adverse health risks associated with obesity and their potential amelioration with combined non-operative and operative therapy.

Healthcare providers, medical authorities, governments, and insurers should recognize and treat obesity as a chronic disease, using a multidisciplinary team approach similar to that used for other chronic diseases, like diabetes and cancer.

Since obesity is a leading cause of chronic disease, disability, and increased healthcare costs, all medical and public authorities should cooperate to address this problem systematically.

III. Obesity-associated co-morbid conditions

1. Introduction
2. Type 2 diabetes mellitus
3. Non-alcoholic (metabolic-associated) fatty liver disease (NAFLD/MAFLD)
4. Cancer
   - Overall cancer risk in patients with obesity
   - Hepatocellular cancer
   - Cholangiocarcinoma
5. Other common co-morbid conditions
   - Obstructive sleep apnoea
   - Venous thromboemboli
   - Urinary stress incontinence
   - Chronic renal insufficiency
   - Idiopathic intracranial hypertension
   - Other gastrointestinal disorders besides NAFLD and cancer
   - Osteoarthritis
   - Depression and other psychological disorders
6. Areas of consensus
7. Conclusions and recommendations

1. INTRODUCTION

Obesity has assumed pandemic proportions globally, with a number of countries now showing prevalence rates between 20 and 40%(169). It is a multi-factorial disorder based on combinations of genetic, behavioural, and environmental factors(170), and therefore requires a multi-disciplinary approach towards management. This includes alterations in lifestyle, a well-defined regimen of diet and exercise, limited use of weight-reducing medications and, finally, interventional therapies which include both endoscopic and surgical approaches. Such approaches require collaboration between a multitude of disciplines, including behavioural therapists, dietitians/nutritionists, physicians, endoscopists and surgeons.

One additional medical issue that is present in many, if not most, patients living with obesity is the co-occurrence of various co-morbidities that also must be kept in mind while deploying management plans for patients with obesity. For instance, patients may need to be evaluated for type 2 diabetes/pre-diabetes, cardiovascular disease, gastro-intestinal manifestations, and even certain cancers. Such assessments are not just to guide the management of whatever co-morbid conditions are identified, but also to aid in the planning of therapeutic options for the obesity itself. For example, the threshold for interventions may be reduced to a BMI ≥27 kg/m^2 in the presence of one or more co-morbidities, as opposed to the usual BMI threshold of ≥30 kg/m^2(171).

The current chapter deals with the identification and assessment of co-morbidities, followed by a discussion of the various treatment modalities that may be used to optimally deal with both the obesity itself and any co-morbid conditions that might exist.

2. TYPE 2 DIABETES MELLITUS

Obesity can be viewed as an epidemic of the 21st century, with a continuously-increasing number of individuals affected each year. Worldwide, 2.2 billion people are living with overweight with a body mass index (BMI) >25kg/m^2 or with obesity with a BMI >30kg/m^2(81). Overweight and obesity are the most common risk factors for the development of number of associated health conditions. These conditions not only adversely affect individuals; they also create significant challenges for healthcare systems around the world(85).

Among the various associated health conditions that obesity is directly associated with are type-2 diabetes (T2DM), arterial hypertension, obstructive sleeve apnoea, dyslipidaemia, non-alcoholic steatohepatitis (NASH), and various diseases affecting bones and joints. Overall, 425 million people have T2DM worldwide, with an estimated additional 50% of cases of diabetes undiagnosed(172). Multiple other diseases — such as coronary heart disease, hyperuricemia, cholecystolithiasis and several carcinomas — also are influenced by obesity(86). The associated health conditions associated with a high BMI are responsible for increased mortality in this population(81). Also, with increasing BMI, quality of life and life expectancy are reduced dramatically(173).

As will be discussed in much greater detail in Chapter VIII of these guidelines, there is now little debate that bariatric and metabolic surgery is currently the most effective long-term treatment for obesity and many of its associated health conditions. This is important both because in terms of decreasing health risks and increasing health-related quality of life. Evidence shows, for example, that much of the increase in quality-adjusted life years (QALYs) experienced following metabolic and bariatric surgery (MBS) are due to the substantially increased number of years that successfully treated patients will spend free of obesity-associated comorbidities(174).

That MBS is superior to non-surgical obesity management was one consensus conclusion of the Second Diabetes Surgery Summit (DSSII), held in 2015 in collaboration with leading diabetes organizations and endorsed by several international professional societies, including IFSO, following three rounds of Delphi voting(175). Based on this Delphi survey, conference attendees also concluded that MBS should be recommended as the treatment of choice for patients with T2DM and class III obesity and for patients with T2DM and class II obesity if hyperglycaemia is inadequately controlled with conservative therapy. They also concluded that MBS might also be considered in patients with T2DM and class I obesity if the patient's hyperglycaemia is inadequately controlled conservatively(175).

Such consensus is further supported by a steadily-growing body of published literature, which includes several high-quality randomized controlled trials (RCTs), which has consistently demonstrated the superiority of MBS at achieving sustained weight loss and reducing glycaemia and insulin resistance relative to both medical and dietary modifications(176, 177, 178, 179, 180, 181, 182).

Evidence further documents that reduced patient weight following MBS is linked to reduced micro- and macrovascular complications of diabetes(183), and that MBS is a more cost-effective treatment of T2DM than non-surgical management alone, with the cost-effectiveness of bariatric procedures even greater in patients with T2DM than among those without(184). For example, while the average cost per QALY gained from bariatric surgery ranges from approximately $5,000 to $10,000 USD(184), intensive conservative interventions intended to achieve glycaemic control cost approximately $41,384 per QALY(185). Thus, the initial cost of bariatric surgery is repaid early on from medications being discontinued, hospitalisations avoided, and complications avoided.

3. NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)/ METABOLIC-ASSOCIATED FATTY LIVER DISEASE (MAFLD)

Non-alcoholic fatty liver disease (NAFLD) is a common chronic progressive parenchymal liver disease with strong pathophysiological underpinnings to adiposity-based chronic disease or obesity. Although not uniformly adopted in medical literature, and to reflect its metabolic underpinnings, recent efforts have called for a nomenclature change to metabolic (dysfunction)-associated fatty liver disease (MAFLD). However, given that the term NAFLD is what has been used and continues to be used overwhelmingly in the medical literature, NAFLD is the terminology adopted here and elsewhere in these guidelines.

A strong connection can be found between overweight/obesity and nonalcoholic fatty liver disease (186) and nonalcoholic steatohepatitis (NASH). Both of these conditions have a major impact upon the regulation of carbohydrate metabolism, including glycogenolysis, gluconeogenesis, and the release of insulin. Both NAFLD and NASH also can progress to irreversible hepatic cirrhosis(187).

Non-alcoholic fatty liver disease (NAFLD) is defined by the presence of fatty liver (more than 5% steatosis) in the absence of excessive alcohol consumption or other causes of liver disease. In 2020, a group of experts reached consensus revisiting the current definition of fatty liver disease, including updating the nomenclature from NAFLD to Metabolic (dysfunction) Associated Fatty Liver Disease (MAFLD), introducing a simple set of “positive” diagnostic criteria for both adults and children(188, 189). Despite the expert panel achieving consensus on the name change, considerable controversy exists with this new concept, which may in the future undergo further changes. We will, therefore, discuss the prevalence of NAFLD, since most published epidemiological studies refer to NAFLD, rather than MAFLD.

a. Epidemiology

In one meta-analysis of 8,515,431 individuals from 22 countries, global NAFLD prevalence was estimated to be 25.2%, with the highest prevalence rates found in the Middle East and South America and the lowest in Africa(190).

Most important is the observation that the epidemiology and demographic characteristics of NAFLD vary considerably between countries and continents. These differences are due to the variable prevalence of risk factors that are modifiable, such as obesity and type 2 diabetes *mellitus (T2DM)*. In individuals with obesity, the estimated prevalence of NAFLD is 70%(191), while among those with T2DM, the estimated prevalence is 55.5%(192).

Although weight loss remains the main management strategy for NAFLD, in a recent study, only about half of those with NAFLD intended to lose weight, though the majority had the perception of being overweight. Persons who perceived themselves as being overweight or overweight/ obese were four times more likely to try to lose weight (adjusted odds ratios = 3.9 and 4.2, respectively, both $P < 0.0001$) than those who viewed their weight as within the normal range(193).

Interestingly, approximately 40% of those with NAFLD did not have obesity and almost one fifth were considered lean. In the general population, prevalence rates for non-obese and lean NAFLD are 12.1% and 5.1%, respectively(194). What is more disconcerting is that, in one study, patients with lean NAFLD had an increased risk of developing severe liver disease, relative to those with overweight NAFLD, after a mean follow-up of 19.9 years(195). In a retrospective study, Ye et al. found that 15-year cumulative all-cause mortality was 51.7% in individuals with NAFLD but without obesity versus 27.2% in those with both NAFLD and obesity and 20.7% in individuals without NAFLD(194).

The prevalence of NAFLD increases through middle-age, being highest in men between the ages of 40 and 65 years old. The prevalence and severity of NAFLD is higher in men than in women during their reproductive age; though, after menopause, NAFLD occurs at a higher rate in women(196).

The worldwide burden of NAFLD continues to increase, correlated with elevations in obesity rates in most countries. Now, it is the most common cause of liver disease worldwide in both adults and children, and one of the main causes of hepatic cirrhosis and indications for liver transplantation in Europe and the USA(197). Over the last ten years, NAFLD has been the most rapidly growing contributor to liver mortality and morbidity(198). It is also the fastest-growing cause of hepatocellular carcinoma (HCC) in the USA, France and the UK, with an estimated annual incidence of HCC that ranges from 0.5% to 2.6% among patients with non-alcoholic steatohepatitis (NASH)-related cirrhosis, while among patients with non-cirrhotic NAFLD its incidence is approximately 0.1 to 1.3 per 1,000 patient-years(199). From 2002 to 2016, there was an increase from 1.2% to 8.4% in the rate of liver transplantations performed in Europe for NASH-related decompensated cirrhosis(200).

Since NAFLD represents a serious healthcare problem, consensus statements and recommendations were recently published to provide a strong foundation for a comprehensive public health response(186), and it is of great importance that governments adhere to these recommendations.

b. Gut microbiota and NAFLD

By virtue of its anatomical location, the unique nature of its blood supply, and its critical metabolic and immunologic functions, the liver is strategically positioned to confront and interact with those microbes, microbial components, and products of microbe-gut interactions that traverse the gut barrier and gain access to the portal circulation(201). Conversely, liver disease or the shunting of portal blood through various collaterals so it bypasses the liver may have serious consequences.

The concept that an interactive, bi-directional axis exists between the gut and the liver is not new. Hints of an enterohepatic circulation of bile can be found in literature dating back to the 19^{th} century, albeit only clearly identified in the 1920s(202) and described in greater detail in the 1970s(203, 204).

The concept of a microbiota-gut-liver axis is also far from new. That the gut's microbiota is relevant to the natural history of liver disease was recognized over 60 years ago when relationships between gut bacteria, their metabolic products, and hepatic coma were first described(205, 206, 207). In these studies, the importance of coliforms was emphasized and these same bacteria and the inflammatory response that they evoke have since been incriminated in the pathophysiology of portal hypertension, as well as in such infectious complications of chronic liver disease as spontaneous bacterial peritonitis, systemic sepsis, and haemostatic failure(208).

Now, research efforts have also begun to focus on the possibility that gut microbiota may be fundamental to the pathogenesis of various liver diseases. Indeed, evidence continues to accumulate to support a role for the microbiota in alcoholic liver disease, non-alcoholic fatty liver disease (NAFLD), total parenteral nutrition (TPN)/intestinal failure-associated liver disease

(IFALD), and even in immune-mediated diseases like primary biliary cholangitis and primary sclerosing cholangitis(207, 209, 210, 211, 212, 213, 214, 215).

It is also interesting to note that the model that was developed to explain the pathophysiology behind hepatic encephalitis many years ago — specifically, the convergence of small intestinal bacterial overgrowth (SIBO) and/or an abnormal microbiota, impaired gut barrier function, a pro-inflammatory state, and the appearance in the systemic circulation of neuro-active molecules generated by bacterial metabolism — has become virtually ubiquitous as the template to explain the role of the microbiota-gut-brain axis in the pathogenesis of several liver diseases. The following players are considered key to the development and/or progression of several liver diseases, be they metabolic, inflammatory, or neoplastic in nature: the gut microbiome and its interactions with luminal contents (including those originating in our diet), the gut barrier, the mucosal immune response, and the metabolic and immune responses of the liver itself.

Changes in gut microbiota in liver disease: Historically, two alterations in gut microbiota populations have been described in individuals with liver disease or its complications: small intestinal bacterial overgrowth (SIBO) and changes in the faecal microbiome.

1. <u>Small Intestinal Bacterial Overgrowth (SIBO)</u>

A link between the gut microbiota and chronic liver disease was first reported by Hoefert over 80 years ago(209). To begin with, by virtue of well-documented changes in gut motility and transit, on one hand, and intestinal permeability, on the other, subjects with chronic liver disease are predisposed, first, to intestinal stasis and, second, to bacterial translocation from the gut lumen to the portal circulation(201, 207, 213, 216). It should come as no surprise, therefore, that SIBO has been shown to be common across a broad spectrum of chronic liver diseases(217, 218, 219).

Small intestinal bacterial overgrowth has also been demonstrated in NAFLD and NASH(217, 220, 221) and its role in the pathogenesis of steatohepatitis among some individuals who have undergone a jejuno-ileal bypass procedure for severe obesity has been well documented(222).

The major issue with SIBO is its very definition, since the techniques used to assess small intestinal bacterial populations — whether invasive like aspiration and culture or non-invasive and based on breath hydrogen analysis — lack sufficient reproducibility and accuracy(223).

2. <u>Quantitative and qualitative changes in the microbiota</u>

Studies using high throughput 454 pyrosequencing of the 16S ribosomal RNA variable region 3 (V3), followed by real-time quantitative polymerase chain reaction (qPCR) analysis of faecal samples, have identified changes in cirrhosis which have been linked to inflammation in the liver, as well as to disease severity and complications of liver disease – like hepatic encephalopathy, spontaneous bacterial peritonitis and bacteraemia(224, 225, 226, 227, 228).

Several mechanisms have been identified that appear relevant to the microbiota's involvement in the pathogenesis of NAFLD/NASH(217, 221, 229, 230, 231, 232, 233):

First, a role for gut microbiota and their metabolites in the pathogenesis of both obesity, *per se*, and metabolic syndrome has been identified.

Activation, by the microbiota, of pro-inflammatory cytokines (e.g., tumour necrosis factor α; TNFα), via Toll-like receptor (TLR) engagement, appears relevant to the progression from steatosis to NASH.

Complex interactions between inflammasomes and the microbiota might also play a role as a consequence of defective/deficient inflammasome sensing, intestinal microbial population change leading to translocation, and the appearance of increased amounts of bacterial products (microbial- or pathogen-associated molecular patterns - MAMPs or PAMPs) in the portal circulation; all are substances with known links to the progression from NAFLD to NASH.

The roles of bile acids: The focus on bile acids has traditionally related to their critical role in fat and fat-soluble vitamin digestion. It is now clear, however, that bile acids have several other physiological functions. These not only include local effects on gut motility, sensation, fluid secretion and permeability, but also signalling/hormonal effects that impact several targets and cell types and influence such activities as energy expenditure, insulin sensitivity, and lipid metabolism(234, 235, 236). Through the activation of farnesoid X receptor (FXR) in the intestinal epithelium, bile acids promote intestinal protection and gut barrier and gut vascular barrier integrity and prevent the development of potentially-pathogenic microbiota(234).

The gut barrier and mucosal immune response: Various definitions have been applied to the term 'gut barrier'. Some definitions limit it to the single-cell thick epithelial layer; others incorporate all elements that contribute to gut defence and integrity. The latter include the commensal microbiota and mucus layer, the columnar epithelium itself, the lamina propria along with its constituent blood and lymph vessels, immune cells, and both intrinsic and extrinsic nerve terminals.

A number of factors relevant to the pathogenesis of liver disease can disrupt gut-barrier integrity (Table 3-1). These include ethanol, inflammatory mediators like interferon gamma and TNFα, proteases released from mast cells and neutrophils, and a number of drugs(237). It has been postulated that an overgrowth of gram-negative bacteria, allied to impaired gut barrier function, allows whole organisms – through a process called *translocation* – and/or the gram-negative bacterial component lipopolysaccharide (LPS), endotoxins and other bacterial products to gain access to the portal system(238). While translocation has been repeatedly demonstrated in a host of animal models, its demonstration in man has proven much more challenging due, in large part, to the limitations of currently-available assays(239).

The immune response in the liver: In liver disease, an overgrowth of gram-negative bacteria, allied to impaired gut barrier function, allows whole organisms, through the process called translocation, and/or lipopolysaccharides (LPS) to gain access to the portal circulation(237). In the liver, they then activate the inflammasome complex, resulting in a cascade of pro-inflammatory cytokine production which ultimately leads to liver injury and may be especially important in the progression from steatosis to steatohepatitis and, ultimately, to fibrosis(240).

Summary: While many details remain to be resolved and more work in humans rather than in animal models needs to be performed, a framework incorporating the gut microbiome, the gut barrier, and the immune responses in the intestinal mucosa and the liver has emerged to explain how microbes in the gastrointestinal tract might play a role in the pathogenesis of NAFLD.

c. Current Medical Treatment of Non-Alcoholic Fatty Liver Disease

Current medical treatment for NAFLD is essentially dependent on life-style interventions and modifying the various components of metabolic syndrome: obesity, type 2 diabetes mellitus, insulin resistance, dyslipidaemia, and hypertension. Drug development for NAFLD has been hampered by the condition's heterogeneity, leading to lack of agreement on hard end-points, as well as a relative lack of good biomarkers that could act as surrogate end-points for use in clinical trials.

<u>Life-style changes</u>: diet and exercise: Lifestyle modification, including significant weight loss through hypocaloric diet consumption and exercise, is considered a first-line intervention for NAFLD, as weight loss is associated with reduced liver fat, which can reverse disease progression(241). Among patients with non-alcoholic steatohepatitis (NASH, an aggressive form of NAFLD associated with hepatic inflammation and fatty deposition), weight loss exceeding 5% total body weight (TBW) can decrease hepatic steatosis, weight loss over 7% TBW can lead to NASH resolution, and weight loss greater than10% TBW can result in either regression or stabilization of fibrosis(242). Clinically-significant weight loss generally requires a hypocaloric diet targeting 1200–1500 kcal/day or a reduction of 500–1000 kcal/day from baseline.

Adults with NAFLD should follow the Mediterranean diet or a diet of similar design and minimize saturated fatty acid intake, specifically red and processed meat. They also should minimize their consumption of commercially-produced fructose-containing products. The Mediterranean diet can reduce liver fat even without weight loss, as it mobilizes fat from hepatic, cardiac, and pancreatic fat deposits(243).

The effects of specific hypocaloric diets — such as low-carbohydrate/high-protein diets, meal-replacement protocols, intermittent fasting, and vitamin supplementation — on histologic NASH end points have not been adequately studied. Therefore, none of these dietary interventions can be recommended as a superior regimen relative to any other, for weight reduction and fat mobilization from the liver.

Even though weight reduction seems the major intervention of benefit in the treatment of NAFLD, sustaining this is the major challenge for which a carefully-conceived and locally-relevant multi-disciplinary approach is needed to maintain motivation, including regular follow-up meetings with patients and employing online resources for health maintenance(244).

Regular physical activity should be considered for patients with NAFLD with a target of 150–300 minutes of moderate-intensity or 75–150 minutes of vigorous-intensity aerobic exercise per week(245). Although resistance (anaerobic) exercise has been considered less effective than aerobic exercise in NAFLD, a recent systematic review suggested that both aerobic and resistance exercises reduce hepatic steatosis equally in NAFLD, while resistance exercise does this with less energy consumption(246). Resistance exercise may, therefore, be more feasible than aerobic exercise for NAFLD patients with poor levels of fitness(246).

<u>Drug Therapy</u>: Drug therapy is indicated for patients who either show evidence of disease progression to bridging fibrosis/cirrhosis or have factors which increase the risk of fibrosis progression, like age >50 years, type 2 diabetes mellitus, or raised serum alanine transaminase (ALT) levels(247). However, no drug therapy is currently approved by the FDA for the treatment of NAFLD/NASH, although a number have been tested in clinical trials and others are currently being tested. The following drug categories have been tested, with the following results:

Insulin Sensitizers: Use of the anti-diabetic drug pioglitazone, when tested against vitamin E and placebo in the PIVENS (Pioglitazone versus Vitamin E) trial, has been linked to improvements in all histological features associated with NAFLD, except fibrosis(248). It also lowered serum ALT levels and partially corrected insulin resistance. Several other studies and a meta-analysis bear out these beneficial effects of pioglitazone(249). However, several side effects of concern were noted in some patients, including weight gain, fluid retention, congestive heart failure (albeit rare), and a small increase in bone fracture rates, particularly in women. This drug has, therefore, not found great favour for the treatment of NAFLD.

Anti-oxidants and cytoprotective agents: Vitamin E, at a dose of 800 IU/day, also was linked to improvements in various liver histology features, including NASH resolution in some patients, in the PIVENS trial(248). This, and other trials, have resulted in the fairly wide-spread use of vitamin E in NAFLD patients, particularly among those with raised alanine transferase (ALT) levels. In one recently-published meta- analysis, vitamin E was found to decrease the risk of death or liver transplantation (as a composite outcome), as well as hepatic decompensation, in patients with metabolic steatohepatitis associated with bridging fibrosis or cirrhosis(250). However, safety concerns must be kept in mind and discussed with the patient before its use. These concerns include an increased incidence of haemorrhagic strokes, as well as of prostate cancer in men older than 50 years old. In clinical practice, these issues usually result in limiting the continuous use of vitamin E to no more than six months, especially if no substantial reduction in transaminase level is observed.

One potentially promising drug, obetocholic acid, which is a farnesoid X receptor agonist, has been shown in clinical trials to improve all histological changes of NAFLD, as well as insulin resistance(251). However, safety and tolerability issues — like increased LDL cholesterol levels and significant pruritis in some patients have resulted in this drug not yet being approved by the FDA.

GLP-1 agonists: Glucagon-like peptide-1 (GLP-1) receptor agonists — such as liraglutide and semaglutide — may have multiple positive effects on NAFLD, which include weight loss, improved blood sugar and lipid levels, and enhanced cardio-vascular outcomes(252, 253). These positive benefits have also been borne out in the results of a recent meta-analysis(254). Both drugs are administered as a subcutaneous injection: liraglutide as a daily dose of 1.8mg and semaglutide 2.4mg once weekly. Side effects may include gastrointestinal symptoms like reduced appetite, nausea, vomiting or diarrhoea in the initial stages, all of which commonly settle down fairly quickly in most patients with continued use. Theoretical concerns were expressed by the authors of the meta-analysis about the potential for an increased incidence of pancreatic cancer, though this has not yet been confirmed empirically in clinical practice.

In clinical practice, GLP-1 agonists are currently considered for use in diabetic patients who also show evidence of NAFLD. However, there also have been positive results published in patients with NAFLD who lack diabetes. This said, the need for injections and the expense of therapy with GLP-1 agonists is a concern in some geographic regions that may preclude their wider use as therapy for NAFLD.

Other medications: Statins do not impact liver fat, but do have cardiovascular benefits in NAFLD patients(255). Ursodeoxycholic acid, although often used, has no demonstrated beneficial effect in NAFLD patients.

Endoscopic and surgical approaches to NAFLD:

As explained in Sections VII and VIII, on the use of endoscopic metabolic and bariatric therapy (EMBT) and metabolic and bariatric surgery (MBS) to treat NAFLD, lifestyle changes and medications frequently fail to induce enough weight loss to reverse either NAFLD or NASH, while considerable therapeutic success has been documented for both EMBT and MBS. Further specifics on the application and effectiveness of these two procedure-based approaches are provided in those two, later sections: on EMBT in Section VII and on MBS in Section VIII.

Monitoring progress and response to treatment: To date, there is no consensus on the optimal strategy for monitoring patients with NAFLD and their response to treatment. Asian-Pacific

Association for Study of Liver clinical practice guidelines recommend that patients with fibrosis be monitored annually by combining non-invasive scores and some measurement of liver stiffness, while those with cirrhosis should be monitored at 6-month intervals, including surveillance for hepatocellular carcinoma(245).

4. CANCER

a. Overall cancer risk in patients with obesity

The prevalence of obesity continues to grow in the US, as does awareness about its associated co-morbidities. The literature is rich in publications that highlight the implications and dramatic diseases associated with the current steady worldwide increase in the prevalence of obesity(169). A major source of concern with this increasing prevalence are the numerous potential adverse outcomes triggered by obesity-associated comorbidities(256, 257). In a survey of non-medical community members conducted by the American Society of Metabolic and Bariatric Surgery (ASMBS) and the Nutrition Obesity Research Centers (NORC) in 2016, 94% of those surveyed perceived that obesity, on its own, increases the risk of early death, even when no other diseases are present, tying cancer as the most concerning health issue(258).

Patients with obesity have been shown to be at increased risk for eleven different cancers. They include oesophageal adenocarcinoma, as well as cancers of the colorectum, endometrium, ovaries, kidneys, and pancreas. Hence, screening for cancer is required in patients considering MBS, though the nature and scope of screening depend on each individual patient. For example, a screening colonoscopy is recommended for patients who are over 45 years of age or have family history of colon cancer; screening for prostate cancer is recommended in all men over the age of 50 years; and an upper endoscopy is required in patients with dysphagia(259). Similarly, patients with severe obesity and Barrett's esophagitis are at a higher risk of oesophageal cancer and should typically, preferentially undergo Roux-en-Y gastric bypass, as this procedure can reduce reflux and may halt the progression of Barrett's esophagitis(260, 261).

The effects of both obesity and adipose tissue on carcinogenesis have been studied extensively(262, 263, 264, 265). The International Agency for Research into Cancer (IARC) has determined that overweight and obesity are associated with elevated risks of developing various types of cancer. Despite the multifactorial aetiology of cancer, there is sufficient evidence to suggest a causative association between excess body fat and at least 13 different cancers(266).

Thus far, the malignancies most commonly attributed to excess body fat, particularly in patients with metabolic syndrome, are adenocarcinoma of the oesophagus, postmenopausal breast malignancies, renal cell carcinoma, cancers of the endometrium, gallbladder, stomach, ovary, thyroid, and colorectum, and multiple myeloma(267). In a 10-year review that analysed the link between obesity and cancer, published by the Centers for Disease Control (CDC) in 2017, obesity was associated with at least 55% of cancers diagnosed in women and 24% in men(267). In another study, obesity was found to be associated with 15 to 20% of all cancer-related mortality(19).

The pathophysiological explanation for the carcinogenic effect of excess adiposity is based on the induction of metabolic and endocrine changes, including increases in inflammatory markers, insulin, sex hormones, and insulin-like growth factor(268).

Our understanding of the underlying mechanisms of this obesity-cancer relationship continues to evolve. Three biological systems — (i) insulin and insulin-like growth factors, (ii) sex hormones, and (iii) adipokines — have been extensively linked to cancer development(269, 270, 271, 272, 273). More recently, other potential influences on the association between carcinogenesis and fat excess have been identified, as well; they are obesity-related hypoxia, shared genetic susceptibility, and migrating adipose stromal cells(265).

This recent growth in evidence linking obesity and cancer, in combination with the continued rise in the obesity epidemic, may be contributing to the reported increase in the number of bariatric surgery procedures being performed. The latest report on bariatric surgery and endoluminal procedures, published by the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO), describes this global increase in bariatric surgery and states that, of the various bariatric procedures, sleeve gastrectomy is currently the one most frequently performed worldwide(26). This surge in popularity of bariatric surgery might be due to the proven safety of bariatric interventions and their effectiveness in inducing weight loss, as well as additional benefits (e.g., improvements in obesity-linked comorbidities like diabetes mellitus and hypertension, quality of life and overall wellbeing) seen following bariatric surgery. The high rate of resolution of obesity-related comorbidities has resulted in long-term positive therapeutic outcomes. It is for this reason that bariatric surgery has now become the standard of care for treating obesity and its metabolic implications(26, 27, 28).

In a systematic review and meta-analysis of controlled studies that evaluated the incidence of cancer following bariatric surgery in 52,257 patients, the authors concluded that bariatric surgery significantly reduced the risk of cancer, lowering the incidence of cancer by 1.1 cases per 1000 person-years. Additional meta-regression analysis identified an inverse relationship between presurgical body mass index (BMI) and cancer incidence following surgery (beta coefficient = -0.2, $p<0.05$)(274).

Other studies have further reiterated the beneficial effects of weight loss on cancer risk reduction after bariatric surgery. A retrospective case-control study of 18,355 patients undergoing bariatric surgery determined that the average amount of weight loss one year postoperatively was 27% among patients who had undergone bariatric surgery versus 1% in matched nonsurgical patients. Percent weight loss at one year was, in turn, significantly associated with reduced overall risk of cancer in an adjusted model (hazard ratio, HR = 0.897, $p=0.005$), though bariatric surgery itself was not a significant independent predictor of cancer incidence(265). Another large multisite case-control study by Schauer et. al. at five sites within the Kaiser Permanente Healthcare System of an overall population of 88,625 patients revealed 2543 incident cancers after a mean follow-up of 3.5 years(275). When the bariatric surgery and non-surgical groups were compared, patients who underwent bariatric surgery had a 33% lower hazard of developing any cancer over the course of follow-up ($p<0.001$), and this reduction was even greater when analysis was restricted to obesity-associated cancers ($p<0.001$). When sub-classified into obesity-associated cancers, the risks of postmenopausal breast cancer, colon cancer, endometrial cancer, and pancreatic cancer were each significantly lower among those who underwent bariatric surgery ($p<0.001$; 0.04; 0.001; and 0.0.04, respectively).

There is no doubt that rapid weight loss after bariatric surgery has a beneficial effect in decreasing the subsequent risk of cancer(276, 277, 278, 279, 280, 281, 282, 283, 284). The relationship between telomere length and cancer is now viewed as one of great importance(285, 286). Telomeres are the ends of chromosomes that are made of non-coding DNA and serve to protect the chromosome from damage. Telomeres typically shorten with advancing age and in some disease states. Carulli and his associates have demonstrated a direct correlation between weight loss and telomere length — the greater the weight loss, the greater the increase in telomere length(287). Moreover, Dersham’s group documented telomere lengthening after bariatric surgery for up to five years after the procedure(288). Taking these observations into account, most authors have hypothesized that the protective effect rendered by telomere lengthening following bariatric interventions is a potential explanation for the reduced cancer risk.

The above-mentioned findings are not only of research and academic interest, but rather, have direct clinical implications. It is essential that policy makers and the general population become aware of the link between obesity and cancer, and how cancer risk is lessened by metabolic surgery. Though further, population-based research remains necessary, if more people start losing weight through metabolic surgery, such reductions in weight might have the effect of preventing the development of cancer in many patients already at higher risk because of their excess weight, reducing the impact of cancer at both a personal and societal level.

b. Hepatocellular cancer

Hepatocellular carcinoma (HCC) is the most common primary cancer of the liver. The number of new cases in 2015 increased by 75% relative to 1990 and, currently, HCC is the sixth most common cancer and third leading cause of cancer-related death worldwide(289). Ninety percent of HCC cases arise in the context of liver cirrhosis, mainly due to chronic hepatitis virus infections and heavy alcohol drinking(290). However, the implementation of hepatitis B virus (HBV) and hepatitis C virus (HCV) eradication programs, combined with the modern epidemic of lifestyle-related diseases such as obesity, hypertension, dyslipidaemia, and type 2 diabetes mellitus, has led to an increase in the incidence rate of HCC linked to non-alcoholic fatty liver disease (186). Indeed, there is clear evidence of a constant rise in HCC incidence, which is commonly attributed to the parallel increase in NAFLD(291). Nowadays, NAFLD has become a dominant factor in hepatic cirrhosis and HCC and is the second leading indication for liver transplantation in the United States(292). The risk of HCC in cirrhotic patients is estimated to range between 1% and 3% per year(293). However, it is important to note that HCC can also develop in the absence of cirrhosis, a phenomenon that appears frequently in patients with NAFLD(294).

Metabolic syndrome and hepatocellular carcinoma: The association of HCC with type 2 diabetes, obesity and hypercholesterolemia is well established(295). Increasing severity of obesity has been linked to increased risks of advanced liver fibrosis and HCC. With a body mass index (BMI) greater than 30 kg/m^2, the risk of cancer almost doubles; while with a BMI higher than 35 kg/m^2, it increases to almost fourfold the rate seen in non-obese individuals. Similarly, type 2 diabetes mellitus is associated with an increased HCC risk, with the strongest association observed in patients with greater disease duration and in those with an increasing number of metabolic abnormalities. Dyslipidaemia is another well-established risk factor for NAFLD, and recent data suggest a possible association between hyperlipidaemia and HCC incidence.

Obesity is often seen in individuals with HBV, HCV, or alcoholic liver disease and is considered an additional HCC risk factor. In one population-based study, obesity (body mass index >30kg/m^2) was associated with a 4.13-fold risk of HCC in anti-HCV positive individuals and a 1.36-fold risk in HBV-infected patients, compared to those with a normal body mass index (<23kg/m^2)(296). Furthermore, when obesity and diabetes were present together, the combination caused more than a 100-fold increased risk of HCC in both HBV and HCV-infected patients relative to those with no such factors, suggesting a possible synergistic effect of metabolic factors and viral hepatitis. In a retrospective analysis conducted in the United States on explanted livers, obesity was also an independent predictor of HCC in patients with alcoholic cirrhosis(297). Another large, prospective study has highlighted the role of obesity in patients with HCC arising in the context of liver diseases caused by other aetiologies, with metabolic risk factors present in up to two-thirds of patients with HCC(298).

Altogether, these data confirm that metabolic syndrome is an important player in the development of HCC.

Pathogenesis of hepatocellular carcinoma: The development of HCC in the context of NAFLD, especially in the absence of cirrhosis, is poorly understood. Chronic inflammation, hyperinsulinemia, adaptive immune responses, hepatic progenitor cell populations, and genetic susceptibility may all play a role in HCC occurrence.

Both obesity and insulin resistance may contribute to HCC development through systemic inflammation and the promotion of oncogenic pathways(299). Effectively, adipose tissue is not only recognized as a reservoir for excess energy, but also as an endocrine organ – since it produces adipocytokines that trigger chronic low-grade inflammation in several organs of the body. Excessive adipose tissue and dysfunction dysregulate adipokine secretion, which contributes to a variety of pathological processes, resulting in obesity-related liver cancer. In addition, increased hepatic lipid storage leads to lipo-toxicity, endoplasmic reticulum stress, and reactive oxygen species-mediated DNA damage. Aberrant DNA damage repair responses may contribute to a permissive environment in which acquired genetic mutations promote HCC development. Furthermore, excess triglycerides and free fatty acids have been shown to inhibit autophagy, again leading to increased cellular stress and DNA damage(300).

The influences of gender, genetic polymorphisms, and altered gut microbiome are also becoming apparent, with the prevalence of HCC higher in men with proportional differences that vary depending on the underlying aetiology(301). A combination of sex hormones and adiponectin production, biological factors like MyD88-dependent interleukin-6 production, and behavioural factors, like smoking, likely contribute to this condition. Moreover, recent data suggest that genetics accounts for approximately half of the interindividual variability in all spectrums of NAFLD. Variations in liver regulatory genes — such as PNPLA3, TM6SF2 and MBOAT7 — are believed to play a key role, not just in NAFLD progression, but also in determining the risk of developing HCC(302). Microbiome dysbiosis is another important factor in NAFLD progression, with some species more prevalent in these patients and having suspected roles in hepatocarcinogenesis. Animal models support a contribution from the gut, with increased intestinal permeability and leakiness potentially promoting the translocation of lipopolysaccharide to the liver, exacerbating inflammation, and driving disease progression and NAFLD-HCC(303).

Hepatocellular carcinoma surveillance: Screening for HCC is currently recommended for all patients with cirrhosis or advanced fibrosis, and should consist of abdominal ultrasounds every six months, with or without alpha-fetoprotein measurements(304, 305). Indeed, in patients who have a good acoustic window, ultrasound is both highly accurate and cost-effective for the detection of HCC. Nevertheless, surveillance in patients with NAFLD is often suboptimal, with up to 52% of HCC cases not diagnosed by screening and presenting with liver-related complications instead(306). The failure of surveillance in this population can be attributed to a number of factors. First, in patients with NAFLD cirrhosis, abdominal ultrasounds are not as sensitive as an early detection tool, relative to other aetiologies, since the presence of fatty liver disease and obesity hampers its performance(307). One retrospective cohort study of patients undergoing ultrasound surveillance for cirrhosis found that patients with obesity had a 3–8-fold higher risk of having an inadequate examination, with increasing BMI associated with a higher risk of missing HCC(308). The option of surveillance with computed tomography (CT) or magnetic resonance imaging (MRI) has been considered for such patients, although the cost-effectiveness of either approach would be impractical if applied to all-comers. Therefore, the use of either CT or MRI to screen for HCC should be restricted to those whose ultrasound is deemed of low quality.

Second, in many individuals with NAFLD, the presence of cirrhosis is only apparent at the time of HCC diagnosis, which is why the opportunity for surveillance and early-stage detection is missed(307). Finally, there is the potential for HCC to arise in non-cirrhotic livers, with nearly half of patients with NAFLD-related HCC estimated not to have significant liver fibrosis. Even so, the incidence of HCC in noncirrhotic individuals is considered insufficient to justify routine screening in such patients, considering the very high prevalence of NAFLD in the general population(309).

Thus, timely diagnosis of HCC arising in individuals with NAFLD is a true challenge for hepatologists and obesity makes it even more difficult.

Hepatocellular carcinoma prognosis: Patients with NAFLD-related HCC should be treated based upon their BCLC stage(310). Notwithstanding this, recent data indicate that patients with NAFLD-HCC generally have a worse prognosis than those whose HCC has been attributed to some other aetiology(311, 312). One contributory factor is NAFLD-HCC generally being diagnosed at a more advanced stage of disease, due to either ineffective or absent surveillance. In addition, this population is often older and has more co-morbidities, limiting the use of curative treatments. Indeed, only a relatively small proportion of NAFLD-HCC patients undergo liver resection or transplantation.

Obesity is also associated with reduced survival in HCC patients. In one study, published by Calle et al, the relative risks of liver cancer-related mortality in patients with a BMI between 30 and 34.9kg/m^2 and in those with a BMI greater than 35kg/m^2 were 1.9 and 4.5 times those of normal-weight individuals, respectively, independent of the underlying aetiology of the liver disease(19). Obesity also may have a negative impact on outcomes after HCC treatment. In a retrospective cohort of HCC patients who underwent orthotopic liver transplantation, a BMI higher than 30kg/m^2 was predictive of HCC recurrence, microvascular invasion, and poor overall survival, doubling mortality risk after transplantation(313). Similarly, another study analysing a cohort of HCC patients revealed lower survival rates in patients who are affected by either overweight or obesity undergoing hepatectomy for recurrent HCC, relative to those with a normal BMI(314).

Possible interventions to reduce hepatocellular carcinoma risk: Weight-loss interventions are strongly recommended to improve NAFLD-related outcomes. Given the strong association between obesity and HCC, every intervention aimed at reducing BMI should decrease the risk of HCC development. A growing body of evidence also shows that a healthy lifestyle can reduce the risk of cancer overall. Good adherence to a Mediterranean diet has been associated with a 50% reduction in HCC incidence(315). Similarly, recent studies have demonstrated that physical activity can also lower the risk of different cancers, including HCC(316). Optimal management of diabetes and dyslipidaemia is also recommended for their established cardiovascular benefits, as this also may reduce the risk of development HCC(317, 318). This said, large randomized controlled trials remain necessary to examine the role of specific antidiabetic and lipid-lowering therapies and their role as chemo-preventative agents for reducing cancer risk. Bariatric surgery has been shown to induce the total resolution of NASH and fibrosis in roughly 85% and 33% of patients, respectively, after one year of post-operative follow-up(319). Although currently-available data remain insufficient, it can be speculated that adopting a surgical approach to weight loss could aid in reducing the future risk of HCC in patients with obesity.

c. Cholangiocarcinoma

Cholangiocarcinoma is a malignant tumour that arises from bile duct epithelia and is the second most common primary liver cancer after HCC. Several factors — including primary sclerosing cholangitis, HBV, and parasitic infections — are strongly associated with cholangiocarcinoma development(320). On the other hand, contrasting data are available on any potential association between obesity and this tumour. Nonetheless, when studies are limited to intrahepatic cholangiocarcinoma, results reveal a more consistent association, with some authors identifying obesity as an independent risk factor for the development of intrahepatic cholangiocarcinoma. In a population-based study conducted in the United Kingdom, patients with obesity (BMI $\geq$30kg/m^2) had 1.5 times the risk of cholangiocarcinoma than those with a BMI <25kg/m^2(321). Leptin can promote cell growth via its receptors, which are found in both normal and cancerous cholangiocytes. Other pro-inflammatory cytokines from adipose tissue, like interleukin-6, can also stimulate several intracellular pathways that support the survival and growth of cancerous cholangiocytes. These mechanisms might explain how obesity promotes the development of cholangiocarcinoma. Nevertheless, data available on obesity remain too limited to definitively confirm this association and more extensive studies are needed.

Similarly, whether NAFLD is a risk factor for cholangiocarcinoma remains unknown. It is biologically plausible that NAFLD promotes cholangiocarcinogenesis directly through the induction of hepatic inflammation or indirectly via cirrhosis. Cirrhosis, itself, has recently been recognized as a risk factor for cholangiocarcinoma. One meta-analysis has identified NAFLD as associated with a significantly-increased risk of cholangiocarcinoma, this risk more pronounced for the intrahepatic versus extrahepatic subtype of this cancer (OR = 2.22 vs. 1.55)(322). This finding is consistent with other studies that have revealed an association between intrahepatic cholangiocarcinoma and chronic liver disease. Even so, as with numerous other conjectures previously posed in the current chapter, further studies to confirm this association remain necessary.

5. OTHER OBESITY-RELATED CONDITIONS

Numerous other co-morbid conditions have been definitively linked to obesity, and it is beyond the scope of this report to mention them all. Among the more common and problematic are:

a. Obstructive sleep Apnoea (OSA):

Patients with obesity are at significant risk of developing OSA, but many patients are unaware of both what OSA is and whether or not they have it(323). In a large, prospective, multicentre study funded by the United States National Institutes of Health (NIH), OSA was identified as one of the factors that increase the rates of morbidity and mortality after metabolic and bariatric surgery (MBS). In addition, OSA may increase the risk of anaesthesia-related complications at the start of, during, and after MBS(324). For all these reasons, it is important for patients considering MBS to be screened for OSA.

One of the most sensitive non-invasive validated OSA screening tools for patients with obesity is the STOP BANG questionnaire, a simple, eight-item questionnaire that can be completed in the doctor’s office(325). Patients who meet four or more of the criteria listed on the STOP BANG tool have greater than an 80% likelihood of having OSA and warrant referral for a sleep study. Once OSA is confirmed in a sleep study, patients require a continuous positive airway pressure (CPAP) machine, and the team must ensure compliance using the CPAP machine before proceeding with MBS to minimize the risk of post-operative complications.

Obstructive sleep apnoea has three stages — mild, moderate, and severe — based on a patient's score on the Apnoea/Hypopnoea Index [AHI]. Any score on the AHI that is <5 is considered within normal population limits, while any AHI score from 5-15 is considered evidence of mild OSA, from 16-30 moderate OSA, and >30 severe OSA(325). The eight criteria listed on the **STOP BANG** questionnaire are: (1) **S**noring; (47) feeling **T**ired during the day; (3) **O**bserved apnoea episodes; (4) **P**revious history of hypertension: (5) **B**ody mass index (BMI) >35 kg/m^2; (6) patient **A**ge over 55 years; (7) **N**eck circumference >35 cm in females or >40 cm in males; and (8) male **G**ender(325, 326).

b. Venous Thromboemboli:

Degree of obesity is directly correlated with the incidence of venous thromboemboli (VTE), in that the higher a patient's BMI is, the greater his or her risk of developing VTE(327). Either a previous personal history of VTE or a family history of VTE increases a patient's chance of having VTE after MBS. Furthermore, as patients age, their risk of VTE after MBS increases.

The most-widely used risk assessment tool for VTE in patients undergoing MBS is the Caprini risk assessment tool(327, 328). Both deciding on whether such a patient will need chemical prophylaxis or not after discharge and determining the appropriate dose of chemoprophylaxis to prescribe are essential. In one large ACS NSQIP (American College of Surgery National Surgical Quality Improvement Program) study, over 80% of the VTE that occurred after MBS did so after the patient had been discharged from the hospital, highlighting the importance of determining which patients will need chemoprophylaxis after discharge(329).

It is imperative that all patients considering MBS are asked about their own personal history of VTE, as well about any history of VTE in first degree relatives. In addition, all patients considering MBS must be assessed for their risk of VTE at the time of surgery so a decision can be made as to whether or not they will require extended chemoprophylaxis at discharge. If a patient has a BMI less than 40 kg/m^2, chronic renal insufficiency, or a BMI >60kg/m^2, their dose of chemoprophylaxis needs to be adjusted for weight.

c. Urinary stress incontinence

Urinary stress incontinence and pelvic floor disorders are more common in women than men with obesity. Evaluating urinary stress incontinence includes inquiring about symptoms like urinary leakage, urinary urge, and nocturia, as well as a physical examination, during which the patient needs to be examined in both a supine and orthostatic position, and both with and without a Valsalva manoeuvre. Urinary stress incontinence has a significant psychological impact on patients and can also negatively impact their overall quality of life. Weight loss is recommended for all women with stress incontinence and a BMI >30kg/m^2. In addition, in a recent meta-analysis by Sheridan et al, MBS was found to be an effective treatment for stress incontinence(330, 331).

d. Chronic renal insufficiency

Patients with obesity are at an increased risk of developing chronic renal insufficiency, regardless of any other obesity-related comorbid conditions they have. As such, all patients with obesity considered for MBS should have their renal function evaluated(332).

Knowing a patient's renal function is especially important when considering which surgical procedure to choose, as sleeve gastrectomy is a lower-risk procedure in renally-impaired patients than either Roux-en-Y gastric bypass (RYGB) or biliopancreatic diversion (BPD). Recently, sleeve gastrectomy (SG) has been used as a bridge to renal transplantation in patients with end-stage kidney disease and severe obesity(333). Significant weight loss after MBS often leads to improved renal function, including an increased glomerular filtration rate(332).

e. Idiopathic intracranial hypertension [pseudo-tumour cerebri]

Idiopathic intracranial hypertension (also called pseudo-tumour cerebri) is not at all uncommon in patients with obesity, usually presenting as headaches and/or visual symptoms. It is more common in women and, similar to obesity itself, is more often observed in socially-deprived areas. It usually responds very well to medical management. However, surgical management, like cerebrospinal fluid diversion and bariatric surgery, are recommended for patients who are refractory to medical management(334, 335).

f. Other gastrointestinal conditions besides NAFLD and cancer

Besides the well-established links between obesity and both liver disease (NAFLD and NASH) and gastrointestinal cancer, overweight and obesity also are well-known risk factors for several other gastrointestinal conditions. One of the most common is *gastrointestinal reflux disease*(101), which is characterized by the chronic regurgitation of acid from the stomach into the oesophagus, causing retrosternal pain. Among the causes of GERD are increased abdominal pressure due to increased amounts of intraabdominal fat, weakening of the lower oesophageal sphincter, and hiatal hernias. The recurring flow of acid into the oesophagus can lead to chronic oesophagitis and, further, to Barrett's oesophagus, which is a precancerous condition(336).

Another gastrointestinal condition associated with obesity is functional dyspepsia, which is characterized by symptoms like fullness, bloating, nausea, abdominal discomfort, and vomiting after food intake. To date, the reasons for these symptoms have not been fully explained, but recently-published research findings suggest that changes in vagal neurocircuits in patients with obesity play an important role in this condition's development(337). Other conditions with increased prevalence in people with obesity are irritable bowel disease and inflammatory bowel diseases, as are prevalence rates for both diverticulosis and, consequently, diverticulitis(338).

Among the various gastrointestinal cancers associated with obesity are colon, pancreatic, hepatocellular, and oesophageal carcinoma, among others. This link with carcinogenesis results from a chronic inflammatory state within adipose tissue, which in turn releases further proinflammatory cytokines(339).

g. Osteoarthritis

Osteoarthritis is more common in patients with obesity than those without, caused by both mechanical and inflammatory factors. It often leads to pain, may be disabling, and can adversely affect overall quality of life. Weight loss, with or without MBS, can reduce the progression of osteoarthritis and may reduce patient's pain and stiffness and improve their joint function(340). In addition, several recent studies have shown that the morbidity of orthopaedic procedures in patients with severe obesity is greater than in patients without severe obesity, and that significant weight loss or offering MBS before the planned orthopaedic procedure might reduce morbidity in patients with severe obesity(341, 342).

A word of caution: it is imperative to ensure that patients with osteoarthritis are not taking non-steroidal anti-inflammatory drugs (NSAIDs) or chronic corticosteroids at the time of their MBS, as these agents my cause post-operative complications, especially after Roux-en-Y gastric bypass.

h. Depression and other psychological disorders

Metabolic and bariatric surgery (MBS) generally leads to improvements in altered-mood symptoms, like depression and anxiety in patients with obesity(343, 344). However, depression is also a potential complication of MBS, especially in patients with a poor support system or post-operative complications. In addition, depression is not uncommon in patients with obesity considering MBS(345), some study results suggesting that both adolescents and adults who undergo MBS may be at a still low, but elevated risk of suicide(346, 347). Why this is so is not yet fully determined. However, forced alterations in what they can and cannot eat, gastrointestinal symptoms due to food intolerance, and unrealized, unrealistic expectations about the extent of weight loss they experience post-operatively all can contribute to depression, feelings of anxiety, and a reduced sense of self-worth, amongst other forms of psychological distress.

It is imperative that all patients considering MBS receive psychological counselling pre-operatively, so they know what behavioural changes will be expected of them after MBS. Such counselling is best delivered by experienced psychologists with expertise in MBS counselling; but it can be delivered within a mental preparedness class or in a group setting, as well as one on one. Counselling and emotional support remain important for all patients undergoing MBS post-operatively, as well(37).

6. AREAS OF CONSENSUS

In addition to the role obesity plays in the development of a host of obesity associated comorbid conditions, and the impact those comorbidities have on patients' health and quality of life, it also is reasonable to assume that comorbidities might have an impact upon whether metabolic and bariatric surgery (MBS) is performed, and which procedure or procedures are entertained. This issue was addressed in the two-round Delphi consensus survey of 94 international experts in the management of obesity that was jointly orchestrated by IFSO and WGO. In this survey, there was almost unanimous agreement (98.7% consensus) that a patient's general level of health and fitness is a "very important" pre-operative factor to consider prior to undertaking MBS. Similarly, 97.5% agreed that the presence of any comorbid illness is very important.

Individually all conditions asked about except thyroid disease were considered "very important" by at least 70% of the experts, including cardiovascular disease (94.9% consensus), liver disease

(94.9%), kidney disease (89.7%), respiratory disease (88.6%), current smoking status (84.8%), advanced diabetes (83.5%) and bone health (73.8%). A patient's level of psychological health and fitness also was considered important (94.9%). These and related issues will be discussed further in Chapter 6 – Pre-Operative Assessment. The Delphi survey results are summarized in Table 3-1, below.

Table 3-1: Consensus reached on obesity-associated comorbid conditions

Importance of pre-operative patient factors on decision making Factors assessed	Level of importance	Percentage consensus	Consensus achieved
Patient's levels of general health and fitness	Very	98.7%	Yes
The presence and/or nature of comorbid illness	Very	97.5%	Yes
Ability to understand/cognitive level	Very	96.2%	Yes
Alcohol or other substance abuse	Very	96.2%	Yes
Psychological health and illness	Very	94.9%	Yes
Cardiovascular health	Very	94.9%	Yes
Liver health (including cirrhosis and portal hypertension)	Very	94.9%	Yes
Patient's level of compliance	Very	92.4%	Yes
Obesity's impact on patient's quality of life	Very	92.4%	Yes
Patient's nutritional status	Very	91.1%	Yes
Physiological more than chronological age	Very	89.9%	Yes
Kidney function	Very	89.7%	Yes
Respiratory health	Very	88.6%	Yes
Social and/or family network and support	Very	84.8%	Yes
Presence/nature of physical disabilities	Very	84.8%	Yes
Current smoking status	Very	84.8%	Yes
Advanced diabetes mellitus	Very	83.5%	Yes
Muscle mass (risk of sarcopenia)	Very	83.3%	Yes
Life span expectations	Very	82.3%	Yes
Patient's level of physical mobility	Very	81.0%	Yes
Bone health	Very	73.4%	Yes
Financial means (e.g., ability to afford vitamins)	Very	59.5%	No
Thyroid disease	Not very	53.8%	No

7. CONCLUSIONS AND RECOMMENDATIONS

Much of the reduction that individuals experience in general health and quality of life stems from the broad range of co-morbid health conditions that commonly accompany obesity, conditions that appear to influence every organ system and both physical and psychological health.

These conditions include life-altering and life-threatening conditions like type 2 diabetes, chronic liver disease, cancer, cardiovascular disease, sleep apnoea, venous thromboemboli, urinary stress incontinence, chronic renal insufficiency, idiopathic intracranial hypertension, other gastrointestinal disorders, osteoarthritis, and psychiatric disorders like depression and anxiety

These conditions are essential to recognize, for several reasons:

Their management sometimes is critical to avoid severe and even life-threatening consequences.

Their presence might influence both whether surgical therapy of obesity is deemed feasible and which surgical procedures to consider.

Many of these conditions, including diabetes and cardiovascular disease, have been documented to improve or even abate altogether following successful metabolic and bariatric surgery.

The risk of other conditions, like cancer, may decline after MBS.

Their recognition and management are two further good arguments for healthcare practitioners to adopt a multi-disciplinary team approach to obesity management.

IV. Psychological impact of obesity and its management

1. Introduction
2. Pre-operative psychological assessment
3. Obesity, psychopathology, and eating disorders
4. Eating patterns and disorders
5. Psychotherapy of obesity
6. Stigma of obesity
7. Areas of consensus
8. Conclusions and recommendations

1. INTRODUCTION

Obesity is a complex disease that both affects and is affected by numerous highly-varied facets of life – physical, psychological, social, cultural; oftentimes economic. Individuals with obesity are also stigmatised, even by healthcare providers(348). It is primarily for this reason that, for obesity management to be successful, a multi-disciplinary approach to both its assessment and treatment is required(349, 350, 351, 352). Moreover, healthcare practitioners must remain ever vigilant to their practices, behaviours, words, and non-verbal signals when interacting with patients living with obesity in order to avoid further stigmatization(353, 354).

This section discusses four aspects of the psychological assessment and management of patients with obesity, starting with general components of pre-operative screening; then specific forms of psychopathology that are either common or potentially markedly problematic in such patients; different eating patterns and disorders and how they must be recognized and managed; psychotherapy for obesity; and, finally, the highly-pervasive issue of weight bias.

2. PRE-OPERATIVE PSYCHOLOGICAL ASSESSMENT

As with any chronic disease, to achieve and maintain long-term health and wellbeing, patients undergoing obesity treatment, including metabolic and bariatric surgery (MBS), behaviour change is required. Behavioural interventions can help patients incorporate obesity management strategies such as self-monitoring and self-care activities, healthy eating, exercise interventions, medication adherence, and other health promoting behaviours.

A psychosocial assessment performed by a qualified health professional specializing in behaviour change and obesity management can be helpful for identifying any underlying psychosocial barriers necessary for behavioural change.

Adherence to obesity treatment has been defined in various ways, including the extent to which a patient self-monitors (e.g., records food intake, sleep, and stress), attends intervention sessions, and follows behavioural recommendations. Research suggests that each of these facets of adherence is associated with better weight loss and cardiometabolic outcomes(355, 356, 357). Attendance at follow-up sessions is particularly important, given the direct correlation between the number of intervention sessions attended and degree of weight loss(357, 358). Data from one recent meta-analysis suggest that higher levels of adherence occur with interventions that incorporate social support (e.g., group sessions, peer coaching, participation of friends/family members), attendance monitoring, and supervised (vs. self-directed) programming(359).

With regard to surgical treatment, regular attendance at post-bariatric surgery appointments with the multidisciplinary team is vital for the prevention and early recognition and treatment of complications. It also aids in identifying any psychological, behavioural, and/or medical intervention non-adherence that could compromise long-term outcomes. It is recommended that patients who have undergone bariatric surgery follow up with the multidisciplinary team at regular intervals for a minimum of two years, and longer and more frequently as needed(360). Though patients may not need to see all members of the team at the same intervals, they should have access to all avenues of support.

To assess for motivation to change, likely level of adherence to treatment, and any potential psychological issues that might impair outcomes, domains that should be included in psychosocial assessments at follow up visits include:

Motivations, goals, and expectations for weight management: A key part of each chronic disease management assessment is exploring factors that have prompted patients to seek treatment, as well as their goals and current level of readiness to manage their disease. Patients seeking treatment for obesity tend to report highly-unrealistic weight loss expectations, with weight loss estimates that they predict would be “disappointing” often more aligned with what can realistically be achieved with behavioural modification programs(361). Unrealistic weight loss expectations, in turn, are associated with attrition from treatment programs(361). Thus, it is important to discuss with patients that obesity management is about improving health and wellbeing and to be clear about weight loss outcomes with existing treatments. Through a psychosocial assessment, healthcare providers can also work collaboratively with patients to identify goals that are aligned with patients' personal values, preferences, and life circumstances. For example, healthcare providers and patients could discuss establishing non-scale goals (e.g., improved blood glucose control, reduced pain, improved mobility, decreased need for medications) to motivate persistence with health behaviours associated with obesity treatments.

Disordered eating behaviours: All patients should be screened for disordered eating, including binge-eating disorder, night-eating syndrome, bulimia nervosa, and restrictive eating disorders. Binge-eating disorder is the most common eating disorder, its prevalence increasing with increasing BMI(362). Conversely, restrictive eating disorders are typically underdiagnosed among people with obesity. Consequently, a thorough assessment should include inquiries into extreme dietary restrictions and compensatory behaviours. Note that, even when patients do not meet the full criteria for eating disorders, they may experience subthreshold eating disorder pathology, such as emotional eating, which warrants assessment and treatment.

Psychiatric history: Obesity is associated with an increased risk of mood and anxiety disorders, most commonly depression(363). Depression, in turn, is a risk factor for obesity, given its association with increased appetite, decreased physical activity, binge-eating disorder, and the weight-gain side effects of many psychiatric medications(363). There is also convincing evidence that obesity can cause depression, due to internalized weight bias, reduced quality of life, and physiological mechanisms like inflammation(364). For all the reasons listed above, it is vital to assess and treat underlying mental health disorders that may be hindering obesity treatment.

Demographic, socioeconomic, and cultural factors: Information should be gathered about each patient's age, ethnicity, disability status, socioeconomic status, educational background, employment, and other cultural factors that may influence health behaviours and patient preferences.

Social support system: The patient's current living situation and broader social support network should also be assessed, including the degree to which friends, family, and co-workers support the patient's obesity treatment.

3. OBESITY, PSYCHOPATHOLOGY, AND EATING DISORDERS

Patients with obesity who intend to start any disease management program must be evaluated by mental health professionals so psychosocial behavioural factors that might jeopardize their obesity treatment are identified promptly. Behaviour change is an important variable that must be addressed in patients living with chronic diseases, including obesity. Dysfunctional eating behaviours can be a barrier hindering long-term obesity management(365). On the other hand, substance use disorders (alcohol and other psychoactive substances), as well as other co-occurrent impulse control disorders — such as compulsive buying, pathological gambling, and addiction to social networks or pornography — may affect some patients after they have lost weight, particularly those undergoing metabolic and bariatric surgery (MBS), thereby decreasing their quality of life and putting them at risk of weight regain and obesity complications. Patients who have undergone metabolic and bariatric surgery are at higher risk of developing alcohol use disorders due to altered pharmacokinetics resulting in increased sensitivity and reduced tolerance to alcohol following surgery(366). It has also been posited that, for some patients, there may be an addictive dimensionality of obesity that, in general terms, stems from dysregulated activity within brain areas known to be related to reward processing and cognitive control, similar to what happens in substance dependence(367).

Psychiatrists and psychologists involved in the assessment and management of patients with obesity need to be sensitive to a wide range of behavioural, cognitive, emotional factors that may be barriers to effective obesity treatment. Such factors lie behind dysfunctional eating behaviours such as binge eating disorder (BED), night eating syndrome (NES), emotional eating, food addition, and grazing, which, in turn, are considered the most important predictors of undesirable weight loss outcomes(368) and need to be promptly diagnosed and managed before and after any obesity treatment modality.

Knowing how to identify psychological and psychiatric factors that predict obesity treatment non-response is one of the challenges faced by professionals working with patients with obesity. Some patients may show depressive symptoms with atypical features or disguised clinical conditions similar to eating disorders. Indeed, the atypicality and peculiarity assumed by the symptoms of many psychiatric conditions in people with obesity convert their assessment into a real psychopathological and nosographic challenge.

Not unlike any other chronic disease, a significant challenge that healthcare professionals face is the low adherence to the systematic multidisciplinary follow-up that is widely recommended for obesity care. Recently, a Canadian cohort of 388 patients who had undergone MBS was studied for one year to identify predictors of adherence to postoperative follow-up(369). Adherence, defined in this study as having attended three or four of the four recommended clinical visits, was higher in patients older than 25 years, those employed part-time or full-time, and those with obstructive apnoea diagnosed before surgery. Another North American study(370) retrospectively examined demographic and psychosocial aspects associated with greater adherence to postoperative follow-up over one year. Adherent patients generally were older and Caucasian, had fewer social phobic traits and lower levels of hostility, and lived closer to the medical services where they were receiving their care for obesity. A more recent New Zealand study(371) found that patients who did not adhere to preoperative follow-up tended to be less adherent to postoperative follow-up, and that non-attendance at any preoperative visit or 50% or more of the postoperative consultations was associated with lower rates of weight loss. More data on psychological profiles related to adherence to psychiatric/psychological follow-up help guide the development of strategies aimed at increasing it, thereby minimizing undesirable outcomes. In addition, more research is needed to understand the systemic barriers to long-term obesity treatment and follow up adherence. For example, in many countries, access to multidisciplinary obesity care is lacking, due in part to the lack of recognition of obesity as a chronic disease in healthcare systems(372, 373).

A. Obesity and psychopathology

Some patients with severe obesity are significantly more likely to have mental health conditions like mood disorder, anxiety, substance use disorder, or personality disorder, as well as higher levels of stress, depression, food cravings, and dysfunctional eating behaviours, lower self-esteem, and worse quality of life(374). However, studies on psychological variables correlating weight loss and mental health in patients with severe obesity before and after obesity treatment have been inconclusive. For instance, no particular personality trait has been found to exhibit superior predictive value with regard to weight or mental status after bariatric surgery(370), though some individuals with obesity have higher rates of neuroticism (a propensity to feel negative emotions), harm avoidance, impulsivity, and low self-esteem(375). The intensity of any psychiatric symptom or disorder is more important than its specificity in predicting bariatric surgery outcomes, in terms of both weight loss and mental health consequences(376). Weight loss appears to improve scores for personality traits like extraversion in some patients undergoing MBS, resulting in improvements in social relationships and greater emotional stability through a reduction in neurotic traits(376).

Dysfunctional eating behaviours seem to be a behavioural marker of obesity treatment non-response, since patients with binges undergoing obesity treatment often have worse outcomes in terms of weight loss. Binges are episodes of food intake which are much greater in volume than normal and are associated with a feeling of lost control over the amount of food eaten, as well as feelings of guilt or shame(377). It was discussed above that dysfunctional eating behaviours should be a significant concern of all healthcare professionals involved in the assessment and follow-up of patients with obesity.

Another concern for psychiatrists and psychologists evaluating and treating patients with obesity, particularly candidates for MBS, is the phenomenon of *addiction transfer*. This term indicates that some individuals who have undergone MBS and who had a pre-existing "addiction to food" before surgery may develop a new substance use disorder, or that the "food addiction" has "transferred" to another substance after surgery. This could include alcohol and/or other substances or engagement in other addictive behaviours like excessive gambling, shopping, internet use and pornography. However, it is not yet established whether these events indicate increased substance use or engagement in behaviours with high addictive potential by individuals who were already experiencing problems like these before surgery, or new cases of problematic substance use or addictive behaviours that originated after surgery(43).

The phenomenon of addiction transfer, also observed in patients undergoing dietary management, seems to occur due to a supposed additive dimension of obesity that, in general terms, would include damage to the functioning of brain areas known to be related to reward processing and cognitive control, similar to what happens in substance dependence(367, 368).

4. EATING PATTERNS AND DISORDERS

a. Compulsive Overeating

Complaints of compulsive overeating are quite frequent in patients with obesity and need to be properly evaluated and treated; otherwise, they may cause non-response to obesity treatment. *Compulsive overeating* is a broad term and not a formal diagnosis. Patients who identify themselves as having compulsive overeating behaviours often have a binge eating disorder, night eating syndrome, emotional eating, food addition, or grazing, either alone or combined. All these conditions include an impulsive or compulsive component, frequently similar to those of people with chemical and behavioural addictions, such as increased motivation to consume palatable foods and greater pleasure related to the consumption of such foods, a gradual increase in the amount of food needed to reach satiety, loss of control over eating, more time spent obtaining and consuming food, stress and dysphoria when they are on diets or unable to eat as usual, eating quickly or too much in the absence of hunger, overeating despite its adverse physical and psychological consequences, and feelings of guilt, demoralization or depression associated with eating(378, 379). Impulsivity and compulsivity are behavioural phenotypes or endophenotypes(379) which are hereditary and variable in the general population(380).

Impulsivity is defined as a predisposition to rapid and unplanned reactions to internal or external stimuli without concern for their negative consequences, resulting from impaired unconscious information processing(381). Impulsive people have impairments in conscious processes of reflection and self-control and a tendency to produce responses of greater magnitude to the potential rewards of the environment, a phenomenon called *reward sensitivity*(381, 382), which predisposes them to a wide range of psychiatric disorders.

Compulsion, in turn, is defined by actions that are inappropriate to a given situation and which persist despite undesirable consequences. Compulsions involve impairments in interrupting an ongoing behaviour when necessary(379) and also increase the chances of mental distress.

Some individuals with obesity may have impairments in conscious processing of reflection and self-control (impulsivity) and may find it very difficult to stop eating (for example), despite knowing that they should do so (compulsion).

Impulsivity and compulsivity result from impairments involving the volitional top-down control exerted by the dorsolateral prefrontal cortex over structures like the ventral striatum and dorsal striatum, associated, respectively, with impulsivity and compulsivity. Impulsivity and compulsivity recruit different neuronal circuits. The former hinges upon a reward-learning system located in the ventral striatum, while the latter depends on more dorsal striatal circuits related to habit formation(379, 383). In substance addictions and in obesity, the consumption of a substance or highly-caloric and palatable foods, respectively, is initially mediated by the ventral striatum and, therefore, initiated impulsively. The repetitive use of that substance or palatable food — primarily subject to voluntary control, but impulsive — causes migration of the ventral circuits to more dorsal striatal circuits, involving processes of neuroadaptation and neuroplasticity, resulting in lost control over food consumption(379). In one study, researchers found that young women with obesity scored significantly worse on neuropsychological measures of attention and impulsivity than women without obesity. This neuropsychological response may be mediated by low-grade systemic inflammation associated with obesity, as younger individuals are not usually exposed to other mechanisms related to cognitive decline in obesity, such as hypertension, metabolic dysfunction, and cardiovascular abnormalities, which are known to alter brain structure. The decline in cognitive performance leading to impulsivity in young women with obesity may suggest the beginning of an early and persistent cognitive decline associated with obesity(384).

b. Binge Eating Disorder

Binge eating disorder (BED) is the most prevalent eating disorder; but it is underdiagnosed and undertreated(385). It is defined essentially as the recurrence of binges. Binges consist of eating an amount of food that is much greater than what most people would manage over a similar amount of time. Such episodes are accompanied by feelings of lost control and may be associated with increased speed of eating, eating until reaching an uncomfortable fullness, eating in the absence of hunger, eating alone due to feelings of embarrassment created by the amount of food ingested, and feelings of shame, demoralization, depression and/or guilt. Binges are not accompanied by inappropriate compensatory behaviours, as in bulimia (in which patients may use laxatives and/or diuretics, induce vomiting, or engage in excessive exercise). Although not all patients with obesity suffer from this condition, BED is common in individuals with obesity. In turn, patients with both obesity and BED tend to have more psychiatric comorbidities and are more refractory to treatments for both their obesity and BED(386). Relative to patients with obesity without BED, patients with obesity and BED have a greater feeling of lack of control, greater sensitivity to rewards, and greater impulsivity associated with food stimuli, as well as feelings of guilt and shame associated with more intense binges(385).

Binge eating disorder is relatively common, with a lifetime prevalence in the general population of 1.4%, though it can increase significantly among individuals with obesity, with no marked differences between genders(387). Comorbidities with other psychiatric disorders — such as depression, anxiety, substance abuse and even personality disorders — are frequent(387, 388). Between 64 and 79% of patients with BED will experience some psychiatric comorbidity throughout their lives, with mood and anxiety disorders the most prevalent(387, 388). Individuals with BED also have pervasive concerns about food, weight, and body image, in addition to deficits identifying and regulating emotions and several interpersonal problems(387). Negative emotions and maladaptive emotion regulation strategies play an important role in the initiation and maintenance of BED; particularly negative feelings associated with interpersonal relationships, like loneliness(388). Higher levels of depression are related to more severe binges; for instance, cravings that trigger binges are more often associated with lowered mood and lower energy levels than cravings that do not trigger them(388). This said, emotions other than depression and sadness are often behind the compulsivity observed in patients with BED. Such other emotions include anger, frustration, guilt, irritability, fury, resentment, and envy. These emotions are highly present in interpersonal contexts, which may be less tolerated by patients with BED or are experienced by them in a distinct and more aversive way(388).

c. Night Eating Syndrome

Night eating syndrome (NES) is characterized by recurrent episodes of night eating, which can be defined either by the occurrence of episodes of food consumption after waking during the night, or by excessive food consumption after the night meal, which cause stress or impairment of the individual's functioning and are not explained by other mental disorders(378). Night eating syndrome often affects individuals with severe obesity and can be explained as a circadian rhythm dysfunction(389). Other symptoms include morning anorexia, a strong urge to eat between dinner and bedtime and/or during the night or early morning, and the belief that it is not possible for them to fall asleep without eating(390).

The prevalence of NES in the general population is usually low (between 0.5% and 1.5%) and tends to increase in individuals with obesity (where it reaches up to 25%)(390). In candidates for MBS, its prevalence can be as high as 60%. Symptoms of NES often overlap with those of other eating disorders. Patients with obesity, NES, and other eating disorders are also at increased risk for mood disorders, anxiety, and sleep disorders(391). Although individuals with NES appear to have similar patterns of sleep onset, completion, and duration as healthy individuals, they wake up an average of 3.6 times per night and often eat in order to fall asleep again(390).

Typically, NES begins in early adulthood and is long-lasting, with periods of remission and relapse often associated with stressful life events(391). Some authors suggest that the motivation to eat differs in individuals with NES versus BED, since in night eaters it consists of seemingly helping them initiate sleep[24]. Night eating disorder must be distinguished from *Sleep-Related Eating Disorder*, a parasomnia in which there are episodes of involuntary eating and drinking while a person still seems asleep(391).

D. Emotional Eating

Patients with obesity often report that their emotions interfere with their eating behaviours. For instance, many indicate that they consume high-calorie foods to alleviate unpleasant emotions, suggesting that they suffer from emotional eating, which is defined as eating triggered by negative emotions or stress(392).

Emotional eating is one of the main causes of the difficulty that individuals with obesity face when managing their disease, in addition to being a possible mediator between depression and obesity(392). The relationship between emotions and eating behaviour is not fully understood; but one of the theories about the origins of emotional eating is that, in some people, food acts as a regulator of aversive or negative emotions(393). There is individual variation in how emotions affect eating behaviour. Several experiments have shown that individuals who restrict their diet to reduce or maintain weight eat more in response to fear and negative mood states than individuals who do not. These studies also show that individuals who experience emotional eating consume more sweet and fatty foods in response to emotional stress, while binge eaters tend towards binge eating when facing negative emotions(394). Despite the intuition that most people – excluding those on diets and emotional or compulsive eaters – decrease their food intake when experiencing negative emotions, only about 40% actually do this(394). This suggests that most people, regardless of their weight and the presence of any eating behaviour disorder, regulate emotions with food, at least at some point in their lives.

Emotion regulation is a multidimensional construct that comprises the ability to respond to multiple personal and social demands with socially-acceptable and flexible behaviours and emotions, in addition to the ability to delay and even repress spontaneous reactions when necessary or convenient(395). It incorporates intrinsic and extrinsic psychological processes, such as monitoring, appreciating, and modifying the magnitude of one's emotional reactions. Ultimately, emotion regulation encompasses any cognitive and behavioural processes that influence emotional intensity, duration, and expression(395). One of the most studied models of emotion regulation proposes two mechanisms: *cognitive reappraisal* and *expressive suppression*(395). The first of these is considered the most adaptive and involves the cognitive strategy of modifying the emotional potential of a given condition, by redefining it in non-emotional terms. Expressive suppression, on the other hand, encompasses modulation of the emotional response. However, both require some ability to perceive and reflect on one's emotions, an ability not uniformly distributed in the population.

Problems in emotion regulation are associated with various mental disorders, such as depression, bipolar disorder, anxiety disorders, borderline personality disorder, and eating disorders(396). There is increasing evidence that eating symptoms — like binges and restrictive behaviours — serve as dysfunctional alternatives to regulating or suppressing unpleasant emotions. Women with bulimia nervosa, binge eating disorder, and anorexia nervosa report greater difficulties perceiving their emotions, greater tendency to avoid them, and less ability to manage them than healthy women(396). Difficulty perceiving one's emotions may lie behind problems regulating them. Difficulties with the perception of emotions are one of the dimensions of *alexithymia*, a transdiagnostic concept(395) characterized by the inability to describe and recognize one's emotions and by externally-oriented thinking, a style of perceiving and thinking disconnected from emotions(397). It is possible that some people with obesity have higher levels of alexithymia and that it may impair their ability to regulate their emotions. It is also possible that individuals with alexithymia have difficulties identifying other people’s emotions. This could happen because, according to some authors, we use our own emotions to interpret the emotions of others(398). Impairments in the proper identification and interpretation of other people’s emotions lead to problems in interpersonal relationships, which trigger unpleasant feelings that may be regulated through high-calorie food consumption. The understanding of deficits in emotion regulation and impairments in abilities of emotion identification present in obesity can help in the development of strategies to prevent and manage binges in people with obesity.

e. Food Addiction

Food addiction is a controversial term some use to describe a set of behaviours – related to the consumption of palatable foods – which is very similar to that observed in those who are dependent on substances like nicotine, cocaine, alcohol, and opioids, as well as in behavioural addictions, with which gambling, sex, shopping, social media, or the viewing of pornography become addictive. From a scientific point of view, however, the mere similarity of some eating behaviours with substance and/or behavioural dependencies does not permit us to categorize them as such(399). Some researchers claim that, despite the similarity that certain eating behaviours have with substance use disorders — like the presence of cravings, loss of control, excessive consumption, tolerance, abstinence, stress and functional impairment, and even the findings of alterations in mesolimbic dopaminergic systems in patients with food addiction(400, 401) — the addictive substance has not yet been found(399), which should disallow use of the term *food addiction*. Whether it is sugar or a combination of sugar and fat, both present in highly-palatable foods, it is nevertheless not yet possible to claim that any specific nutrient acts directly on the brain, triggering reward-motivated behaviours(399). On the other hand, there is evidence that obesity has important impacts on the activity of different brain areas(402), including those related to reward processing(403), introducing even more controversy to the subject. It is, however, not yet possible to precisely identify whether the changes observed by neuroimaging in the connectivity and activity of brain areas related to reward processing and cognitive control in those who report food addiction (the vast majority of whom suffer from obesity), are truly triggered by food or are phenomena specifically associated with obesity. These neuroimaging findings are often used to justify the validity of the food addiction construct.

Obesity and addictions share neurobiological processes that result in compulsive consumption, which in turn results from dysregulation of reward-processing circuits and biochemistry, where the protagonist is dopamine. The particularly-reinforcing character of food in obesity characterizes its addictive dimension(404). Impairments in the ability to exert self-control are essential psychopathological elements in any addiction. *Self-control* can be defined as the efforts that an individual makes to modify thoughts, feelings, and behaviours to achieve long-term goals or interests; it allows for the coordination or direction of lower-level, more automatic cognitive processes, ensuring that our behaviour is in line with our aspirations(405). The neurobiological processes leading to both addictions and obesity result from the interaction between a tendency to produce greater responses to potential environmental rewards (which is called *reward sensitivity*) and impairments in self-control, which is why more impulsive individuals are more vulnerable to weight gain when exposed to an obesogenic environment(382).

The similarities between substance use disorders and food addiction are not exclusively phenomenological and psychobiological, but also involve family history, more common onset in adolescence or early adulthood, chronic evolution with relapses, and even the potential for spontaneous resolution without any treatment(406). One of the possible reasons behind difficulties agreeing on the convergence between substance use disorders and food addiction is that the negative consequences of the former are much more obvious than of the latter, including family dysfunction, dropping out of school, financial problems, and even prison(406). With food addiction, such outcomes are rarely observed and, when they do, usually lack the same magnitude of severity as observed in substance users. Likewise, children are not likely to miss school because they are overeating, and no adult is committing a crime by eating too much.

f. Grazing

Grazing (also called picking, nibbling, snack eating) is defined as eating small portions of food in an unplanned manner between meals. Reviewing these different concepts, the criteria most frequently endorsed by experts include repetitiveness, consumption of small amounts of food, and lack of planning. Loss of control is not considered by all authors to be a dimension of grazing, since, for many authors, this criterion should not be used to differentiate grazing from BED. For instance, grazing may be a sub-syndromic form of BED which, as such, increases the likelihood of undesirable outcomes, in terms of weight loss in patients undergoing obesity treatment.

g. Addiction Transfer after Bariatric Surgery

There is concern between mental health professionals that a phenomenon named *addiction transfer* could be triggered in some patients by the surgical treatment of obesity. The concept behind addiction transfer in patients undergoing MBS is that patients who have undergone MBS and are, thus, no longer able to consume previous quantities of food due to the physical restrictions preventing the consumption of food imposed by the surgery, could start to over-consume alcohol and/or start using other substances and/or develop other addictive behaviours, such as excess gambling, shopping, internet use, or pornography viewing.

Nonetheless, it is not well established whether such manifestations result from increased substance use or engagement in behaviours with high addictive potential by individuals who already had such problems before surgery or whether, in reality, they are new cases of problematic substance use or addictive behaviours(43).

Substance and/or behavioural addictions are defined by their cardinal components: salience, mood modification, tolerance, withdrawal, conflict, and relapse. These components are more important from a diagnostic point of view than quantitative variables such as, for instance, the amount of alcohol or high-calorie foods consumed per day, or the time spent on social networks or viewing pornography on the internet. By salience, it is understood that the substance or addictive behaviour occupies a central place in the person's life, becoming what is most important to the affected person. A person with addiction uses a drug or engages in a behaviour to induce emotional arousal or alleviate aversive feelings, needs increasing amounts of the substance (or greater amounts of time involved with addictive behaviours) to achieve the same arousal effect or relief (tolerance), and may develop withdrawal symptoms (dependence) if exposure to the drug/behaviour decreases or is interrupted. Patients with an addiction disorder frequently experience situations of interpersonal conflict related to their addiction and report relapses after struggling to resist it(407). Risk factors for developing addictive behaviours include genetic characteristics (e.g., children of parents with alcoholism are 2-4 times more likely to develop alcoholism themselves), lack of parental/family support, and the presence of psychosocial stressors. Personality traits — like the desire for new experiences, impulsiveness, low self-esteem, aggressiveness, emotional lability, inattention, antisocial behaviour, and stubbornness — are common in those with drug addictions. However, to date, there is no consistent evidence that an "addictive personality" exists. Therefore, given the nosological and etiological complexity of addictions, the idea that bariatric surgery “generates” new addictions may seem overly simplistic. Except in patients with chronic or severe alcoholism, in which physical signs of the disease are unmistakable, identifying problematic use of alcohol and other substances can be a real challenge, as the assessment of problems related to substance use is limited by its need for accurate self-reporting. However, despite the notion shared by most mental health professionals working with patients seeking or considering bariatric surgery that problematic alcohol use is a contraindication for the procedure, some investigators have identified higher rates of weight loss among patients with a history of substance abuse than among those with no such history(43). It has been postulated that these surprising results may be a consequence of such patients with prior substance use disorders using some of the same skills they employed to overcome their substance use disorder to deal with the life changes required after their surgery. This contradicts the concept of addiction transfer, a phenomenon still considered controversial among experts. Many experts do not admit its existence and argue that, for there to be addiction transfer, first it is necessary to accept that food addiction exists in persons with obesity; and second, that this addiction takes a different form after surgery, as discussed above. Furthermore, the lack of consensus on the meaning of "addiction" makes the discussion even more confusing. For many, "addiction" is synonymous with compulsivity, a vague term(408) often used by lay people, which includes different categories of behaviour, from drinking to gambling or compulsive shopping, while, among scholars, "addiction" is a medical term used in diagnosis and should be defined in a standardized way(408) that incorporates the cardinal components listed above.

The perspective of behavioural neuroscience, which defines the phenomenon of addiction in light of alterations in the brain's response to different stimuli, makes the debate even more complicated, as there is biochemical evidence suggesting a "kinship" between the compulsion for food and the compulsion for substances. This evidence involves, for example, the role of presumed dopamine deficiency in the brain of individuals with obesity, perpetuating pathological eating behaviours that compensate for the decreased activation of dopaminergic circuits(409). Many neuroimaging studies have demonstrated that individuals with obesity have brain responses to food intake or even visual or auditory food cues that are very different from those exhibited by lean individuals. These responses involve several brain regions, like the ventral striatum, amygdala, hippocampus, and medial prefrontal cortex, all areas linked to motivation and reward processing, as well as the dorsolateral prefrontal cortex, a brain region associated with cognitive control(402). Several other neuroimaging studies have shown that MBS can reverse anomalous activation patterns in brain systems linked to reward and cognitive control(410), giving some credence to the hypothesis that, even though they might not be phenomenologically identical, eating, drinking, compulsive gambling, and compulsive shopping are very similar from a neuroscience perspective. Dysfunctional eating behaviours, like those present in patients with BED, consist of psychological experiences very similar to those described by patients who suffer from substance use disorders, including feelings of loss of control; of pleasure and excitement related to the consumption of high-calorie foods; and of guilt and remorse that frequently are an end result.

Alcohol pharmacokinetics seem to change after MBS. In patients undergoing Roux-en-Y gastric bypass, plasma alcohol levels can reach their peak very quickly(43). Patients themselves often say that their "resistance" to alcohol changes after surgery, referring to the perception that they are more sensitive to the effects of alcohol, manifested as being able to drink fewer drinks than they used to pre-operatively. It has been proposed that the faster a psychotropic drug's action and the shorter the time over which its effects are experienced, the greater its addiction potential(43), a hypothesis called the *pharmacokinetic etiological model of addictions*. If this hypothesis truly explains why many patients develop alcohol-related problems after surgery, alcohol addiction after surgery cannot be considered transference of dependence.

Unfortunately, most studies on substance use and bariatric surgery have focused primarily on alcohol-related problems, with little information on other legal or illegal psychoactive substances, including benzodiazepines. For the time being, taking into account the changes in the response of brain regions processing rewards and in cognitive control observed in patients with obesity, as well as the many questions that remain about the validity of phenomena like food addiction and addiction transference, the rule is for healthcare professionals to be extra careful to rule out addiction when evaluating candidates for MBS, especially when there are reasons to suspect it.

5. PSYCHOTHERAPY OF OBESITY

Psychotherapy is an important component of the overall treatment of obesity and can be used for other purposes in patients who have undergone MBS as well. The most studied therapeutic targets of psychotherapy in patients with obesity are dysfunctional eating behaviours which, as discussed above, increase the likelihood of an undesirable outcome with all the different modalities of obesity treatment.

Different psychotherapeutic techniques aim to generate a mental attitude that facilitates achieving the main goals of obesity treatment, including long-term maintenance of weight loss achieved during treatment by controlling, among other barriers to treatment response, dysfunctional eating behaviours. Such techniques encompass different strategies to achieve such goals. For instance, psychoeducational techniques help to change habits and lifestyles, while techniques based on *cognitive-behavioural therapy* (CBT) focus on cognitive restructuring(411) and *dialectical behaviour therapy* (DBT)-based techniques aim to improve self-regulatory strategies(412). Interpersonal psychotherapy can be helpful for assisting patients with obesity to develop ways to improve their social support, reduce interpersonal stress, and facilitate emotional processing in social contexts, as well as to help them improve their social skills. Finally, techniques based on transcendental meditation, like mindfulness, have been increasingly used treating obesity, helping to minimize automatic eating behaviours, cravings, and food impulsivity by regulating the balance between aversive emotions and emotional eating(413). Mindfulness-based techniques can be employed alone or as part of other programs focused on emotion regulation, such as DBT.

Cognitive behavioural therapy techniques should be differentiated from interventions aimed at changing habits or health behaviours, although there is not always a clear distinction between them. Interventions to change habits and health behaviours include actions to encourage healthier eating and physical activity. They can employ behavioural strategies like self-monitoring, goal specification, stimulus control, problem solving, and relapse prevention, which will be discussed below. Techniques based on CBT, in turn, use all these strategies associated with a therapeutic component aimed at cognitive restructuring(100). Self-monitoring, one of the pillars of the behavioural treatment of obesity, includes the systematic recording of weight, nutrition, and exercise, which seems to increase awareness of behaviours that lead to weight gain(414). Specification of goals is recognized as an evidence-based strategy for behaviour change and consists of helping patients to set clear and tangible goals, which ultimately helps to direct their attention and efforts, as well as to minimize the effects of distractors, while increasing energy, motivation, and persistence(415). Such goals can further extend beyond weight, nutrition, and exercise to include, for example, self-care activities and self-acceptance, among others.

Stimulus control-based interventions are useful for identifying stimuli that trigger automatic and dysfunctional eating behaviours, as well as for extinguishing their associations(416). Structured problem-solving techniques involve methods to help patients identify personal problems underlying their dysfunctional eating behaviours, and to assist them in developing adequate tools to solve these problems(415). Relapse prevention techniques were initially developed to treat patients with problematic substance use, but also seem to be effective for managing dysfunctional eating behaviours in obesity. They encompass not only identifying aversive emotions and thoughts that often trigger binges, but also interventions that help to minimize the potentially-devastating impact of relapses.

Meanwhile, CBT-based techniques encompass all the strategies discussed above, with an added cognitive component of therapy, defined as the assessment and modification of thoughts, beliefs, emotions, and motivations about weight loss(417). Dysfunctional beliefs — like “I don't deserve to be lean” or “I'll never be able to exercise routinely” — must be replaced, constantly and automatically monitored, and promptly addressed. Patients can additionally be taught to create healthier responses to these mental automatisms, as well as to value minimal achievements and react differently to weight gain(417).

Psychotherapeutic approaches that focus on emotion regulation, such as DBT, have been increasingly studied as alternatives for patients with obesity. *Emotional regulation*, a domain of self-regulation, is defined as the repertoire of cognitive strategies used to influence emotions in ourselves and others(418). Inability to regulate emotions can lead to dysfunctional eating behaviours, as previously discussed in detail.

Dialectical behaviour therapy is an integrative intervention that was originally developed for emotional dysregulation in highly suicidal and self-aggressive patients with borderline personality disorder. The technique combines CBT strategies with techniques from other orientations, like mindfulness, which then can be applied individually or in groups(419).

6. STIGMA OF OBESITY

a. Introduction

The recently published Canadian Adult Obesity Clinical Practice Guidelines highlight the pervasiveness of weight bias, obesity stigma, and discrimination experienced by people living with obesity(353, 420). While prevalent across multiple settings like schools and workplaces, weight bias, obesity stigma, and discrimination are also found in healthcare settings(421, 422). Even healthcare providers who support obesity management often hold biased beliefs and attitudes about obesity and about people living with obesity(423). For individuals seeking obesity care, including bariatric surgery, exposure to weight-biased attitudes among the professionals they turn to for support can impact treatment outcomes(353).

Weight bias can also deter people living with obesity from seeking support from healthcare providers, which can have ramifications for their overall health and well-being. More importantly, weight bias experiences can also directly increase morbidity and mortality beyond obesity-related health impairments(420). While the Canadian Adult Obesity Clinical Practice Guidelines(420) provide recommendations to reduce weight bias in healthcare settings, specific guidance to healthcare providers who offer bariatric surgical approaches can help enhance the bariatric experience for patients and providers.

In this section, we provide an overview of current evidence on how bariatric surgery healthcare professionals can modify, align, or enhance their practice to achieve the goal of reducing weight bias, obesity stigma, and discrimination. To support standard practice within chronic disease management, we use people-first language throughout this chapter(424). Our specific recommendations for healthcare providers who work in bariatric surgery settings are based on a narrative review of the current literature and it should be noted that the approach we employed to derive these recommendations did not follow the systematic methodology of the original Canadian Clinical Practice Guidelines. We, therefore, recommend that readers also review the Canadian guidelines and consider the additional recommendations included here as supplementary.

Table 4-1: Key definitions used in this chapter

Term	Definition
Obesity	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(352). With obesity understood as a chronic medical disease and not simply a consequence of poor health behaviour choices, obesity management takes on many of the principles of chronic disease management(425). The term “obesity management” is used to describe health-related improvements beyond weight-loss outcomes alone. If weight loss occurs because of the intervention, this should not be the focus over improvements in health and quality of life (QoL)(426). Obesity care should be based on evidence-based principles of chronic disease management, must validate patients’ lived experiences, and must move beyond such simplistic approaches like “eat less, move more” to address the root drivers of obesity(420).
Weight bias	The negative weight-related attitudes, beliefs, assumptions, and judgments in society that are held about people living in large bodies. They can be implicit (subconscious negative attitudes toward people in large bodies), explicit (overtly negative attitudes toward people with obesity) or internalized (the extent to which individuals living with obesity endorse negative weight-biased beliefs about themselves)(353).
Weight (or obesity) Stigma	Weight bias manifested through harmful social stereotypes that are associated with people living with obesity(353).
Weight (or obesity) Discrimination	The unjust treatment of individuals because of their weight/obesity status(353).

One of the key drivers of weight bias and stigma is the belief that any amount of weight loss is achievable and, indeed, desirable to improve health. Thus, for many people, the most measured outcome of bariatric surgery remains weight loss (this is often emphasised by referring to it as "weight-loss surgery"). Yet, such framing can exacerbate weight-biased attitudes. These attitudes manifest as the belief that people who undergo bariatric surgery are somehow "cheating" or undeserving of healthcare resources(426). Furthermore, even though some weight regain after bariatric surgery is normal(427), patients may perceive this as personal failure, which can have a negative psychosocial impact on them(425, 428).

Reducing weight bias, stigma, and discrimination in bariatric surgery healthcare settings therefore requires an understanding of the prevalence, drivers, and impact of these constructs. Canada's Adult Obesity Clinical Practice Guidelines include a new definition of obesity as the presence of excess or abnormal adiposity that impairs health(420). With obesity considered a chronic disease, treatments should be life-long, and outcomes should go beyond just weight loss, instead focussing on improving health. Due to the past focus of obesity interventions on weight loss as the primary outcome and pervasive social bias against people with obesity, expectations of weight loss tend to exceed what obesity management interventions can achieve(425).

b. Prevalence and impact of weight bias, stigma, and discrimination in surgical settings

It is now widely accepted that weight bias and obesity stigma are both commonplace and harmful(428). Approximately 40% of adults report having personally experienced some form of weight bias or stigma(429). Although recent research has identified the family setting as one of the most common settings for stigma to manifest(428, 430), the healthcare setting remains a source of weight bias globally(431) and stigma is also experienced by people who have undergone bariatric surgery(432).

Clinicians are not exempt from weight-biased attitudes, with one study finding medical doctors' implicit and explicit weight-biased attitudes comparable to the general public(433). Unfortunately, we could not find any studies that examined the prevalence of weight-biased attitudes specifically among bariatric surgery providers, indicating an important gap in the literature.

The stigma that many individuals who may qualify for bariatric surgery are forced to endure may affect them in several ways. Often, these patients have had long histories of weight bias and stigma experiences by the time they decide to consider bariatric surgery. Some of these experiences may have occurred in the clinical setting, which may affect their willingness to interact with healthcare professionals in bariatric surgery clinics. Considering that patients who undergo bariatric surgery need more sustained interactions with healthcare professionals, it is important to keep this in mind and try to support patients who undergo bariatric surgery by providing an empathic and non-judgmental clinical environment(434).

In bariatric settings, the categorization of "severely obese" — a designation based on body mass index — is often used to designate anyone who has a BMI > 40, or a BMI >35 accompanied by one or more associated comorbidities. This categorization can be experienced by patients as stigmatizing. The Canadian CPGs have avoided this terminology to reduce weight bias and stigma.

Negative evaluations of individuals who undergo bariatric surgery (i.e., due to the misperception that bariatric surgery is the "easy way out") can also impact weight bias experiences for patients. For example, patients who undergo surgery are perceived as lazier, sloppier, and less competent than individuals who have managed their weight through behavioural interventions(435). Educating patients and the public about obesity as a chronic disease and changing the perception that obesity is a lifestyle choice may reduce weight-biased beliefs and attitudes.

Managing any chronic disease requires effort on the part of patients, as well as evidence-based treatments. Obesity is no different. Framing bariatric surgery as an obesity treatment, rather than as a weight-loss tool, could also address the misconceptions about bariatric surgery. Bariatric surgery healthcare providers should avoid showing examples of extreme weight loss outcomes ("outliers") in presentations or promotional materials, as this promotes unrealistic weight loss expectations and continues to position obesity treatment outcomes as weight-loss focused. Providing information about the significant effort that is required to manage obesity and undergo bariatric surgery may also help reduce weight bias and stigmatizing experiences for people living with obesity.

Many patients who undergo bariatric surgery expect weight bias and stigma to decrease after they have had bariatric surgery, as a result of their weight loss. However, weight bias experiences after bariatric surgery can still come from friends, family members, and colleagues, and from other healthcare professionals outside the bariatric surgery setting. Many patients experience anxiety in social situations, for fear of attracting attention when only eating small amounts or when experiencing gastrointestinal symptoms(432). Some patients are afraid to tell their family or friends that they have had bariatric surgery, for fear of being shamed for taking “the easy way out.” This highlights the importance of having more follow-up care, including psychological support after bariatric surgery. Helping patients to cope with these weight-biased experiences with their families, friends, and colleagues should be part of any pre- or post-bariatric surgery care plans.

Experiencing weight bias and stigma, along with weight bias internalization, can impact bariatric treatment outcomes. For example, in 2012, Lent et al identified a link between pre-operative weight bias internalization scores and post-operative weight loss, suggesting that being screened for weight bias internalization is an important step prior to undergoing bariatric surgery(436).

Given the focus in the Canadian clinical practice guidelines on health, rather than weight loss, as the target of intervention, it is important to better understand how weight bias and stigma might impact health behaviours like physical activity and healthy eating among individuals who are considering undergoing bariatric surgery. In a study examining the mediating role of weight bias internalization in the relationship between self-efficacy and preoperative physical activity levels, associations were identified between lower self-efficacy and higher rates of weight bias internalization(437). Developing interventions that target preoperative weight bias internalization may, therefore, assist in increasing preoperative physical activity levels among patients seeking or considering bariatric surgery(437). That said, more research is needed to better understand the effectiveness of interventions and track outcomes over time.

Weight bias internalization also is associated with less weight loss, lower mental health related quality of life, poorer dietary and supplement adherence, lower levels of moderate to vigorous physical activity, and increased barriers to and lower self-efficacy of physical activity(438). Additionally, weight bias internalization is correlated with greater eating-disorder psychopathology, overvaluations of weight/shape, depression, and lower self-reported mental health(58, 434, 439).

Recommendations for reducing weight bias, stigma, and discrimination in healthcare settings (Extracted with permission from the Canadian Clinical Practice Guidelines, Reducing Weight Bias in Obesity Management, Practice and Policy Chapter, Version 1)(353)

1. Healthcare providers should assess their own attitudes and beliefs regarding obesity and consider how their attitudes and beliefs may influence their delivery of care.
2. Healthcare providers should recognize that internalized weight bias (bias towards oneself) in people living with obesity can affect behavioural and health outcomes.
3. Healthcare providers should avoid using judgmental words, when working with patients living with obesity.
4. Healthcare providers also should avoid making assumptions that any ailment or complaint a patient presents with is related to their body weight.

Promising strategies to reduce stigma in healthcare settings include:

1. Improving provider attitudes about patients with obesity and/or reducing the likelihood that negative attitudes influence provider behaviour.
2. Educating healthcare providers about obesity and weight bias to reduce weight bias in clinical settings, including bariatric surgery clinics and hospitals(440). Providing weight bias sensitivity training to all staff and having zero tolerance policies for disparaging remarks about patients who undergo bariatric surgery, fat jokes, and any other form of explicit weight bias. Education about weight bias and professional conduct should be part of resident training and training for all healthcare professionals involved in bariatric care. Similar policies need to be implemented in other hospital units where patients who are undergoing bariatric surgery could be seen, like diagnostic imaging.
3. Altering the clinic environment or procedures to create a setting where patients with obesity feel accepted and less threatened.
4. Empowering patients to cope with and challenge stigmatizing situations and attain high-quality healthcare.

Additional recommendations for reducing weight bias, stigma, and discrimination in surgical settings

1. Settings where surgery is performed should provide pre- and post-surgery resources (e.g., a contact list of professionals who specialize in bariatric surgery) to ensure patients receive adequate care that is sensitive to their needs(434).

2. It is important to screen the parents of adolescents undergoing bariatric surgery. A study by Singh et al., published in 2020, is of particular relevance to weight-bias guidelines for bariatric surgeons, as it suggests a need to provide counselling to parents of children who meet the requirements for bariatric surgery(441). Further research is needed on reducing weight bias in parents of children living with obesity.

3. Pre-screening all individuals who are considering bariatric surgery for weight bias internalization(425).

5. Bariatric healthcare providers should assess internalized weight bias and the meaning of weight for people with obesity, particularly because of the moderating effects of weight bias on obesity treatment outcomes.

6. Clinicians would be advised to address internalized weight bias as part of the course of any psychological or behavioural intervention (i.e., self-compassion as a resource; inducing empathy and influencing controllability attributions; and the careful and considered use of language). Addressing self-esteem as part of any obesity management intervention is likely to be of benefit to the individual.

Shifting from a weight focus to a health focus(420)

1. Healthcare providers should speak with their patients and agree on realistic expectations, person-centred treatments, and sustainable goals for behaviour change and health outcomes.

2. Healthcare professionals should explicitly acknowledge the multiple determinants of obesity, discuss the chronicity of obesity care, disrupt stereotypes of personal failure or success attached to body composition, and redefine success as health and well-being.

7. AREAS OF CONSENSUS

Due to its multifactorial nature, obesity requires a multidisciplinary approach. Behavioural features, particularly those related to eating behaviours, must be evaluated by mental health professionals trained in the assessment and therapeutic management of patients with obesity, since, as discussed above, the psychopathology of this population is characterized by atypical clinical presentations and psychopathological “disguises”.

In a just-conducted two-round Delphi survey of 94 intercontinental experts in obesity management, spanning all fields of obesity management, consensus was reached that patients seeking or considering MBS, a population that usually includes more severe cases of obesity, when exhibiting food addiction and emotional eating, are more likely to have other psychiatric conditions, like depression and anxiety, as well. Likewise, the experts reached consensus agreement that these patients are also at increased risk of suicide, though no consensus was achieved regarding the controversial role that bariatric surgery itself might play inducing suicide in patients with depression undergoing such surgery. Interestingly, consensus was reached that, when patients seeking or considering MBS present with a depressive condition characterized by predominantly somatic symptoms (e.g., asthenia, fatigue, and psychomotor retardation), they tend to more frequently experience improvements in such symptoms after surgery, which seems to reflect the perception that obesity not only changes the clinical presentation of depressive conditions, but seems to produce characteristic clinical presentations, such as mood disorders of metabolic origin, that are more likely to respond to weight loss, as discussed extensively elsewhere by Mansur et al.(442). The Delphi panel also consensually agreed that significant weight loss after MBS is often accompanied by reduced depressive symptoms in patients with obesity and depression, regardless of their clinical presentation, including those patients in whom cognitive features predominate. The experts did not agree that most patients with depression experience worsening of their depressive symptoms after bariatric surgery, which may reflect their understanding of the impact of weight loss on mood symptoms, regardless of their metabolic origin. Regarding patients with obesity and other potentially-severe psychiatric conditions, like schizophrenia or bipolar disorder, the experts agreed that such conditions should not be considered absolute contraindications against the surgical treatment of obesity. They similarly agreed that, once such patients’ psychiatric disorders are stabilized, they should be considered eligible for MBS.

Consensus also was reached regarding the importance of a comprehensive psychological assessment for all patients who are seeking or considering MBS, which may reflect the experts' awareness of the role that dysfunctional eating behaviours, like food binges, play in undesirable outcomes of obesity treatment. Although they consensually agreed with the existence of psychopathological phenomena, like emotional eating and food addiction, as well as with the importance that such behavioural phenomena not yet included in official nosological classifications have in the emergence of food binges, they did not agree that all individuals with obesity have food binges. They consensually agreed that the presence of binges appears to worsen some behavioural outcomes after bariatric surgery, but did not agree that a relationship exists between the presence of binges and increased rates of suicide or suicidal behaviours after bariatric surgery. They also agreed that patients who have undergone bariatric surgery and who had a history of binges are more likely to regain weight post-operatively than candidates with no history of binges.

The controversial nature of food addiction was acknowledged by the expert panel, who consensually agreed with the possibility that this phenomenon might not exist, since food contains no substances capable of acting directly on brain areas related to reward processing. Interestingly, however, they also consensually agreed that sufficient empirical evidence exists to consider food addiction a valid clinical entity, which may reflect the dissociation between real-life clinical observation and neuroscience. They also agreed that only a minority of patients with food addiction develop alcohol or other substance abuse after MBS, but also that food addiction is more common in patients who have undergone MBS who exhibit problematic use of alcohol or other substances. Regarding substance use, the expert panellists did not agree that virtually all patients who undergo bariatric surgery will develop problematic alcohol use after surgery. There also was no consensus reached that patients undergoing bypass are more susceptible to problematic alcohol use post-operatively. Despite some anecdotal reports in the literature about improved behaviours related to alcohol use in some patients undergoing bariatric surgery, the Delphi experts consensually disagreed that such cases exist, which may reflect their perception that such cases may not be frequent enough to render them worth citing. This potentially reflects the reality of the few patients with personality traits that, together, facilitate their recovery from both problematic alcohol consumption and obesity.

Table 4-2: Consensus reached on psychological issues and their management

Statements	Most common selection	Percentage consensus	Consensus achieved
Patients undergoing MBS virtually always develop problematic alcohol use post-operatively.	Disagree	95.60%	Yes
Patients with severe psychiatric conditions, like schizophrenia or bipolar disorder, should not undergo MBS, unless the psychiatric condition is well controlled.	Agree	95.60%	Yes
A comprehensive psychological evaluation should be completed before MBS	Agree	93.60%	Yes
Patients undergoing MBS with predominantly cognitive depressive symptoms (e.g., difficulty concentrating, memory loss) usually do not exhibit any improvement in their depressive symptoms after surgery.	Disagree	89.70%	Yes
Most patients with depression experience worsening of their depressive symptoms after MBS.	Disagree	87.50%	Yes
Patients undergoing MBS who predominantly have somatic depressive symptoms — like asthenia, fatigue, and psychomotor retardation — tend to have fewer depressive symptoms after bariatric surgery.	Agree	84.60%	Yes
The best psychotherapeutic strategy for patients with obesity and a high risk of binge eating behaviour is...	CBT	83.70%	Yes
Patients seeking or considering MBS surgery with emotional eating are more prone to having other psychiatric conditions, like depression or an anxiety disorder.	Agree	83.00%	Yes
Patients with severe psychiatric conditions, like schizophrenia or bipolar disorder, should not undergo MBS, irrespective of whether the psychiatric condition is well controlled or not.	Disagree	79.10%	Yes
Patients with depression and obesity who experience significant weight loss after MBS usually also experience improvement in their depressive symptoms.	Agree	75.00%	Yes
Patients seeking or considering MBS with food addiction are more prone to having other psychiatric conditions, like depression or an anxiety disorder.	Agree	73.90%	Yes
Overall, patients who have undergone MBS have an increased risk of suicide.	Agree	70.90%	Yes
Bariatric surgery increases the suicide rate among patients undergoing MBS who already have clinical depression.	Agree	68.40%	No
Patients undergoing gastric bypass are more susceptible to developing problematic alcohol use post-operatively.	Agree	57.00%	No

8. CONCLUSIONS

The treatment of obesity must be performed by a multidisciplinary team and include a comprehensive psychological assessment and follow-up by a trained psychotherapist, preferably with considerable expertise managing patients with obesity.

Identifying dysfunctional eating behaviours — like binge-eating disorder, emotional eating, and food addiction — that could undermine the effectiveness of any obesity treatment modality is crucial during early assessments.

Though the concept of ‘food addiction’ remains unproven and controversial, obesity manifests many of the same symptoms.

It is also important to assess for behavioural factors that might identify patients at higher risk for developing problems associated with alcohol and other substance abuse after MBS, currently considered the most efficient treatment for severe obesity.

Patients with severe psychiatric disorders, like schizophrenia and bipolar disorder, must have it controlled prior to undergoing metabolic and bariatric surgery (MBS). The presence of this conditions, in itself, is not an absolute contraindication to MBS.

Obesity should be treated as the chronic disease that it is, both to reduce stigmatization as the result of weak willpower and to reinforce the importance of regular life-long follow-up, especially after MBS.

Healthcare providers who work with patients living with obesity need (a) to be vigilant regarding their own potential weight bias so as to eliminate it; (b) to recognize that patients with obesity typically have suffered from such bias long-term, including bias exhibited by other healthcare providers; and (c) to strive to educate patients, families, other practitioners, and the general public regarding obesity’s legitimate status as a chronic disease.

V. Lifestyle changes and other non-operative management

1. Introduction
2. Nutrition
3. Exercise
4. Pharmacology
5. Areas of consensus
6. Conclusions and recommendations

1. INTRODUCTION

The two lifestyle factors that are typically the target of weight-loss interventions are dietary approaches intended to reduce energy in-take and physical activity to enhance energy expenditure. The combination of these two lifestyle factors for weight loss is consistent with current clinical guidelines for the treatment of obesity(349, 350, 426, 443, 444, 445, 446).

Numerous studies have found that the magnitude of initial weight loss achieved is related to the level of dietary adherence and overall caloric deficit, rather than the macronutrient composition of the diet(447). Thus, there is general consensus that attention should focus on strategies that will lead to the long-term selection of healthy, calorically-appropriate dietary regimens. A patient-centred approach is needed to increase the likelihood that patients will be offered a healthy and sustainable dietary plan. Consideration of pre-existing individual dietary preferences, genetic background, and metabolic profiles will help to optimally match patients with specific types of diet strategy. As therapists, we need to be able to identify patients' capacity to sustain healthy dietary changes(448) by identifying challenges like the food environment, socioeconomic factors, cooking skills, job requirements, medical comorbidities, and caregiving responsibilities, among others. Successful obesity management requires lifelong treatment and there is a pressing need to help patients navigate day-to-day realities in the face of maintaining permanent and intentional behavioural changes. To prevent weight regain, we need to better understand how family, community, and society as a whole can help to support and sustain healthy lifestyles.

Long-term adherence can be considered one of the main behavioural challenges. One possible explanation for declining adherence is that the perceived costs of adherence gradually exceed the perceived benefits(449). Behavioural approaches that have been shown to facilitate long-term weight loss can be conceptualized as utilizing different approaches to change the cost-to-benefit ratio and, thereby, promote longer-term adherence. Such approaches include strategies to (a) increase support from peers or professionals and maximize motivation; (b) make it easier to follow the routine by providing food or meal-replacement or via reducing boredom by varying the intervention; (c) facilitate the development of self-regulating skills through self- monitoring, and establishing this skill set prior to embarking on weight loss efforts, and (d) varying the dose, intensity, and/or behavioural support for physical activity(448). Many of these approaches have been documented to produce small, but statistically-significant improvements in longer-term weight maintenance, but no approach has worked to change the overall pattern of weight loss and regain. This lack of success would suggest that we need a better understanding of the motivating factors underlying adherence and how patient perceptions of the cost-to-benefit ratio change over time.

Within the continuum of care for people with obesity, lifestyle modification — including diet, physical activity, and behaviour modification — is considered the first-line treatment(444). Behavioural interventions are also important adjuncts to anti-obesity medications and bariatric surgery(450). Core components of behavioural modification include goal-setting, self-monitoring, and stimulus control. Behavioural modification is frequently supplemented with cognitive restructuring, problem-solving, and relapse prevention planning(450, 451). Motivational interviewing, a patient-centred therapeutic approach used to help patients overcome ambivalence to change, can also be used, along with more traditional behavioural approaches, to increase patients' intrinsic motivation and enhance their weight loss(450).

Self-monitoring is the cornerstone of behavioural treatment. It involves recording food intake, weight, physical activity, and associated factors like emotions, thoughts, and activities)(414). Via self-monitoring, patients become aware of patterns they need to address through behavioural treatment. For example, they may learn they need to implement more adaptive stress management strategies, address maladaptive thoughts related to eating, and/or restructure their home environment to reduce their access to stimulating foods. Behavioural interventions also involve setting small, realistic, action-oriented goals, problem-solving to overcome barriers to achieving goals, and planning how to prevent relapse.

2. NUTRITION

a. Introduction to nutrition and weight loss

Effective behaviour management and psychological well-being are fundamental to achieving treatment goals for people with obesity and other chronic metabolic diseases. Together with other lifestyle factors – like exercise and behaviour modification — diet and nutrition play an instrumental role in achieving weight loss. Well-controlled studies in patients with obesity and type 2 diabetes have shown that intensive lifestyle interventions that incorporate several different strategies can help to achieve weight loss(349, 425, 452, 453, 454, 455, 456). Moderate weight loss, defined as a 5 to 10% reduction in baseline weight, can be achieved through conventional treatment and is associated with clinically-significant improvements in metabolic risk factors related to obesity and coexisting disorders(457).

To achieve successful weight loss and sustain it over time, European Association for the Study of Obesity (EASO) guidelines recommend changes in lifestyle behaviours; reduced energy intake while ensuring adequate nutrition quality; and as much of an increase in energy expenditure as possible(452). Regarding dietary interventions, an individualized diet that achieves a state of negative energy balance should be encouraged(458). A personalized dietary approach is also essential to meet individual values, preferences, and treatment goals and, thereby, provide a dietary strategy that is safe, effective, nutritionally adequate, culturally acceptable, and readily affordable to facilitate long-term adherence.

All this notwithstanding, over the last 40 years, several diets have become popular despite the lack of any reliable scientific support. These dietary strategies can be classified into five categories (Adapted from Freire R et al, Nutrition 2020)(459):

1. Diets designed to manipulate macronutrient content (e.g., low-fat, high-protein, and low-carbohydrate diets).
2. Diets that primarily restrict specific foods or food groups (e.g., gluten-free, Paleo, vegetarian/vegan)
3. Dietary approaches that incorporate cultural aspects and proximity foods from a specific geographical area (e.g., a Mediterranean diet).

4. Very-low calorie diets (VLCD)

5. Diets that manipulate when people can eat (e.g., fasting).

b. Dietetic strategies

i. Manipulating macronutrient content

Low-carbohydrate diets can be either normal-fat/high-protein or high-fat/normal-protein. However, despite the theory behind the carbohydrate insulin model (i.e., the carbohydrate-insulin model (CIM) predicts that increases in fasting and post-prandial insulin in response to dietary carbohydrates stimulate energy intake and lower energy expenditures, leading to positive energy balance and weight gain), clinical trials comparing low-carbohydrate and low-fat diets versus iso-protein diets have identified similar degrees of weight loss with the two dietary approaches(460, 461).

Low-carbohydrate diets permit the consumption of 50 to 100 grams of carbohydrates per day or <40% of a person's daily calories from carbohydrates(462, 463, 464). Intake of high-protein foods (e.g., meat, poultry, fish, shellfish, eggs, cheese, nuts, seeds) is encouraged. So is a greater intake of fats (e.g., oils, butter, olives, avocados). Low-carbohydrate diets are largely characterized by the consumption of low-carbohydrate vegetables (e.g., green salads, cucumber, broccoli, squash), while the intake of starchy foods — like rice, pasta, and bread — is restricted. Low-carbohydrate diets generally result in rapid weight loss, amounting to roughly 10% of a person's initial weight over the first six months(465). However, weight regain typically occurs thereafter, commonly associated with reduced adherence(466). Moreover, one group of authors, after conducting a stringent meta-analysis of 32 controlled studies, concluded that energy expenditure and fat loss were more significant with low-fat than with isocaloric low-carbohydrate diets(461).

Ketogenic diets, which are a type of very low-calorie-high-fat diet, involve a minimum of 70% of energy from fat, while severely restricting carbohydrate intake. This is done to mimic a fasting state and induce ketosis via the resulting depletion of glycogen stores. The subsequent increased breakdown of fats results in fatty acids being metabolized to acetone, after which ketone bodies replace glucose as a primary source of energy, thereby leading to weight loss(467), as well as an observed reduction in hunger and appetite(468, 469). In general, clinical trials have revealed significant weight reduction among individuals on ketogenic diets, though adverse effects — like constipation, halitosis, headaches, muscle cramps, and weakness — have commonly been observed(470). Other adverse effects, like lipemia and increased cardiovascular risk factors, have also been documented, due to either the amelioration(471, 472) or worsening(473) of the lipid profile and development of hepatic steatosis(474).

Nutritional deficiencies have also been associated with ketogenic diets. They include deficiencies in thiamine, folic acid, magnesium, calcium, and iron. Because carbohydrate-rich staples are a good source of vitamins and minerals, restricting them could have important clinical consequences. While weight loss can promote reproductive function in women with overweight/obesity, inadequate folic acid and iodine intake both increase the risk of poor foetal development in women of childbearing age(475) .

More importantly, observational data have demonstrated increased mortality associated with the long-term intake of both low-calorie diets and high-carbohydrate diets, this risk minimized when the energy derived from complex carbohydrates is from 50% to 55% of total caloric intake. Animal-derived protein and animal-derived fat also may be associated with a higher risk of mortality, whereas plant-derived protein and fat lower such risk(476).

In conclusion, ketogenic diets are associated with good short-term adherence, reduced body weight, and some amelioration of cardiovascular risk factors. However, in the long term, such differences appear to be of little clinical significance, likely due to increased carbohydrate intake long term. Moreover, many low-carbohydrate diet studies have identified an association with a significantly higher risk of all-cause mortality.

High-protein diets generally entail >30% of all calories from protein sources. Considering nutritional adequacy, high-protein/high-fat diets promote greater intake of animal products and saturated fat, with the detrimental effect of increased low-density lipoprotein cholesterol(477). Popular high-protein/high-fat diets — like the Atkins and Zone diets – appear to achieve significant weight loss for short periods of time(478). Increased protein intake has been linked to increased satiety and energy expenditures(479). While this approach appears to offer advantages for weight loss and body composition in the short term(461, 480), the limited number of long term (up to 2-year follow-up) studies that have been reported have revealed no significant differences in weight loss(481).

In conclusion, in the short term, though high-protein/low-fat diets appear to promote at least short-term weight-loss, current evidence indicates that, in the long term, a different ratio of macronutrients, associated with caloric restriction within a healthy diet, may promote similar degrees of weight loss(461, 482).

ii. Low-fat diets

Clinical guidelines support the promotion of long-term adherence, with hypocaloric low-fat diets the treatment of choice(386). Well-designed, controlled studies have demonstrated that modest weight loss using a low-fat, calorie-restricted diet in conjunction with lifestyle changes can significantly reduce the incidence of type 2 diabetes mellitus (T2DM) in pre-diabetic populations(456, 483). Generally, such diets contain <30% of their calories as fat, and especially focus on avoiding saturated and trans fats, commonly resulting in 5% reductions in weight over the first six months(484). Longer-term (one-year) results include >10% weight reduction(485), along with beneficial changes in biochemical parameters associated with increased cardiovascular risk, like reduced serum levels of low-density lipoprotein cholesterol and triglyceride, and increased levels of high-density lipoprotein cholesterol(484). Four percent weight regain at two years has also been reported(485).

iii. Restricting specific foods or food groups

There has been a recent surge in the number of diets excluding specific food groups as alternative diets for weight loss. This category includes vegetarian and vegan diets, the latter excluding all animal products, as well as the Paleo diet, which restricts many food groups including grains, dairy, and legumes; and increasingly-popular gluten-free diets.

Some evidence has supported the therapeutic use of plant-based diets as an effective treatment for overweight and obesity. However, further long-term trials are required to verify these results, as some studies have failed to identify any superiority over other weight-loss approaches(486). Moreover, a sufficient, well-designed vegetarian diet often requires collaboration with a trained nutritionist/dietitian and adequate long-term nutritional supplementation.

According to MESH(487), the Paleo (Paleolithic) diet is a nutritional plan based on the presumed diet of our pre-agricultural human ancestors. It consists mainly of meat, eggs, nuts, roots, vegetables, and fresh fruits, while it excludes grains, legumes, dairy products, and refined dietary sugars. Although evidence suggests general health benefits and weight loss, most have entailed only short-term follow-up of small groups of individuals, meaning that their results might not be generalizable to the overall population(488). Also, in follow-up studies, the reported health benefits of this approach disappeared after 24 months, and adherence was low. Another important limitation of the Paleo diet is the potential risk of deficiencies to various nutrients, which include vitamin D, calcium(489), and iodine(490). Further research is needed to support the claims of Paleo diet proponents.

With respect to gluten-free diets, little has been studied about the impact of gluten on weight control. It is not known whether gluten presents obesogenic properties or, if it does, what the metabolic mechanism might lie behind this effect(491).

iv. Mediterranean diets

The term ‘MedDiet’ reflects the traditional dietary pattern that existed in olive-tree growing areas of Crete, Greece, and Southern Italy in the late 1950s. This was characterized in the landmark Seven Countries Study after investigators observed an association between this diet and the lowest rates of coronary heart disease and longest life expectancy in all the countries that were examined(492). The main features of the MedDiet are (a) high fat intake, mostly as extra-virgin olive oil, used generously to cook and dress vegetable dishes; (b) high consumption of low-glycaemic-index, carbohydrate-rich foods, like whole grain cereals, legumes, nuts, fruits, and vegetables; (c) moderate to high fish consumption; (d) moderate to little poultry and dairy product consumption; and (e) low consumption of red meat and meat products(493). In terms of weight loss with the Mediterranean diet, the quality of fat and carbohydrates seems to be more important than the amounts of these macronutrients(494). In one meta-analysis of randomized clinical trials, the MedDiet was found to be a useful tool for reducing body weight and obesity-related metabolic alterations, particularly when total energy intake was restricted(495). In an RCT, the MedDiet yielded results comparable to those achieved with low-carbohydrate diets and superior to those of low-fat diets`, in terms of weight loss and changes in other biochemical parameters(466).

The PREDIMED-Plus trial is an ongoing, six-year, multicentre, parallel-group, randomized trial designed to compare the effects of a hypocaloric traditional MedDiet combined with physical activity promotion and behavioural support on cardiovascular disease morbimortality, relative to usual care advice, consisting exclusively of an energy-unrestricted traditional MedDiet (control group)(496). One-year results appear to document the intervention's effectiveness at significantly changing dietary habits, reducing adiposity, and decreasing the magnitude of cardiovascular risk factors in patients with metabolic syndrome, which is encouraging. However, the critical questions that the PREDIMED-Plus study still must answer are whether these changes can be maintained long term and, if so, whether such changes are associated with a substantial reduction in incident cardiovascular disease(497).

v. Very-low calorie diets (VLCD)

Several retrospective and prospective clinical trials through the 1990s revealed significant initial weight loss when very-low-calorie diets (VLCD), typically providing 400 to 600kcal/day via total meal replacements, were used. However, the 1998 expert obesity panel convened by the National Heart, Lung, and Blood Institute did not recommend the use of VLCDs due to concerns that long-term weight loss, especially after cessation of the VLCD, was not significantly different from that achieved with standard low-calorie diets(498). While studies reviewed for the 2013 guidelines suggest that short-term total meal replacement weight loss might be larger than that achieved with food-based diets, the potential for weight regain after total meal replacements appears high(469).

Very-low-calorie diets promote quick weight loss and use commercial formulas, liquid shakes, soups, or bars to replace all regular meals. Several meta-analyses comparing weight loss in individuals on very-low-calorie diets versus a low-calorie diet of 800 to 1,200 calories per day have shown that VLCD patients lose weight at a more rapid rate, but also that the rate of initial weight loss has no effect on weight maintenance after six or 12 months(485, 499). Recently, a VLCD diet plan immersed in a comprehensive primary care multidisciplinary program was demonstrated to be effective at inducing T2DM remission(500). Very-low-calorie diets achieve glycaemic control by reducing hepatic glucose output, increasing insulin action in the liver and peripheral tissues, and enhancing insulin secretion. These benefits occur soon after starting the diet, which suggests that caloric restriction plays a critical role(501). Interestingly, long-term analysis of the DiRECT (Diabetes Remission Clinical Trial) program revealed sustained remissions at 24 months in more than a third of people with type 2 diabetes. Sustained remission was linked to the extent of sustained weight loss. This study highlights the importance of developing a structured, integrated primary care-based weight management program — especially in patients whose type 2 diabetes is within six years of diagnosis — when striving to sustain remissions to a non-diabetic state, off all anti-diabetes drugs.

vi. Conclusions

Diets with equivalent caloric intake result in similar weight loss and glucose control, regardless of macronutrient contents. It is important that total caloric intake is rendered appropriate for each given patient's weight management and glucose control goals. The metabolic status of the patient — as determined by lipid profiles, and renal and liver function tests — is the main determinant of the diet's macronutrient composition. Current trends favour the low-carbohydrate, low glycaemic, Mediterranean, and low-caloric intake diets, though there is no evidence that any one of these dietary approaches is best for weight loss and optimal glycaemic control in patients with obesity and type 2 diabetes. Published studies are limited by varying definitions, high dropout rates, and poor adherence. In addition, for many patients, weight regain often follows successful short-term weight loss, indicative of the low durability of results obtained with many dietary interventions. Medical nutrition therapy and a multidisciplinary lifestyle approach remain essential components for managing weight and type 2 diabetes. The ideal diet is the one that achieves the best adherence when tailored to a patient's preferences, energy needs, and health status.

vii. Intermittent fasting (IF)

Intermittent fasting (IF) is an eating regimen that alternates between periods of eating and periods of voluntary fasting or very low-calorie intake. During the fasting period, there is a change in the use of the energy substrate: since no glucose is available, the body uses fat as its main source of energy. During fasting periods, patients can drink unlimited quantities of very-low-calorie fluids like water, coffee, tea, and light broths. Since such intake limits micronutrient intake, a general multivitamin supplement is recommended to provide adequate micronutrients. On "non-fasting" days, patients are encouraged to follow a diet low in sugar and refined carbohydrates, which reduces glucose and insulin secretion.

Several different fasting strategies exist, which involve fasting for different periods of time. Such strategies include (a) Alternate-day fasting (zero calorie intake on fasting days); (b) Alternate-day, modified fasting (>60% energy restriction on fasting days); and (c) Fasting or modified fasting two days per week.

A common and appealing feature of intermittent fasting is that dieters do not have to restrict calories every day. Weight loss likely occurs because individuals do not fully compensate on non-fasting days for the calorie deficit that occurs on fasting days. It has been suggested, however, that intermittent fasting generates weight loss that is no superior to that achieved with continuous calorie restriction plans. One randomized, one-year clinical trial evaluated the effects of intermittent fasting versus continuous energy restriction on weight loss, weight loss maintenance, and cardiometabolic risk(502). Both the magnitude of weight loss and rate of weight loss maintenance were similar in the two diet groups. However, the degree of weight regain was greater in the intermittent fasting group. Participants in the fasting group also reported more hunger than participants in the continuous energy restriction group. Intermittent fasting also may be especially difficult to sustain long term, as increased feelings of hunger may limit long-term adherence.

One systematic review and meta-analysis has evaluated the effects of fasting interventions on the regulation of anthropometric and metabolic parameters in subjects with overweight or obesity(503). Fasting was associated with significant reductions in body weight, body mass index (BMI), fat free mass, fat mass, waist circumference, low density lipoprotein cholesterol, triglycerides, systolic blood pressure and diastolic blood pressure. However, there was no significant difference in changes for total cholesterol, high-density lipoprotein cholesterol, or blood glucose and insulin concentrations.

A Cochrane review(504) evaluated the role of intermittent fasting on preventing and reducing the risk of cardiovascular disease (CVD) in people with or without a documented history of CVD. Although body weight and BMI both declined, these reductions did not satisfy the criterion for clinical significance (≥5% reduction). Also, no differences were noted in waist circumference, total cholesterol, low- or high-density cholesterol, triglycerides, fasting plasma glucose, glycated haemoglobin, or either systolic or diastolic blood pressure.

Intermittent fasting also is not free of adverse effects(502), since some patients experience some degree of dizziness, mild headache, mild nausea, and temporary sleep disturbance. Such unpleasant feelings of discomfort could seriously compromise long-term adherence.

viii. Adherence as a determinant of success

Based on the results discussed above, there is no single best dietetic strategy for weight management. Reducing daily calorie intake is the most important determinant of weight loss, and improvements in cardiometabolic factors largely depend on the degree of weight loss achieved.

The best diet for weight management is one that can be maintained long term. Healthcare providers should consult with patients before choosing a diet strategy, because successful weight loss and its maintenance depend on a patient's choices, preferences, and long-term adherence to the diet plan. Adherence to a diet is defined as the degree to which participants meet diet requirements(505). Many factors influence adherence to a dietary program, including food preferences, cultural or regional traditions, food availability, food intolerances, and the dieting individual's level of motivation. Higher-level adherence is a predictor of success. People with obesity are often stigmatized as having a lack of dietary adherence. However, a recent study demonstrated no differences in dietary adherence between lean individuals and individuals with obesity. More importantly, the investigators found that adherence was not associated with either weight status or hunger. They, thus, asserted that the belief that people with obesity do not adhere to dietary instructions due to the lack of willpower is untrue, and may in fact perpetuate weight bias and stigmatization(506).

As described by the World Health Organization's (WHO) evidence for action, 2003(507), adherence is a multidimensional phenomenon determined by the interplay of five "dimensions", of which patient-related factors are just one determinant. The common belief that patients are solely responsible for their treatment is misleading and most often reflects a misunderstanding of how other factors affect people's behaviour and capacity to adhere to treatment.

The five dimensions are:

1. Social and economic factors
2. Health system/healthcare team-related factors
3. Therapy-related factors
4. Socioeconomic factors
5. Patient-related factors

The ability of patients to optimally adhere to treatment is frequently compromised by more than one barrier. Interventions to promote adherence require several components to target these barriers, and health professionals must follow a systematic process to assess all these potential barriers. A continuous effort should be made to improve the provision of information to patients. However, motivation, which drives sustainable good adherence, is one of the most difficult determinants of treatment success for the healthcare system to provide long term. Developing patient-centred treatments and multiple treatment options and integrating patient input during the process of intervention development and evaluation, all help to address these barriers.

In summary, then, several popular diets for weight loss are not supported by scientific evidence; and, to date, no optimally-effective weight loss diet exists for all individuals. Food quality matters in a weight loss diet that is aimed to promote health. For individuals to lose weight, it is fundamental that they adopt a diet that creates a negative energy balance. However, adherence is a critical predictor of success.

c. Nutritional screening prior to metabolic and bariatric surgery (MBS)

Adherence to a dietary program is not only important in patients who elect to forgo endoscopic or surgical options. If anything, as will be explained in greater detail in Chapter 9 (Post-Operative Follow-up and Outcomes), it may be even MORE important in patients who elect to have an endoscopic or surgical intervention.

To have metabolic and bariatric surgery (MBS), patients must meet specific program and insurance requirements. Patients begin working towards clearances from designated medical specialists, psychology/behavioural health, and nutrition as part of an inter- or multi-disciplinary program. Patients are expected to schedule and attend appointments and be examined or have procedures conducted to determine if they are healthy enough to withstand surgery(446).

Several recent clinical practice guidelines (CPG) and best practices have been published that encompass nutrition care in patients who plan to have or have had MBS, including recommendations for a preoperative medical work up, as well as having a Registered Dietitian (RD) to provide a nutrition assessment, education, and ongoing evaluation and monitoring(33, 446, 508, 509, 510, 511). In addition, it is well known that the care of any patient undergoing MBS must begin pre-operatively; including screening for micronutrient deficiencies, if excellent patient outcomes are to be achieved(33, 508, 509, 511). However, research continues to show that many patients do not have some of the recommended labs or biochemical work-up completed prior to surgery. Research also points to pre-existing nutrient deficiencies as a prime predictor of more severe or additional nutrient deficiencies after surgery(512, 513).

Preoperatively, an RD must assess every patient's nutritional status, evaluate their patients' knowledge of healthy and modified post-operative eating strategies to ensure safe dietary progression, and examine their expectations for their own MBS outcomes. One of the factors that can potentially undermine patients' success is their nutrient status. If recommended screening for a micronutrient has not been conducted pre-operatively, a patient's status may be compromised. Research continues to show that patients who have a nutrient deficiency preoperatively generally develop more severe and other nutrient deficiencies post-operatively(33, 509, 512, 513).

Research also shows that any type of major surgery creates physiological stress which tends to compromise the status of some nutrients(514, 515). Additionally, we now know that 12 micronutrients (vitamins A, C, D, E, B6, B12 and folate; as well as iron, zinc, copper, magnesium, and selenium) are involved in every stage of a fully functioning immune system, which includes maintaining physiological barriers and innate, inflammatory, and adaptive immune responses(516, 517). Many of these micronutrients are often deficient post-bariatric surgery(33, 446, 508, 509, 518). This means not only that patients' energy level might lag postoperatively, but that they may be more susceptible to viruses and other recurrent infections that can impair their ability to fully function, be physically active, eat healthfully in small amounts, and take their recommended vitamins and minerals(516, 517).

d. Practicalities of the dietary assessment

Numerous issues must be considered when collecting a dietary history, as a person's dietary intake is influenced by many factors. These include their cultural background, economic status, working patterns, and ability to cook and prepare food. Collecting such information can be challenging, as people with obesity may feel uncomfortable sharing dietary information for fear of being judged(353). Asking a person with obesity to recount a "typical day" and "where food fits in" allows a conversation-style approach that may be perceived by patients as less judgemental and threatening, and provides insights into the context of that patient's eating behaviours(519).

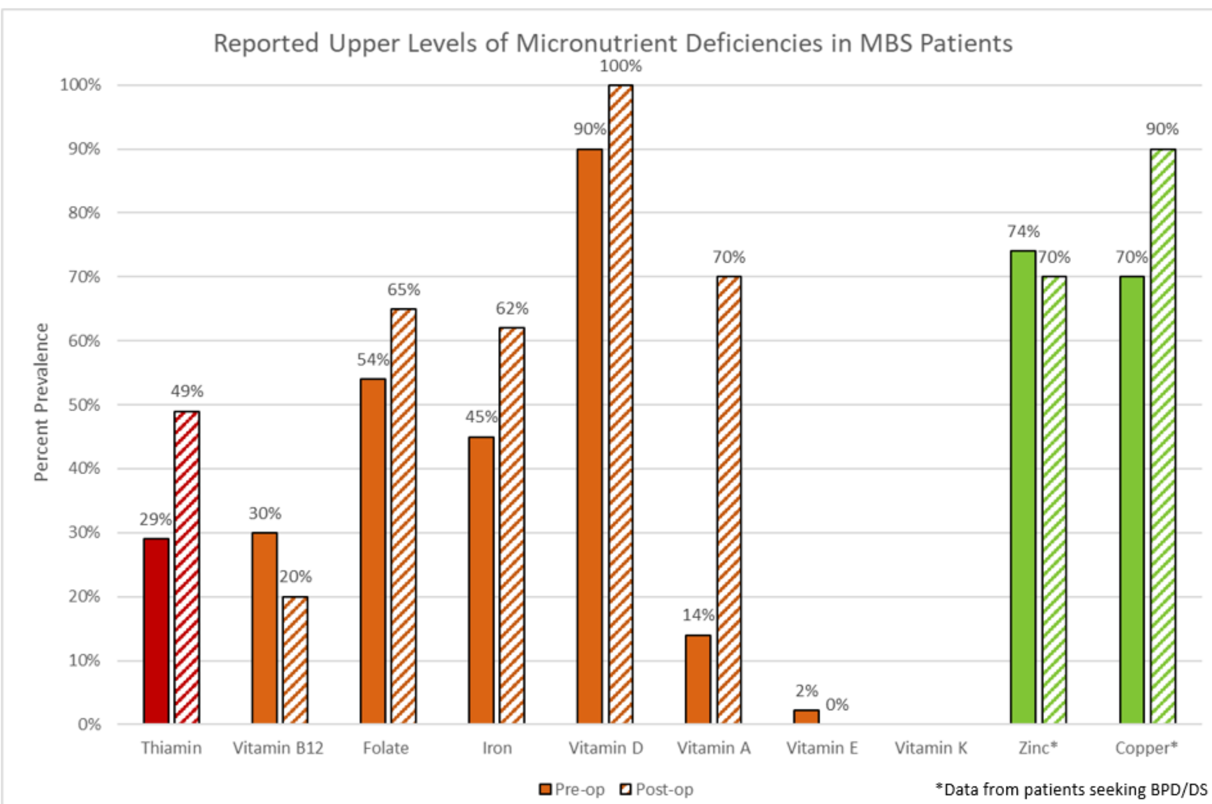
Additional information also may be needed about shift work and sleep patterns, as these can impact dietary intake too(520).

Dietitians also collect information on diseases that can affect nutritional intake and nutritional status, such as coeliac disease, Crohn's disease, and ulcerative colitis(521).

e. Prevalence of micronutrient deficiencies before and after surgery

The importance of micronutrient screening is highlighted by the high prevalence rates of many micronutrient deficiencies. Figure 5-1, below, depicts a consistent increase in reported nutrient deficiencies from pre- to post-operatively following MBS. Note that, though thiamine does not have the highest deficiency rate, it is a nutrient that, if not supplied daily, can reach deficiency levels within a very short period of time. In 2015, Stroh et al reported data from a systematic review containing 255 post bariatric surgery cases of patients who developed beriberi or Wernicke-Korsakoff syndrome (WKS) within 4-12 weeks postoperatively(522). Patients must have adequate stores of these nutrients to prevent early *de novo* deficiencies.

Figure 5-1: Common Micronutrient Deficiencies Pre- and Post-Bariatric Surgery



Since research continues to identify patients having at least one micronutrient deficiency at the time of surgery, it is important to screen patients both pre- and post-operatively for deficiencies of vitamins B1, B12, D, folate, and iron(33, 446, 508). The micronutrient deficiencies identified in Figure 5-1 have been reported in clinical practice guidelines with a focus on micronutrients. Patients undergoing malabsorptive procedues such as the duodenal switch, are at greater risk of fat-soluble vitamin and trace mineral deficiencies(32, 511). Although currently, there is insufficient evidence to support formal recommendations for newer bariatric procedures such as OAGB with bilio-pancreatic limb greater than 150 cm and SADI-s, at a minimum, current recommendations for malabsorptive procedures should be followed to provide some level of prevention for the various micronutrient deficiencies for which patients are most at risk(508, 509).

Pre- and post-operative screening for all bariatric surgeries is recommended for most vitamins and minerals, except for vitamins A, E, and K, and for zinc and copper, which are affected primarily by malabsorptive procedures. Some medications, such as proton-pump inhibitors (PPI), are known to decrease acid production and stomach pH, which increases the probability of vitamin B12 and other nutrient deficiencies. Additionally, some nutrients interact with other nutrients and/or medications if taken at the same time, such as calcium and iron. Generally, patients are advised to avoid taking calcium at the same time as iron, and to take them no less than two hours apart(33, 446, 508).

There may be valid reasons why a patient does not have all the recommended laboratory tests completed. For example, their insurance might not cover certain tests for which costs are otherwise prohibitive; or their bariatric surgery program may have decided not to incorporate certain lab tests into its clinical pathway, due to seemingly low prevalence rates for certain related disorders in that specific geographical location. There also might not be enough time to correct a nutrient deficiency if one or more is identified a short time before surgery. As dietitians/nutritionists, we may need to advocate or lobby for better insurance coverage for labs, timely screening, and treatment of deficiencies if we want our patients undergoing MBS to thrive and have the best outcomes possible. For patients to succeed with weight loss and weight maintenance and have optimal outcomes, patients should be in the best nutritional status possible prior to MBS. Ultimately, preoperative nutrient screening, treatment, and ongoing monitoring should be incorporated as part of the standard MBS clinical pathway. Further details on the post-operative monitoring and management of nutritional status in MBS patients are provided in Section IX.

d. Specific pre-operative recommendations

PRE-OP NUTRITIONAL PREPARATION

Many programs prescribe some type of preoperative diet with the goal of preventing further weight gain and decreasing liver fat, thereby creating a better visual field for the surgeon and better recovery for patients. A very low-calorie diet (VLCD < 800 kcal) or low-calorie diet (LCD < 1000 kcal) with some combination of liquids and solids containing healthy rather than saturated fats is generally used(523).

A multitude of choices exist for protein supplements, so it is common for specific products to be recommended to meet a patient's protein and caloric goals. Meal replacements are "nutritionally complete", either over the counter or commercially available in a liquid, powder, or snack bar form. These products are fortified with all 24 vitamins and minerals to meet a specific portion of patients' daily caloric goal: for example, 25% of 2000 kcals/day for four meals a day(524, 525). Protein supplements must not be confused with meal replacements, because they do not contain all 24 vitamins and minerals. In some cases, patients may use protein supplements and not a meal replacement during their preoperative phase without recognizing the difference. This confusion may exacerbate nutrient deficits at the time of surgery(526). For this reason, MBS programs should encourage patients to take a multivitamin and mineral supplement during their pre-operative preparation phase(508, 509).

PERIOPERATIVE PREGNANCY RECOMMENDATIONS

i. Pre-operative considerations

It is well known that the majority of patients seeking bariatric surgery are women of child-bearing age; and that bariatric surgery generally increases fertility(527). A higher body mass index (BMI) also is associated with higher rates of adverse maternal and perinatal outcomes(528). Twenty to twenty-five percent of all pregnant women have overweight or obesity at their first prenatal visit(529). As BMI increases in females with obesity and during pregnancy, they experience up to a three-fold elevated risk of developing gestational diabetes, hypertension, and preeclampsia(528, 529).

Patients who have had MBS and who are planning pregnancy should be assessed for adherence to vitamin and mineral recommendations and either continue taking supplements or begin taking them at least three to six months prior to attempting conception(510, 530). A multivitamin and mineral supplement should be taken daily that contains the following nutrients: copper (2 mg), zinc (15 mg), selenium (50 μg), folic acid (5 mg), iron (45-60 mg or >18 mg after AGB), thiamine (>12 mg), vitamin E (15 mg), and beta-carotene (vitamin A, 5000 IU) (level 4). Note that the retinol form of vitamin A should be avoided during pregnancy due to teratogenicity risk and supplementation should be adjusted to maintain concentrations within normal limits for pregnancy(508, 530).

ii. Post-operative considerations

Since the first 12 months after MBS are when a patient's dietary intake is most limited and weight loss greatest, most clinical practice guidelines recommend that patients wait to become pregnant until more than 18 months have passed post-operatively or until they are weight stable (446, 508, 511, 531). However, many patients become pregnant much sooner than that. In one cohort of 1016 female patients observed over a four-year timespan, only 3.8% became pregnant over the course of data collection and the mean time interval between MBS and pregnancy was 16.6 (±4.8) months. However, 41% of those who became pregnant did so within their first postoperative year(532).

It is important to educate patients about both the increased fertility they may experience post-operatively and the associated increased risks to both the mother and baby and additional nutrient needs that will occur if pregnancy occurs within the first 18 months postoperatively. One group of investigators(511) reported that, in their survey of bariatric and metabolic surgeons, only 39% reported discussing contraceptive options and only 25% of their patients were referred to another healthcare practitioner for birth control options. Bariatric surgery, particularly those procedures that alter absorption, may also change the efficacy of oral contraceptives.

One of the concerns related to pregnancy after MBS is the increased likelihood of a small-for-gestational-age baby being delivered(528, 529, 530, 533). Protein recommendations for patients after MBS have been reported to range from 60 g/d to 1.5 g/kg ideal weight per day, but higher amounts of protein — up to 2.1 g/kg ideal weight per day — may be needed during pregnancy(446, 530). In fact, foetal growth has been reported as directly correlated with maternal protein intake(533). Consequently, continued protein supplements may be necessary to help patients meet the protein needs of both bariatric surgery and pregnancy(528).

As maternal blood volume increases as part of normal pregnancy, the serum levels of many micro- and macronutrients may decrease. Anaemia is a common concern among women who have undergone MBS and an even greater concern when they are pregnant. It is important to interpret lab results assisted by obstetrical guidelines and considering markers of inflammation(508, 511, 530, 534, 535).

To ensure a healthy pregnancy and baby, the following laboratory parameters should be checked at least once per trimester, using pregnancy-specific ranges to identify deficiencies:

- serum folate
- serum vitamin B12
- serum ferritin
- iron studies including transferrin saturation and complete blood count
- serum vitamin D with calcium and parathormone (PTH)
- phosphate and magnesium
- serum vitamins A, E, and K1 – particularly with malabsorptive procedures(33, 446, 508)
- serum protein and albumin,
- renal and liver function tests
- serum zinc, copper, selenium

Keep in mind that, during the first trimester of pregnancy when hormone levels are changing rapidly, hyperemesis is common. If continued vomiting occurs, and there is a risk of refeeding syndrome (a potentially-fatal condition that may occur if food intake is increased following periods of malnourishment, caused by sudden shifts in essential electrolytes that help to metabolize food), intravenous thiamine, as well as potassium, magnesium, and phosphorus are recommended(536).

If refeeding syndrome is not a concern, intravenous thiamine should still be given at a minimum dose of 100 mg daily, along with an intravenous vitamin B complex(530). It is vital to avoid depleting thiamine levels further by giving intravenous thiamine before or along with any intravenous dextrose or glucose solution(537, 538).

Supplementation and additional screening during pregnancy should consist of:

Checking vitamin B12 levels, particularly if the patient has been taking metformin
An extra 400mcg folic acid daily over the first 12 weeks prior to planned conception.
Please note that European guidelines recommend 5mg folic acid daily for women with a BMI >30 or diabetes(532).
Replace vitamin A in supplements from retinol to beta carotene form to avoid possible toxicity(33, 508).

PAEDIATRIC RECOMMENDATIONS

The most important component of paediatric education is providing not only information on what paediatric patients need to do, but how and why they need to do each of the tasks required of them to adhere to their MBS program. For example, taking supplements requires remembering to take them and creating a new habit by incorporating them into their daily schedule. Using different prompts, such as alarms or phone apps, may be helpful. It is also important to include another family member in this process(529).

Iron deficiency anaemia is common in females with heavy menses. Adolescent females should be screened for heavy menses and must be monitored closely for potential iron deficiency anaemia after MBS. Additionally, even without MBS, adolescents may be fussy eaters and eat a limited variety of foods which may lead to nutrient deficiencies. It is critical to assess individual nutrition status both pre- and postoperatively. Evaluating labs is a vital part of this assessment. A Registered Dietitian with expertise in MBS is best equipped to assess nutritional status, including screening for nutrient deficiencies(508, 509, 529).

3. Exercise

a. Physical Activity and Obesity

Increased physical activity (PA) is an essential component of any comprehensive lifestyle intervention, where PA is characterized by any muscle movement that causes appreciable caloric expenditure. Physical exercise (or physical training) is a specific type of PA: one which is planned, structured, and repetitive and has a purpose of either improving or maintaining physical fitness(539). In individuals living with obesity, exercise promotes health benefits like weight loss, reduced blood pressure, improved physical function, enhanced lipid profile, lower fasting glucose levels, improved mental health, and better overall quality of life(540, 541, 542). Such studies also have shown that the risk of all-cause mortality can be reduced by 16-30% in moderately active individuals, relative to those who are sedentary, irrespective of their BMI and waist circumference. When the BMI is above 30kg/m^2, it can be responsible for twice as many deaths as obesity to any degree(543).

b. Recommendations for Exercise Programs

Training programs must follow the basic principles of specificity, progression, overload, reversibility, and biological individuality (as defined in Table 5-2)(544). In addition, they need to be comprehensive, regardless of a person's body weight, including activities that improve their cardiorespiratory and neuromotor function and flexibility. Such assessments must include anthropometric measurements — like the person's weight, height, and BMI — and information regarding that person's demographic characteristics, physical limitations, cardiometabolic status, emotional issues, personal preferences, and pre-existing daily physical activity habits (Table 5-3). They also need to focus on identifying exercises that each given patient will be both capable of doing and willing to do, to increase program adherence and effectiveness(539, 541, 542, 545).

Aerobic exercises — like running and walking — improve a person's general physical fitness, mental health, and cardiometabolic status, among other advantages. Strength training — also known as resistance training and including activities like lifting weights, functional training (which consists of exercises aimed at facilitating activities of daily living), and certain types of fitness class — either reduce the amount of muscle mass that is lost or actually increase muscle mass (hypertrophy). Strength training also can improve someone's posture, physical function, and bone density and reduce their risk of injury.

Neuromotor exercises that involve balance, proprioception, agility, motor coordination, and gait improvement are especially relevant for patients undergoing some surgical intervention for obesity, due to sudden changes in their centre of gravity caused by rapid weight loss.

Flexibility exercises maintain or improve joint range, are linked to body function, and seem to decrease bodily pain either caused or exacerbated by excess weight.

To maintain body weight and health, roughly 150 minutes per week of aerobic exercises, of moderate to vigorous intensity, are recommended. To lose weight and avoid weight regain, more than 200 minutes per week might be necessary. Sessions can be continuous or partitioned into 10-minute blocks, the latter especially suited for obese individuals with cardiovascular and orthopaedic comorbidities, and for those who are extremely sedentary or highly obese. Such reduced goals (e.g., weight maintenance) can exert health benefits even when they have no impact on a person's weight (Table 5-4). Strength exercises should be performed two or more times per week and focus on the main muscle groups (Table 5-5)(539, 541, 542, 545, 546).

There is a dose-response relationship between physical activity and health outcomes(539, 546). However, excessive exercise volume or loads are associated with increased injuries, immune function impairment, and hypoglycaemic episodes. Therefore, both the physical assessment and the guidance provided by a Physical Education professional specialized in obese and bariatric patients are essential(539, 547, 548, 549, 550).

Even when following a physical training program, the total amount of time spent in sedentary behaviours should be reduced. Adding breaks for short walks during prolonged periods of sitting can improve endothelial function, enhance carbohydrate and lipid metabolism, and increase electromyographic activity in muscle. It also improves quality of life and decreases someone's risk of developing cardiovascular disease and certain types of cancer(539, 551, 552).

c. Exercise and bariatric surgery

Studies have shown that most patients undergoing bariatric surgery are insufficiently active preoperatively(553). Low levels of cardiorespiratory conditioning can increase the incidence of complications during surgery and elevate the rate of hospital readmission over the first 30 days after bariatric surgery(554). When initiated before surgery, a physical training program can decrease the inflammatory effects of obesity, reduce a patient's weight and pain level, improve functional capacity, enhance cardiometabolic parameters, and increase quality of life(551, 552, 555). It also increases the likelihood of long-term success from the surgery. In addition, self-perception regarding the benefits of physical exercise is a predictor of better adherence to physical activity programs postoperatively(556, 557, 558).

The physical activity program of any patient undergoing bariatric surgery should start during their in-hospital peri-operative phase. Post-operatively, they should be encouraged to get out of bed, sit, stand, and begin walking as soon as possible, as studies have documented that early mobilization reduces the length of hospital stay and rates of postoperative complications(559).

After patients are discharged by the medical team, a full training program should begin, focusing on cardiorespiratory conditioning, flexibility, strength, and neuromotor exercises, in addition to patients being encouraged to adopt an overall active lifestyle(539, 546, 558).

Aerobic and resistance training promote benefits before and after bariatric surgery, regardless of body weight(552, 560). Cardiorespiratory training seems to accelerate fat loss during interventions longer than 12 weeks, probably due to increased time participating in moderate-to-vigorous physical activities(561). It is worth remembering that both the absence and inadequacy of physical activities are determining factors for weight regain, type 2 diabetes, hypertension, and losses in physical function(552).

Over time, some of the benefits of bariatric surgery — such as weight loss, type 2 diabetes remission, increased function, and reduced joint pain — may see their effects attenuated. Physical exercise plays an important role during this later post-surgical period(562). Individuals in the late postoperative period (i.e., 12 to 24 months after surgery) experience greater weight loss, increases in lean mass, and reductions in fat mass when they join exercise programs, relative to individuals who remain sedentary(557, 562).

The initiation of any physical exercise program must be grounded in the concept of health promotion, supported by educational processes that extend beyond the mere dissemination of knowledge. It must help patients to face potential future difficulties, strengthen their sense of identity, and incorporate creative solutions and health-based knowledge in their very mindsets. In addition to sharing information, practitioners who treat and follow patients who have bariatric surgery need to assist them to generate strategies to become more active and, consequently, healthier.

Table 5-2: Principles of physical training(544)

Specificity	According to the specificity principle, adaptations are specific to the muscles trained, the intensity of the exercise performed, the metabolic demands of the exercise, and the joint angle trained. For instance, if the goals of the training program were to maximize strength gains, then performing low-intensity, high-volume exercise would not be specific to the objectives of that particular program.
Progression	During a training program, adaptations occur that change the relative intensity or volume of training. To maintain the same absolute training stimulus (i.e., intensity or volume of training), the resistance needs to be continuously modified.
Overload	The basis of the overload principle is the idea that for training adaptations to occur, the muscle or physiological component being trained must be exercised at a level to which it is not normally accustomed.
Individuality	The individuality principle refers to the concept that people respond differently to a given training stimulus. The variability of the training response may be influenced by such factors as pretraining status, genetic predisposition, and sex.
Reversibility	When the training stimulus is removed or reduced, the ability to maintain performance at a particular level is also reduced, and eventually the gains that were made from the training program will revert to their original level.

Table 5-3: General guidelines for prescribing exercise for obese individuals

General Guidelines	It is important that the development of the exercise program is supervised by an exercise physiologist. The program should emphasize isometric exercises, which cause less muscle injury than isotonic exercises. Resistance training is crucial to preserving and recovering lean mass. Each individual must establish an exercise routine. Electronic devices (pedometer, phone apps) and environments with attractive distractions (e.g., music, television, scenery) can improve adherence. Individuals can change their exercise activities frequently, as long as they have some other exercise activity or activities already in place.
Types of exercise	Each patient's personal tastes must be considered (walking is usually well accepted) Exercises done in water (e.g., water aerobics, swimming) generally place less stress, especially on lower extremity joints and the back. Exercises are best that are easy to do and convenient to perform. Movements that involve large muscle groups should be emphasized. Cycle ergometers can be very useful.
Frequency/duration	Exercise should be performed throughout the day. For example: 10 minutes of walking three times daily (e.g., morning, afternoon, evening). Patients with severe obesity should start with 3–5-minute walks several times per day. In addition to regular exercise, an overall active lifestyle should be encouraged (e.g., taking stairs instead of elevators; walking instead of driving, when possible).
Assessments should include:	Anthropometric measurements (e.g., height, weight, body mass index) Demographic details A daily routine and time spent in sedentary behaviours Personal goals Previous exercise program(s) Any cardiometabolic or musculoskeletal disorders

Table 5-4: Aerobic exercise suggestions for obese individuals with and without comorbidities

AEROBIC PROGRAM			
	Times/week	*Duration (in minutes)	Exercise intensity[1]
Obesity	5 or more	30 - 60 (or 10+10+10)	Light to somewhat hard*
Type 2 diabetes mellitus	3 to 7	20 - 60	Somewhat hard
Osteoarthritis	3 to 5	10 - 30	Somewhat hard
Osteopenia/Osteoporosis	3 to 5	30 - 60	Somewhat hard
Heart disease	3 to 5	15 (or 5+5+5) - 30	Extremely light to hard**
Hypertension (controlled)	3 to 7	30 - 60	Light to somewhat hard***

*Depending on the degree of obesity and/or weight loss goals; **Depending on the level of control of heart disease; ***Depending on physical capacity and hypertension control.
Exercise intensity according to Borg Scale Rating of Perceived Exertion(563).

Table 5-5: Strength training suggestions for obese individuals with and without comorbidities

STRENGTH TRAINING PROGRAM					
	Times/week	Sets	Repetitions	Exercise intensity	Interval (seconds)**
Obesity	2 or more	2-3	2-20	Somewhat easy to somewhat hard	45-120
Type 2 diabetes mellitus	3-4	2-3	10-15	Somewhat easy to somewhat hard	60-90
Osteoarthritis	2-3	1-2	Pain limit	Somewhat easy	60-120
Osteopenia/Osteoporosis	2-3	2-3	8-12	Somewhat easy to somewhat hard	60-120
Heart disease	2-3	1-3	8-15	Somewhat easy	90-120
*Hypertension	2-3	1-2	8-12	Easy to somewhat hard	90-120 (or more)

*Strength training is not recommended for individuals with a systolic blood pressure (BP) ≥ 180mmHg or diastolic BP ≥ 110mmHg. **The duration of rest between sets.

4. PHARMACOLOGY

a. Management of obesity with medications

The 2013 American Heart Association (AHA), American College of Cardiology (ACC), and The Obesity Society (TOS) joint practice guidelines recommend, as the initial intervention for treating obesity, a comprehensive lifestyle program emphasizing dietary and behavioural modifications, and regular exercise for all patients with overweight or obesity(349). While these interventions remain the cornerstone of weight management, they may be insufficient to achieve or maintain clinically-significant weight loss, due to adaptive physiological changes that occur during weight loss, including the upregulation of orexigenic hormones and decreased metabolic rate(564, 565, 566). For individuals who are unable to achieve or maintain clinically-significant weight loss and have either a body mass index (BMI) ≥30 kg/m^2 or a BMI ≥27 kg/m^2 accompanied by weight-related comorbidities (e.g., type 2 diabetes [DM2], obstructive sleep apnoea, hypertension, hyperlipidaemia, etc.), anti-obesity pharmacotherapy may be considered as an adjunct to help offset adaptive changes in energy expenditure and appetite and improve adherence to lifestyle interventions(567).

In the United States, the Food and Drug Administration (568) has strict criteria for anti-obesity medication approval. To be approved, a medication must demonstrate at least 5% placebo-adjusted weight loss at one year, or ≥ 35% of patients must achieve at least 5% weight loss (which must be at least twice that induced by placebo). The approval criteria also require that a medication improve metabolic biomarkers, including lipids, blood pressure, and glycaemia. There are six medications currently approved for the treatment of overweight and obesity in the United States:

- Phentermine
- Phentermine/topiramate
- Orlistat
- Bupropion SR/naltrexone
- Liraglutide 3.0mg
- Semaglutide 2.4mg

The European Medicines Agency (EMA) has similarly-strict criteria for medication approval, but has only approved orlistat, bupropion SR/naltrexone, and liraglutide. In addition, sibutramine was approved by the FDA in 1997 and by the EMA in 1999, but withdrawn in 2008 and 2010, respectively, due to cardiovascular safety concerns. Sibutramine remains available in Brazil and Russia, however, so it too will be discussed here.

The decision of which medication to initiate should be based on several factors, including (1) the presence of comorbidities that might improve with medication (e.g., liraglutide 3.0mg helps to improve DM2 as a patient's weight falls), (2) medication contraindications, (3) potential drug-drug interactions, and (4) each patient's unique challenges with weight loss. The individual medications are summarized in Table 5-5, below.

Table 5-5: Anti-obesity pharmacotherapy

Medication	Mechanism of action	Dosing/administration	Clinical effects	Most common adverse events	Contraindications
Phentermine(568)	Norepinephrine-releasing agent	8.0mg-37.5mg daily (the 8.0mg dose can be administered TID, though caution should be exercised with doses later in the day, as they can induce insomnia)	Appetite suppressant	Irritability Insomnia Tachycardia Dizziness Dry mouth Hypertension	Agitated states History of drug abuse History of CVD (CAD, stroke, arrhythmia, HF, uncontrolled HTN) Glaucoma Hyperthyroidism Concurrent MAOI use (during or for 14 days afterwards)*
Phentermine /topiramate(569)	Norepinephrine releasing agent / carbonic anhydrase inhibitor and blocks voltage-gated Na channels and Ca channels	3.75/23 mg daily for 14 days, followed by escalation to 7.5/46 mg daily for 12 weeks. If needed, then escalate to 11.25/69 mg daily for 14 days followed by 15/92 mg daily	Appetite suppressant and enhanced satiety	Insomnia Paraesthesia Dysgeusia Dizziness Constipation Dry mouth	Same as phentermine. above. In addition: Nephrolithiasis Patients trying to conceive a child*,**
Orlistat(570)	Lipase inhibitor	60-120mg TID with meals	Reduces fat absorption in the gut	Faecal urgency Faecal incontinence Steatorrhea Flatus with discharge Oily spotting	Chronic malabsorption syndrome Cholestasis*
Bupropion/ naltrexone(571)	Norepinephrine and dopamine reuptake inhibitor/opioid	8/90 mg daily (in the morning) with dose escalation to 8/90 mg BID; then 16/180 mg in the	Appetite suppression	Diarrhoea Constipation Headache Nausea/vomiting	History of suicidal behaviour***

	receptor antagonist	morning, 8/90 mg in the evening; then 16/180 mg BID		Insomnia Dry mouth Dizziness	Concurrent MAOI use (during or for 14 days afterward) Uncontrolled HTN Abrupt discontinuation of benzodiazepines, alcohol, barbiturates, or antiepileptic medications Opioid agonist or partial agonist use*
Liraglutide 3.0mg(572)	Glucagon-like peptide-1 (GLP-1) receptor agonist	0.6mg daily with gradual dose escalation (1.2mg daily, 1.8mg daily, 2.4mg daily, 3.0mg daily)	Appetite suppression	Nausea Vomiting Dyspepsia Hypoglycaemia Acute pancreatitis Constipation Abdominal pain Diarrhoea Headache Increased lipase Fatigue Dizziness Cholelithiasis	Personal or family history of medullary thyroid cancer or MEN 2*,¶¶
Semaglutide 2.4mg¶	Glucagon-like peptide-1 (GLP-1) receptor agonist	0.25mg weekly, with gradual dose escalation to 2.4mg weekly	Appetite suppression	Nausea Vomiting Diarrhoea Constipation Dyspepsia Headache Nasopharyngitis Cholelithiasis	Personal or family history of medullary thyroid cancer or MEN 2*,¶¶

				Acute pancreatitis	
Sibutramine	Norepinephrine and serotonin reuptake inhibitor	5mg daily titration dose (if available), then increase to 10mg daily. Subsequent increase to 15mg daily, if <2kg weight loss in one month		Tachycardia HTN Palpitations Headache Dry mouth Constipation	Concurrent MAOI use (during or for 14 days afterward) Uncontrolled HTN Tourette's syndrome Cardiovascular disease Thyrotoxicosis Severe hepatic or renal failure*

*All medications are contraindicated in pregnancy and while breastfeeding
** The FDA requires a Risk Evaluation and Mitigation Strategy (REMS), given the increased risk of orofacial clefts with topiramate when taken during the first trimester of pregnancy[i]
***Black box warning: increased risk of suicidal thoughts and behaviours in children, adolescents, and young adults taking antidepressants for major depressive disorder and other psychiatric disorders. However, no evidence of suicidality was found in phase 3 studies
¶ This medication is not yet approved by the EMA for the treatment of overweight and obesity
¶¶ Black box warning: risk of thyroid C-cell tumours in rodents. However, no evidence was found of comparable malignancy in humans.
Abbreviations: BID, twice daily; CAD, coronary artery disease; CVD, cardiovascular disease; eGFR, estimated glomerular filtration rate; ESRD, end stage renal disease; HD, haemodialysis; HF, heart failure; HTN, hypertension; MAOI, monoamine oxidase inhibitor; MEN2, Multiple Endocrine Neoplasia syndrome type 2; TBWL, total body weight loss

b. Main treatment outcomes for medications

Obesity is considered a chronic disease. Therefore, almost all medications prescribed for it have been approved for long-term use. One exception is phentermine, which is only approved by the FDA for three-month use, because there have been no long-term safety trials for monotherapy. Many providers prescribe phentermine off-label for longer durations since it has been approved for chronic weight management in combination with topiramate ER. After initiating anti-obesity pharmacotherapy, the patient should be reassessed regularly to evaluate both the tolerability and the effectiveness of the medication regimen.

- When initiating treatment, reassess patients at regular intervals (preferably once/month) to assess both the tolerability of the medication regimen and its efficacy, typically defined as ≥5% total body weight lost (TBWL) over three months.
- If a patient does not tolerate a medication or develops unsafe side effects, or if the medication does not induce ≥5% TBWL over three months, it should be discontinued, and another agent may be considered.
- When a patient reaches a weight-loss plateau (no weight loss over 1-3 months) or experiences weight regain, consider either dose escalation of the current medication or the addition of another anti-obesity medication to target multiple pathways simultaneously. Avoid abrupt discontinuation of a medication, even if initiating another medication, as this may lead to weight regain.
- Once a desired weight has been achieved and the patient has experienced improvement in metabolic biomarkers, it is reasonable to try to reduce the overall number of medications the patient is on, or the doses of medications. However, regular follow-up with the provider is crucial at this time to monitor for symptoms (e.g., increasing hunger, cravings) and weight regain.
- Patients require long-term treatment and follow-up to maintain weight loss and prevent weight regain.

Estimated expected weight loss and specific discontinuation criteria for each medication, if specified, are listed in Table 5-6, below.

Table 5-6: Guidelines for anti-obesity medication use

Medication	Estimated % TBWL	Percentage of patients achieving ≥5% weight loss: intervention vs. placebo	Discontinuation criteria
Phentermine	At 28 weeks: 7.5mg daily: 5.45% 15mg daily : 6.06% Placebo: 1.71%	49% vs. 16% at 28 weeks	Not specified
Phentermine/topiramate	At 1 year: 7.5/46mg daily*: 7.8% 15/92mg daily: 9.8% Placebo: 1.2%(573, 574)	70% vs. 21%	7.5/46mg daily*: <3% weight loss at 12 weeks – discontinue or increase dose 15/92mg daily: <5% weight loss at 12 weeks
Orlistat	At 52 weeks: 120mg TID: 9.6% Placebo: 5.61% At 208 weeks: 120mg TID: 5.25% Placebo: 2.71%(575)	50.5% vs. 30.7%	Not specified
Bupropion/naltrexone	At 56 weeks: 160/16mg BID**: 5.0% Placebo: 1.3%(576)	48% vs. 16%	<5% weight loss at 12 weeks
Liraglutide 3.0mg	At 56 weeks: 3.0mg daily: 8.0% Placebo: 2.6%(577)	63.2% vs. 21.7%	<4% weight loss at 16 weeks
Semaglutide 2.4mg	At 68 weeks 2.4mg weekly: 14.9% Placebo: 2.4%(578)	86.4% vs.31.5%	Not specified
Sibutramine	At 24 weeks: 10mg: 6.1% 15mg: 7.4% Placebo: 1.2%(579)	At 24 weeks: 10mg: 64% vs. 15mg: 52% vs. Placebo: 13%	If clinically-significant weight loss goals are not met

Abbreviations: BID, twice daily; TBWL, total body weight loss; TID, three times daily
*7.5/46mg daily refers to the doses for phentermine and topiramate, respectively
**160/16mg BID refers to the doses of bupropion and naltrexone, respectively

5. AREAS OF CONSENSUS

In our panel of 94 international experts in obesity management, strong (> 90%) consensus was reached regarding the vital importance of a thorough nutritional assessment prior to MBS, on the importance of a patient's pre-operative nutritional status, and on the importance of identifying and correcting nutritional deficiencies before proceeding with surgery. These results are summarized in Table 5-7, below.

Table 5-7: Consensus achieved on nutritional status

Statements	Most common choice	% consensus
A comprehensive medical and nutritional evaluation should be completed before bariatric surgery.	Agree	100.00%
Nutrient deficiencies should be evaluated and corrected in all candidates for metabolic and bariatric surgery.	Agree	98.90%
A patient's nutritional status is very important prior to metabolic and bariatric surgery.	Agree	91.10%

6. CONCLUSIONS AND RECOMMENDATIONS

Despite evidence demonstrating that the surgical treatment of obesity generally achieves better long-term outcomes than totally non-surgical management, the non-surgical management of obesity nonetheless remains crucial, for several reasons, which include:

For patients who either elect against or are not deemed suitable for MBS

As adjunctive therapy to enhance surgical outcomes; and

To prevent potentially life-threatening complications like severe nutritional deficiencies in patients who either elect for or against MBS.

Obesity management should begin with a thorough assessment of every patient’s nutritional status and dietary practices, levels of activity, and medications, as well as of their levels of physical and psychological health and fitness and their treatment goals.

Any nutritional deficits that are identified must be corrected.

From that point onward, again whether surgery is elected for or rejected, non-surgical management must be tailored to each individual patient, as no one diet, exercise program, or medication will be accepted by or found effective in all patients, and none has been documented as first-line or superior to all others.

Long-term and often life-long monitoring is required to monitor the effects of treatment, identify treatment non-response or intolerance, and detect any adverse effects of whatever treatments that have been chosen.

VI. Assessing & preparing patients for bariatric procedures

1. Introduction
2. Roles of the multi-disciplinary team
3. Pre-operative patient evaluation and preparation
4. Special circumstances
   Elderly patients
   Adolescents
   COVID-19
5. Areas of consensus
6. Conclusions and recommendations

1. INTRODUCTION

As will be elaborated in Chapter 8 of these guidelines, a growing body of evidence supports the premise that metabolic and bariatric surgery (MBS) is currently the most effective treatment for patients with moderate to severe obesity, in terms of achieving and maintaining long-term weight reduction, alleviating obesity-associated conditions like type 2 diabetes mellitus and other components of metabolic syndrome, improving quality of life, and reducing mortality(580). Nonetheless, MBS carries risks and is sometimes either unnecessary or inadvisable, depending on a broad range of factors.

In addition, not every MBS procedure is suitable for every patient, again for a variety of reasons that include the goals of surgery, the patient's pre-operative health status and comorbid conditions, nutritional concerns, surgical history, and any anticipated issues pertaining to post-operative follow-up and compliance.

For all these reasons, deciding which patients warrant MBS and which MBS procedure each suitable patient should be offered requires a thorough, multi-disciplinary pre-operative assessment. This chapter provides guidelines for this assessment, which should include evaluations of each patient's medical, surgical and psychological history; current physical and psychological health and fitness; nutritional status, including any nutritional deficiencies; past level of activity and any barriers to increased activity and exercise; past and/or current addictive or obsessive behaviours; social support network; and economic welfare (e.g., can the patient afford necessary nutritional supplements). It also must include a review of past weight-loss attempts. Such detailed assessment can only be accomplished satisfactorily when a patient has access to a multi-disciplinary team.

2. ROLES OF THE MULTI-DISCIPLINARY TEAM

Patients seeking bariatric surgery should have access to comprehensive assessments by key members of a multidisciplinary team, which should include, at the very least, an obesity physician, bariatric surgeon, dietitian, and behavioural health professional(351, 446). Each member of this team should complete their own assessment of each patient to optimize patient outcomes and satisfaction. They also can serve to educate patients in the need for each component of their self-care to accentuate compliance.

Education on nutrition and the need for exercise, behavioural strategies for successful weight loss and weight maintenance, self-monitoring, mindless eating, and goal setting all are recommended during the pre-operative period, and this is best accomplished with a multi-disciplinary team. Some programs specifically include therapists who guide and monitor patients' exercise routines and activity levels. Moderate-intensity exercise of 30 minutes per day, totalling at least 150 minutes per week, can be recommended, as such a level of exercise has been associated with an additional 3.6 kg weight loss, relative to not exercising regularly after bariatric surgery(581).

Essential areas of pre-operative query include:

a. Nutrition

Most patients seeking bariatric surgery have made many previous weight loss attempts, often achieving short-term success, but suffering eventual weight regain(582). Bariatric and metabolic surgery (1) is an effective treatment option for severe and complex obesity, improving metabolic status and aiding weight loss. However, MBS also impacts a patient's nutritional intake and most procedures also impact the absorption of micronutrients to some degree(33, 508). Those procedures that are more malabsorptive – like biliopancreatic diversion and biliopancreatic diversion with duodenal switch, one anastomosis gastric bypass with long biliopancreatic limb, and single anastomosis duodenal ileal switch – also impact fat and protein absorption(508). In addition, many people with obesity have nutritional deficiencies. Therefore, it is important that patients have access to a dietetic and nutritional assessment and receive appropriate dietetic support and preparation for metabolic and bariatric surgery. Pre- and post-operative nutrition are discussed further in Chapter 5 (Lifestyle changes and other non-operative management) and Chapter 9 (Outcomes and follow-up).

Elements pertaining to nutrition that should be considered within a dietetic assessment include each patient's:

- Current nutritional status
- Nutritional intake
- Diet quality
- Eating patterns and behaviours
- Disordered eating
- Fluid and hydration
- Understanding of post-operative nutritional guidelines
- Understanding of recommendations for postoperative vitamin and mineral supplementation

After surgery, patients must be able to follow nutritional guidelines, such as adherence to a high-protein diet and vitamin and mineral supplementation. Barriers to adherence include financial limitations(583), special diets (e.g., vegan/vegetarian), and food intolerance. The team has a responsibility to ensure that patients are able to afford and access the appropriate diet and vitamin and mineral supplements after surgery.

b. Psychosocial Assessment

Though bariatric surgery is a powerful intervention, long-term outcomes are influenced by psychosocial factors, including the patient's mental health functioning(584), substance use(366) and any maladaptive eating behaviours(585). Thus, a presurgical psychosocial assessment by a behavioural health professional with specialty knowledge in bariatric surgery is recommended by professional societies as best practice(350, 586).

Overt psychological contraindications for surgery include severe, uncontrolled mental illness; current substance abuse/dependence; and current compensatory behaviours such as self-induced vomiting(586). Though psychosocial assessments do sometimes uncover such overt psychiatric contraindications that would put patients at high risk for poor outcomes, they are best viewed not as a “yes/no” or gatekeeping process, but as an opportunity to identify and reduce vulnerabilities that may compromise post-surgical outcomes(586).

To help maximize the chances of long-term, post-operative success, behavioural health professionals educate patients about psychosocial risks and make individualized treatment recommendations, including but not limited to the following:

- Establishing mental health treatment and achieving stability
- Consulting with current mental health providers to corroborate patients’ report of stability
- Completing treatment for any substance use disorder(s) and demonstrating a period of sobriety/abstinence
- Engaging in therapy to address disordered eating behaviours, like binge eating

The psychosocial assessment also serves as an opportunity to develop rapport with patients so they feel comfortable following up after surgery if problems arise(586).

c. Obesity medicine assessment

Obesity is not only a devastating disease that requires a multidisciplinary approach for treatment, but also continues to be a risk factor for chronic medical conditions like cardiovascular disease, diabetes, chronic kidney disease, nonalcoholic fatty liver disease, metabolic syndrome, and many cancers(4).

Obesity medicine physicians work with a team of other healthcare providers who include dieticians, mental health professionals, and surgeons to guide a comprehensive preoperative assessment and manage patients throughout their preoperative and postoperative journey.

The obesity medicine physician helps with selecting a bariatric procedure based upon patients’ individualized goals of therapy, including specific weight-loss targets and/or improvements in specific obesity-related complications, as well as upon their personalized risk stratification and patient preferences.

The obesity medicine physician plays other important roles on the multidisciplinary team, which include identifying patient candidates for bariatric procedures, discussing which types of bariatric procedures should be offered, outlining patient management before procedures, and optimizing patient care during and after procedures(350, 420, 444).

During the preoperative period, the obesity medicine physician starts by assessing the patient for causes of obesity through a careful medical history and evaluation of obesity-related complications. The medical history should include the patient's chronology of weight gain and family history of obesity; as well as a comprehensive evaluation of symptoms of obesity — including hunger, satiety, satiation, and cravings — to help tailor treatment options to the cause of obesity(587). Additionally, an obesity medicine assessment should entail a thorough physical examination and appropriate laboratory testing to assess each patient's surgical risk.

During the postoperative period, the obesity medicine physician monitors patients for weight-loss progress (paying special attention to those individuals with sub-optimal weight loss after bariatric surgery); makes medication adjustments for patients with comorbidities like diabetes mellitus, hypertension, and/or hypothyroidism; evaluates micronutrient status and provides supplements, as needed; and helps to orchestrate the detection and management of long-term complications, like obesity relapse (i.e., weight regain), gastroesophageal reflux, deteriorating bone health, and post bariatric surgery hypoglycaemia. Follow-up should be scheduled depending on the bariatric procedure performed and the severity of comorbidities(350, 420, 444).

d. Obesity surgical assessment

A bariatric surgeon is one of the primary facilitators for the surgical management of a patient with obesity. The decision to undergo such surgery is a major one and both the assessments performed and opinions expressed by a bariatric dietitian, psychologist, and physician must also be taken into consideration. The intention of the final discussion between the patient and the team must be to help everyone make an informed and value-based decision in the patient's best interest(588).

The field of bariatric surgery offers multiple surgical options with no clear "best amongst all" procedure. Different operations lead to different results in patients, depending on the patient's specific needs and goals(589). Bariatric surgery also entails a life-long commitment to compliance to lifestyle modification and nutrient supplementation(350). Hence, shared decision making (SDM) has gained significance in the field of bariatric surgery over the last few years(590).

Shared decision-making entails explaining all treatment options to each patient. The surgeon may then recommend a particular procedure, based on all the collated information, and then work with the patient to reach a final decision. Factors that warrant consideration during the decision-making process are the patient's grade of obesity; status of associated co-morbidities, like type 2 diabetes, gastroesophageal reflux disease (GRD), and heart disease; patient mobility; the patient's lung and liver health; and so on. Future compliance with medications, supplements, and lifestyle modifications also must be assessed prior to surgery; and any history of addictions, especially smoking, must be taken into account.

Most importantly, a patient's choice of procedure must be discussed at length, during which time, they must be informed about the various pros and cons of each procedure to help them make a final, informed choice. The final decisions about whether to have surgery and which type of procedure to have must result from a two-way, informed discussion between the patient and bariatric team.

Bariatric surgery is a life-long partnership between a patient and that patient's bariatric team. Initial decision-making sets the tone for this relationship. In our endeavours to achieve the best outcomes for our patients, decision making must involve the patients themselves. Optimal results are achieved when both the surgical team and the patient work in tandem to arrive at educated choices.

3. PRE-OPERATIVE PATIENT EVALUATION & PREPARATION

Bariatric surgery should be considered for patients over 18 years of age with a BMI $\geq$ 35kg/m^2, who have at least one obesity-related complication, including type-2 diabetes (T2DM), hypertension, hyperlipidaemia, pseudotumor cerebri, osteoarthritis, non-alcoholic fatty liver disease or non-alcoholic steatohepatitis, severe reflux, or obstructive sleep apnoea(350). Bariatric surgery is also indicated for patients with a BMI $\geq$40kg/m^2, independent of the presence of obesity-related complications. Bariatric surgery may also be considered in patients with a BMI between 30 and 34.9 kg/m^2 with obesity-related complications, especially T2DM, who have been refractory to nonsurgical attempts at weight loss(591, 592). The BMI criterion should be adjusted for ethnicity (e.g., BMI thresholds decreased by 2.5kg/m^2 for Asian patients). Bariatric surgery should also be discussed in adolescents with similar indication criteria, and potentially-eligible adolescents referred to bariatric centres with experienced bariatric and paediatric teams for further discussion and investigation(529).

a. General considerations for bariatric surgery candidates

All patients must be committed to their educational process for bariatric surgery and to adhering to long-term medical and nutritional follow-up. The most common contra-indications to bariatric surgery include unstable psychiatric illness, substance abuse, reduced life expectancy, and active malignancy.

b. Weight history

Assessing a patient's weight history, including all previous weight loss attempts, provides powerful insights into a person's life story(352). Many people with obesity have tried numerous weight-loss interventions, often with initial success followed by weight regain(582). Discussing what has worked well or less well may guide future treatment plans. It is also helpful to establish whether the person's weight is currently stable or if they are presently losing or gaining weight(352).

c. Pre-operative nutritional evaluation

Multiple studies have shown that patients living with obesity have a high risk of inadequate nutritional status, vitamin and mineral deficiencies, and malnutrition(33). In a large, multicentre observational study of 106,577 patients undergoing bariatric surgery, 6% of patients had protein deficiency and this was associated with a 20% increased odds of death or serious morbidity(593). Pre-operative evaluation and optimization of nutritional intake and micronutrient levels prior to surgery (more specifically vitamin D, vitamin B12, iron and albumin levels) is thus recommended(33).

The nutritional assessment has several components, including each patient's current weight, body mass index [BMI] and waist circumference, current meal patterns and eating behaviours, nutritional status, and psychosocial factors. Body mass index (BMI) is the measurement most commonly employed to assess a person's weight status. The BMI is used as a measure of adiposity, but should be interpreted with caution(352, 594). For instance, it is not an accurate reflection of someone's true level of obesity in highly-muscular individuals and different reference values should be used for people of different ethnic family origins(352, 594). Among people with a BMI less than 35kg/m2, waist circumference helps to determine health risks(352, 594). As a measure of health risk, among men, a waist circumference that is less than 94cm is classed as indicating low, 94 to 102cm as high, and more than 102cm as very high risk. Among women, corresponding categorizations are less than 80cm, 80 to 88cm, and more than 88cm(594).

Routine pre-operative blood work should include a complete blood count and serum levels of creatinine, liver enzymes, lipids, thyroid-stimulating hormone, and either haemoglobin A1C or fasting plasma glucose. Nutritional evaluations should include an iron panel, vitamin D, calcium, parathormone (PTH), vitamin B12, folic acid and albumin. Patients undergoing malabsorptive surgeries should also have serum levels of vitamins A and E measured, while gastric bypass patients should be screened for *Helicobacter pylori*. Oligo-elements (zinc, copper, selenium) can also be considered prior to hypo-absorptive surgeries. Taking a routine multivitamin complex with thiamine and correction of deficiencies in preparation for surgery are recommended. A more detailed evaluation has been summarized in recently-published clinical practice guidelines(446).

d. Pre-operative weight loss

Preoperative weight loss has been shown, in a randomized clinical trial, to decrease both the perceived difficulty of bariatric surgery and operating time(595). Other benefits that have been reported include reduced odds of 30-day mortality and leaks(596). The amount of pre-operative weight loss and type of protocol remain debated, but most bariatric centres currently use some form of pre-operative weight-loss protocol. There is no compelling evidence of long-term benefits; however, pre-operative weight loss may make the surgery technically less difficult and reduce peri-operative complications.

e. Smoking and nicotine cessation

A minimum of six weeks cessation of smoking and all other nicotine use is recommended for all patients undergoing bariatric surgery to decrease the rate of peri-operative complications (e.g., pneumonia)(597). In addition, nicotine contributes to ulcer development by potentiating acid and pepsin secretion, diminishing prostaglandin synthesis, increasing bile salt reflux, increasing *H. pylori* infection risk, and decreasing mucosal blood flow and gastric mucus production(598).

Following gastric bypass surgery, smoking is associated with an increased risk of marginal ulcers and strictures.

f. Pre-operative testing

Cardiac evaluation – Each patient's cardiac evaluation should be based on individual risk factors and follow national guidelines (e.g., American Heart Association guidelines(599)). Patients with obesity tend to present with comorbidities at a younger age, and their anthropometric features might limit the use of traditional cardiovascular risk stratification. Alternative techniques to measure cardiac risk have emerged, especially in nuclear medicine. Positron emission tomography-computed tomography (PET-CT) might be the diagnostic imaging technique of choice(600). Patients with known or suspected heart disease should be directed to either a cardiologist or bariatric physician.

Pulmonary evaluation: Impaired pulmonary function is common in patients with severe obesity, and may include volume restriction, altered respiratory mechanics, and sleep apnoea(601). Sleep apnoea is highly prevalent (77 to 90%), independent of BMI, and most cases are not diagnosed before bariatric surgery consultation(602, 603). Sleep apnoea can result in significant respiratory, cardiovascular, and neuropsychiatric complications. Patients undergoing bariatric surgery who have non-recognized OSA may experience higher complication rates, including prolonged hospital stays, an increased rate of thromboemboli, more reoperations, elevated 30-day mortality, more challenging airway management, and increased intensive care unit admissions(602, 604).

The gold standard for diagnosing OSA is an overnight polysomnogram (PSG), but this test is impractical and costly and typically reserved for select patients. A standard clinical evaluation with validated sleep questionnaires (STOP BANG or Berlin Questionnaire) and nocturnal oximetry can be used to screen for OSA. Employing a standardized screening algorithm(605) in patients in whom the clinical suspicion of OSA is high is recommended.

Endoscopy: Controversy still exists regarding indications for preoperative endoscopy in patients undergoing bariatric surgery. The decision to perform endoscopy should be based on each individual patient's clinical symptoms and risk factors, and the type of procedure being considered. Patients considering bariatric surgery who have gastro-oesophageal reflux disease (101) symptoms, dysphagia, or symptoms suggestive of other upper gastrointestinal (GI) pathology, as well as those on chronic anti-acid therapy should undergo preoperative endoscopy(606). The *American Society for Metabolic and Bariatric surgery (MBS)* recently issued a statement that routine preoperative endoscopy is justifiable, even in asymptomatic patients, and should be done at the surgeon's discretion(607). Post-operative endoscopy is also suggested three years following sleeve gastrectomy and every five years thereafter, until better evidence emerges to clarify the exact risk of developing Barrett’s oesophagus. Another benefit of endoscopy is to screen for *Helicobacter pylori*, which is recommended in any patient undergoing any gastric bypass procedure.

Other considerations: Patients with obesity are at increased risk of several GI and hepatobiliary diseases, including non-alcoholic fatty liver disease and steatohepatitis. Abdominal ultrasound is recommended for patients presenting with a clinical suspicion of biliary disease or significantly-elevated liver enzymes(33). Little evidence exists on the need for a bone density evaluation, though it is usually considered in postmenopausal women, in patients with significant risk factors for low bone mass, or in accordance with national screening recommendations for the general population.

g. Pre-operative management of medication

Patients should receive clear instructions on which medications to continue and discontinue in the peri-operative period. Anti-inflammatory drugs are typically discontinued one week before surgery and resumed afterwards, depending on the type of surgical procedure and the drug’s potential benefits. Anti-platelet and anticoagulant medications are stopped before surgery, with bridge therapy considered in patients at elevated risk of thrombosis.

The efficacy of direct oral anti-coagulants (DOAC) after bariatric surgery is still unknown, such that some vitamin K antagonist like warfarin is advised(608). Patients should be educated, in advance, that their surgery will impact their option to use DOAC. Limited data suggests that a sleeve gastrectomy does not appear to affect the pharmacokinetics or pharmacodynamics of prophylactic rivaroxaban, but data remain too limited to draw clear conclusions on its efficacy after bariatric surgery(609).

Long-acting medications may also need to be converted after bariatric surgery to short-acting preparations or their dose adjusted, based on the medication’s clinical effectiveness. The drugs for which absorption appears to be most consistently-diminished are cyclosporin, thyroxine, phenytoin, and rifampin. Individual dose adjustments and therapeutic monitoring may be required. A pharmacology consultation should be considered in patients with complex medication regimens prior to surgery(610).

Though few if any data have been published on the use or stoppage of oral contraceptives around the time of MBS, in the United Kingdom, the Royal College of Obstetricians and Gynaecologists has published guidelines for patients with obesity through the Faculty of Sexual & Reproductive Health (FSRH)(611) that include the following statements:

- Non-oral contraceptives have been studied in only small numbers of women following bariatric surgery, but appear to be safe and effective.
- For women with a BMI $\geq$35 kg/m^2, risks associated with the use of combined hormonal contraception/contraceptives (CHC) generally outweigh the benefits.
- Women of reproductive age who are receiving counselling regarding MBS should have a discussion about contraception and have a plan for contraception in place prior to surgery.
- Women should be advised that the effectiveness of oral contraception (OC), including oral emergency contraception (EC), could be reduced by bariatric surgery and that OC should be avoided in favour of non-oral methods of contraception.
- Women should be advised to stop CHC and to switch to an alternative effective contraceptive method at least four weeks prior to planned major surgery (e.g. bariatric surgery) or any expected eriod of limited mobility.

The current authors emphasize, however, that few published empirical data exist on either the effectiveness or safety of various forms of contraception among patients with obesity, particularly prior to or after MBS.

h. Pre-operative management of type 2 diabetes mellitus (T2DM)

Few data exist regarding the management of T2DM in patients who undergo bariatric surgery over the peri-operative period. Poorly-controlled T2DM has been associated with prolonged lengths of hospital stay and increased complications after orthopaedic and colorectal surgery(612). However, randomized controlled trials suggest that neither pre- nor post-operative intensive management of T2DM in bariatric surgery patients results in better haemoglobin A1c levels at one year(613).

Patients on a liquid diet will need some adjustments of their dose of hypoglycaemic agents. Sulfonylureas, meglitinides, and SGLT2 (sodium-glucose cotransporter-2) inhibitors should be avoided by patients on a very-low calorie diet. Alpha-glucosidase and alpha-amylase enzyme inhibitors and thiazolidinediones also may be stopped during this period of time. Insulin requirements also significantly drop over this period. Intermediate- and long-acting insulin are typically reduced by 50%, while short-acting insulins are adjusted based upon capillary blood glucose measurements(614).

Given the current literature and the above-listed consensus opinions, the following recommendations are made:

4. SPECIAL CIRCUMSTANCES

a. Elderly patients

1. Introduction

Obesity is the most long-lasting pandemic humanity has ever dealt with. The World Health Organization (WHO) estimates that more than 600 million individuals currently have obesity worldwide(615). Unfortunately, this is not limited to any particular age range, as patients from childhood through the oldest-old face escalating rates of obesity and obesity-related comorbid diseases(616, 617). In the United States, which is one of the most extensively affected countries globally, roughly 32% of men and 36% of women >60 years old currently suffer from obesity(617, 618, 619).

Remarkably, obesity conveys a higher risk of several other comorbid conditions that negatively impact quality of life and constantly increase the risk of death(580). This is also true in the geriatric population: obesity accentuates physical disabilities, worsens the severity of chronic metabolic diseases, and escalates the risk of other geriatric syndromes(617).

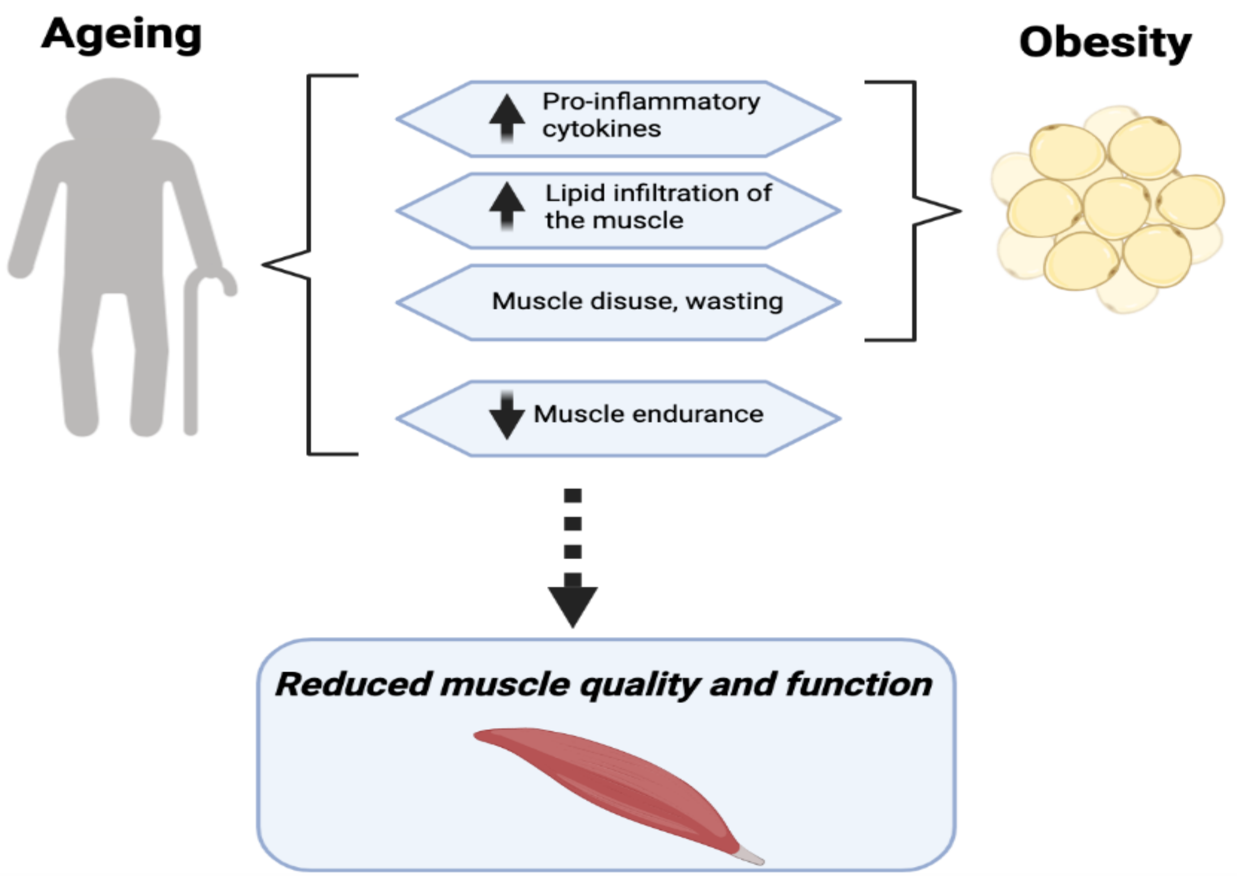
In this context, older adults with obesity must not be denied treatment. Nonetheless, one also must carefully assess the risk-benefit ratio of any proposed therapy. Pre-emptive individualized healthcare seems central to reducing the risks of procedure-related adverse events (AEs)(620). This section discusses important topics in the bariatric treatment of seniors with obesity.

2. Non-operative management

Nutritional counselling is the first step in every therapeutic algorithm for obesity(621). It is the least invasive approach with virtually no associated risk of adverse events. Besides regulating caloric intake, dietary counselling may also assess for and treat other nutritional deficits that are more prevalent among the elderly(622).

Another typical geriatric disorder, *sarcopenia*, is also frequently associated with excess body weight. This condition, also known as *sarcopenic obesity*, causes physical function to deteriorate and escalates a person's risk of falls (Figure 6-1)(623)[10]. Nutritional counselling, especially when accompanied by an exercise regimen, may address both excess weight and decreased muscle quality and function. Ultimately, this also may reduce the risk of falls and improve quality of life(624).

Figure 6-1. Schematics of the pathophysiological interaction between ageing and obesity. From Bales *et al*.(624)



Of note, exercising is an important therapeutic approach to fighting obesity. In the elderly, data show that it helps preserve fat-free mass during energy-restriction weight loss, which is critical to improving sarcopenic obesity(625). Therefore, exercises and nutritional counselling together comprise the first therapeutic step and should be indicated for all individuals who seek medical help.

The next possible treatment option is pharmacotherapy. Most currently-employed anti-obesity medications are suitable for seniors. Use of sibutramine, metformin, orlistat, fluoxetine, sertraline, phentermine/topiramate, fenproporex, mazindol, liraglutide, and amfepramone, alone or in various combinations, concomitantly or sequentially, has already been reported in the literature(626, 627). However, data on the outcomes of pharmacotherapy in the elderly remain scarce. Adverse events may occur more frequently than in younger adults, though most are transient and non-serious(626). Therefore, an individualized approach, considering comorbid conditions and medication-specific adverse effects, is warranted to minimize the risk and increase the benefit of pharmacotherapy.

Bariatric endoscopy procedures have also been proposed to address overweight and obesity in the geriatric population. Intragastric balloons (IGB) and endoscopic sleeve gastroplasty (ESG) are probably the endoscopic approaches most commonly employed worldwide. Recent guidelines do not establish an age limit for such approaches, however, which presumably grants attending physicians some discretion to adopt their use based on each patient's physiological age and general health status(628, 629). Both endoscopic therapies seem somewhat effective in terms of percentage of total body weight loss (%TBWL), which generally is from 10-20% at 12 months of follow-up(629, 630, 631). However, some studies have detected a higher risk of severe complications in adults over 60 years old than in those 60 years old or less(632).

Since IGBs and ESG are generally less invasive than standard bariatric surgery, they should be considered carefully for older patients with mild obesity or those with greater surgical risk(633). Nonetheless, since the elderly often are more fragile at baseline, one should expect an augmented risk of complications with any proposed therapy. Accordingly, an appropriate, individualized approach is needed to minimize adverse events and boost the benefits of treatment.

3. Operative management

Metabolic and bariatric surgery (MBS) is the gold-standard therapy to address moderate to severe obesity in the general population(580). Recent guidelines also recommend it with a metabolic purpose for patients with mild obesity and refractory diabetes(175). However, most studies in the bariatric field have evaluated outcomes in the general adult population, and few specific data on the elderly exist.

To help fill such a literature gap, the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO), in partnership with the World Gastroenterology Organization (WGO), conducted a two-round consensus survey of international experts specialized in the management of obesity using standard Delphi survey methodology. This survey included 94 experts worldwide who voted on, among many others, 15 statements specifically concerning the use of MBS in the elderly. Among the 15 proposed statements on MBS in the elderly, consensus (either ≥70% agreement or disagreement) was reached by the expert panel on ten. We present below the results of the survey and corresponding discussion of these results. These results are summarized together in Table 6-2.

a. Patient preparation and selection

Consensual statements	**Most selected option**	**Level of agreement**
Life-span expectations should be taken into account when considering bariatric surgery for elderly patients.	Agree	90.2%
Besides the extent of obesity and the patient's consent, patient's age should be the only consideration when surgeons are planning bariatric surgery in the elderly.	Disagree	87.2%

Statements <u>not</u> reaching consensus	**Most selected option**	**Level of agreement**
In terms of bariatric surgery, a patient should start to be considered elderly based upon their (chronological vs. physiological) age.	Based on physiological age	51.3%

Like younger individuals, several patient-related factors other than age alone should be taken into account when considering MBS in an elderly adult. Among others, these factors include life-span expectations, cognitive level, general health and fitness, muscle mass (risk of sarcopenia), bone health, patient's level of compliance, the impact of obesity on quality of life, and nutritional status (please see section 6.3.c, above).

In terms of bariatric surgery, no consensus was reached regarding when a patient should be considered elderly, though slightly more voters (51%) felt this should be based on physiological than chronological age. Accordingly, physiological more than chronological age has been singled out as a factor that warrants consideration before MBS for all individuals. In summary, chronological age appears to play a minimal role in this context.

b. Perioperative morbidity and mortality

Consensual statements	Most voted option	Level of agreement
The overall risk of bariatric surgery may be prohibitive in patients who are elderly.	Disagree	77.2%
The 30-day postoperative mortality risk of 0.4% in patients over 65 years (versus 0.1% in younger patients) contraindicates bariatric surgery in this patient group.	Disagree	86.5%
Peri-operative risk in the elderly is comparable to that of younger patients.	Disagree	71.0%

Several observational studies have already demonstrated that the overall risk of bariatric surgery in the elderly is acceptable. Of note, however, is that the literature is somewhat contradictory. While some studies have identified risk levels similar to those of younger patients(634, 635, 636, 637, 638), others have revealed slightly higher operative risk(639, 640). Accordingly, meta-analyses also disagree on this topic. For example, Marczuk et al. pooled nine studies encompassing a total of 4391 individuals who underwent RYGB (N=366 >60 years old and N=4025 ≤60 years old) and detected significant elevations among the elderly in both morbidity (odds ratio, OR = 1.88, 95% CI [1.07, 3.30], p=0.03) and mortality (OR = 4.38 [1.25, 15.31], p=0.02)(641). Conversely, another meta-analysis by Giordano et al. uncovered comparable complication rates in patients older than 60 years old versus 60 or younger, independent of the type of procedure performed(642).

Still, the absolute risk of MBS in the elderly is low and tends to be diminishing over time as perioperative healthcare continues to be refined and improved. Current data show that the 30-day postoperative mortality rate varies from 0.01% up to 0.8%, depending on the study and type of procedure (laparoscopic *vs*. open; RYGB *vs.* SG)(642, 643). In our Delphi consensus survey, most experts acknowledged increased perioperative risk in the elderly (agreement = 71%), though it seemed far from being prohibitive (agreement = 77%). Ultimately, the benefit of controlling obesity outweighs the surgical risk. Therefore, MBS is a viable and safe option to address obesity in elderly patients who are deemed fit for surgery.

c. Bariatric procedures in the elderly

Consensual statement	Most voted option	Level of agreement
Laparoscopic Roux-en-Y Gastric Bypass should be considered a viable option for patients who are elderly.	Agree	86.8%

Numerous studies have identified laparoscopic RYGB (LRYGB) as a viable option to treat obesity in the elderly(641, 643, 644, 645, 646). Interestingly, though total weight loss may be lower, the metabolic response and comorbidity amelioration rates seem greater in geriatric than in younger patients(635). This is especially true when laparoscopic SG is compared to LRYGB(646), as the latter is associated with slightly higher late complication rates than the former(643).

Concerning absolute numbers, a recent systematic review showed a mean percentage of excess weight loss (%EWL) of 66.2% at the study's endpoint and a 30-day mortality rate as low as 0.14%. The mean total postoperative complication rate was 21.1%, with wound infections the most common complication (7.58%) followed by cardiorespiratory complications (2.96%)(644). The serious adverse event rate was extremely low and explains why most experts consider LRYGB a viable option among elderly patients with obesity.

Consensual statement	Most selected option	Level of agreement
Operating time directly impacts the rate of complications in the elderly.	Agree	83.7%

Prolonged operative times are usually associated with increased rates of postoperative adverse events, mainly wound infection and pulmonary and cardiac complications(647). For LRYGB, data show that every additional 10 minutes in operative time increases the odds of leaks, any adverse event, and one-year mortality. For LSG, every additional 10 minutes leads to an increase in the one-year leak rate(648). To the best of our knowledge, however, no study has demonstrated that

MBS in the elderly requires more prolonged operative times than in younger patients. Conversely, one case-matched study uncovered no difference in the duration of the surgical procedure comparing younger adult and geriatric patients(649). Still, since prolonged operative time is a predictor of postoperative complications in the overall population, one should expect that this association also applies to geriatric patients.

Consensual statement	**Most selected option**	**Level of agreement**
Only high-volume bariatric services and experienced bariatric surgeons should operate on patients who are elderly.	Agree	82.4%

The definition of "high-volume" bariatric services is neither clear nor standardized in the literature. Data show a definite volume-outcomes relationship, but there is no inflection point to justify selecting a specific threshold to define "high-volume" centres(650). Therefore, IFSO advocates three levels of a centre's complexity, based on a more thorough assessment than just volume alone. This includes both the surgeon's and institution's characteristics to categorize centres as a Primary Bariatric Institution (PBI), a Bariatric Institution (BIs), or a Center of Excellence Bariatric Institution (COEBI). To summarize IFSO's conclusions, Primary Bariatric Institutions should generally only perform primary bariatric procedures in patients with moderate to severe obesity. Centres that fall within the second category, as a Bariatric Institution, must have at least five years of experience in the field and a surgeon who has been performing >50 bariatric surgeries yearly. Bariatric Institutions, contrary to Primary Bariatric Institutions, may also host revisional cases and patients with super-obesity (BMI $\geq 50 kg/m^2$). Finally, Centres of Excellence Bariatric Institutions are those committed to providing the highest level of excellence in the bariatric field(651).

Based on this definition, it seems appropriate that MBS in the elderly should be restricted to centres designated as either a Bariatric Institution or Centre of Excellence with surgeons who are performing >50 MBS procedures annually. Noteworthy is that bariatric surgery is generally safe and standardized despite a patient's age. However, preoperative care and patient selection are far more challenging, which validates the abovementioned consensus statement[7,39].

Statement <u>not</u> reaching consensus	Most selected option	Level of agreement
Patients who are elderly can undergo hypo-absorptive procedures.	Agree	69.6%

Hypo-absorptive bariatric procedures refer to those entailing any intestinal bypass. The most common ones are LRYGB, one-anastomosis gastric bypass (OAGB), Duodenal Switch, and SADI-S (single anastomosis duodeno–ileal bypass with sleeve gastrectomy). Although numerous data assert the safety of LRYGB in the elderly(641), other hypo-absorptive procedures have been poorly investigated in this population. San Martín *et al*. published one of the few studies to examine SADI-S outcomes (then called *sleeve gastrectomy with jejunal bypass*)(637). Among their 72 patients ≥60 years old, 29 underwent this bariatric procedure and no early complications were observed in this subset of patients. Of note, however, is that the authors did not report long-term data on nutritional or metabolic disorders. For this reason, we cannot recommend performing other hypo-absorptive bariatric procedures in the elderly outside of strict research protocols.

Statement <u>not</u> reaching consensus	Most selected option	Level of agreement
In terms of weight loss, patients who are elderly tend to respond more, less, or about the same to LRYGB than patients who are younger.	About the same	65.8%
In terms of weight loss, patients who are elderly tend to respond more, less, or about the same to LSG than patients who are younger.	About the same	60.8%

In terms of weight loss, the literature is contradictory. While some studies demonstrate similar weight loss(636, 642), others show that younger patients respond more to LRYGB than elderly patients(635, 641). As for LSG, differences between young and elderly patients also appear variable, with some studies revealing similar results(645) while others demonstrate better outcomes in younger patients(634, 652). These discrepancies probably explain the lack of consensus achieved by the IFSO/WGO expert panel on the above-mentioned assertions.

Statement <u>not</u> reaching consensus	Most selected option	Level of agreement
For elderly patients with metabolic syndrome, the gold standard procedure should be …	LRYGB	60.3%

Assessing efficacy, safety, and risk-benefit ratio is central to defining the gold-standard therapy for any disorder. In this sense, while LRYGB seems to generate more pronounced metabolic improvement(646) , it also appears to pose a higher risk of late complications(643). Conversely, LSG is usually associated with reduced operative times, shorter hospital stays, and fewer adverse events(643, 646, 653, 654, 655). Thus, no gold-standard procedure has yet been established in the geriatric population. The decision between LSG and LRYGB must therefore be individualized, considering baseline health status, presence of metabolic diseases, surgical risk, and team expertise.

d. Outcomes

Consensual statement	Most selected option	Level of agreement
Bariatric surgery in the elderly improves their overall quality of life (QoL).	Agree	96.7%

Besides promoting weight loss and ameliorating obesity-related comorbidities, MBS has been shown to improve quality of life in the overall population(656, 657). Consistent with this, available data also show that older patients with obesity similarly experience improvements in QOL, as measured using the *Bariatric Analysis and Reporting Outcome System* (BAROS). This also appears true for elderly with extreme obesity (BMI > 50kg/m^2) undergoing MBS(658).

Consensual statement	Most selected option	Level of agreement
The amount of weight loss achieved should <u>not</u> be the primary indicator of treatment success in patients who are elderly.	Agree	86.2%

Although weight loss has traditionally been employed as the primary goal of bariatric surgery, positive outcomes extend beyond just losing weight. This has become increasingly evident as surgical treatment has drifted away from a purely-bariatric perspective towards a more metabolic one. Accordingly, recent studies have shown that weight loss alone is insufficient to assess the cardiometabolic success of bariatric surgery(659). Thus, alternate endpoints are needed to define surgical success more accurately.

In 2015, the *American Society for Metabolic and Bariatric Surgery* (ASMBS) listed eight outcomes of interest arising from the operative treatment of obesity. Weight loss was one of them, along with the remission of diabetes, hypertension, dyslipidaemia, obstructive sleep apnoea, and gastroesophageal reflux disease, rate of complications, and improvement in quality of life(660). The elderly usually present with more comorbid conditions by the time MBS becomes indicated(638). Thus, metabolic improvement seems particularly important in this patient population, possibly outweighing the bariatric goal of surgery. In summary, clinical success in the elderly should be individualized by thoroughly evaluating all eight of the afore-mentioned outcomes.

Consensual statement	**Most selected option**	**Level of agreement**
The cost-benefit of bariatric surgery is greater in younger than older patients, greater in older than in younger patients, or about the same in youths and seniors.	Greater in younger patients	79.7%

Metabolic and bariatric surgery is well-established as a cost-effective treatment for obesity in adults(661). In 2018, Borisenko *et al*. published an interesting study comparing the cost-utility of non-operative and surgical management of obesity(662). By analysing European databases, the authors found that the latter approach was associated with a reduction of €2742 in mean costs to the healthcare service relative to the former. Moreover, there was a gain of 0.8 life-years and 4.0 quality-adjusted life-years (QALYs) with operative management. Of note, delaying surgery for up to three years resulted in a minor decrease of €2058 (£1459) in associated healthcare costs and a reduction of 0.7 QALYs. The authors concluded that currently-used surgical methods are cost-saving over a person’s lifetime(662). It must also be noted that cost-effectiveness takes time to become manifest. Due to their reduced baseline lifespan expectations, one should therefore anticipate that the cost-benefit ratio of MBS in older patients is somewhat inferior to that observed in those who are younger.

4. Conclusions

Obesity is a pandemic that has not spared the elderly. This subset of patients also suffers from the limitations and comorbid conditions that the excess weight is often accompanied by. As such, older individuals with obesity require treatment. For this, we recommend using a step-up approach, starting with nutritional counselling and exercises, but also including medications, bariatric endoscopy, and bariatric surgery if necessary. Several particularities exist in the perioperative management of geriatric patients with which bariatric surgeons must become familiar if they are to improve outcomes and reduce potential surgical risks.

b. Adolescents

Global rates of obesity are currently increasing in children and adolescents, while the rate of obesity in adolescents is increasing without a similar increase in the rate of adolescent metabolic and bariatric surgery (1, 663, 664). In addition, children and adolescents with severe obesity are at risk of significant obesity-related comorbidities — like type 2 diabetes mellitus, hypertension, etc. — and most children and adolescents with obesity grow up to have obesity in adulthood(665).

In adolescents, MBS requires a multidisciplinary team [e.g., a paediatric psychologist, endocrinologist, and dietitian, in addition to a bariatric surgeon] with experience dealing with children and adolescents and their families. In addition, MBS in adolescents should be performed by experienced bariatric surgeons with a proven track record performing MBS in adults and life-long follow-up is needed post-operatively(666).

Short-term studies show that MBS in adolescents is like MBS in adults, in terms of major complications, readmissions, and mortality. In addition, MBS in adolescents is generally safe and leads to excellent outcomes, including durable weight loss and improvements in obesity-related medical problems and quality of life. Sleeve gastrectomy is the most common procedure performed in adolescents, followed by Roux-en-Y gastric bypass, while biliopancreatic diversion [duodenal switch] and one-anastomosis gastric bypass are not recommended for adolescents(664).

Enough empirical evidence has been published to affirm that MBS is the most effective therapy for severe obesity in adolescents. Despite its effectiveness in adolescents, lack of physician and public knowledge and the lack of published long-term results for MBS in adolescents remain barriers preventing the referral of adolescents for MBS(667).

c. COVID-19

The worldwide spread of severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2) has occurred in the context of another alarming pandemic, which is obesity(668).

As evidenced by extensive studies evaluating the correlation between comorbidities and the course of coronavirus disease 2019 (COVID-19), obesity has emerged as a significant and independent determinant of COVID-19 severity(669, 670, 671, 672, 673). In a meta-analysis by Huang et al.(674), which analysed 45,650 patients from 30 studies with body mass index (BMI)-defined obesity and three studies with visceral adipose tissue (506)-defined obesity, both univariate and multivariate analyses revealed significantly higher odds ratios for severe COVID-19 in patients with a high BMI, in terms of hospitalization, intensive care unit (ICU) admission, need for invasive mechanical ventilation (IMV) support, and mortality. Furthermore, patients with severe COVID-19 had significantly higher VAT accumulation, suggesting that excessive visceral adiposity may have a crucial role in determining the risk of severe COVID-19. In line with these data, other meta-analyses(675, 676, 677) have revealed strong linkage between obesity, ICU admission, COVID-19 progression, and complications, with a linear dose-response association between BMI and both COVID-19 severity and mortality. Other studies have suggested that visceral adipose tissue (506) is more specifically the marker of worse clinical outcomes in patients with COVID-19(678, 679). One meta-analysis of five studies encompassing 539 patients showed that visceral but not subcutaneous adiposity was associated with enhanced COVID-19 severity (OR 1.9, P = 0.002; I 2 49.3%)(680).

The pathophysiology involved in the interplay between COVID-19 infection and obesity is likely multifactorial(681). The association between obesity and a chronic inflammatory state and VAT secretion of pro-inflammatory cytokines (IL-6) may play a significant role(682). SARS-COV2 infection induces the activation of both innate and adaptive immunity after the recognition of viral antigens and triggers the production of a large quantity of pro-inflammatory cytokines. The co-existence of obesity and COVID may lead to a hyperinflammatory state, which can exacerbate lung and systemic damage after the viral infection(681).

Obesity is characterized by increased leptin-resistance, enhanced by SARS-COV-2 infection, that is linked to dysregulated cytokine production(683) and enhanced immunosuppression by T-regulatory cells, resulting in host immunity incompetence managing attacks from pathogens and, consequently, accelerated infection(684).

Further hypothesized pathogenetic factors include the overexpression in adipose tissue of the receptors and proteases for viral entry, resulting in an ectopic viral reservoir(685), prothrombotic and vasoconstrictive states(686), and limited cardiorespiratory reserve(687).

In addition, obesity is associated with comorbidities (e.g., diabetes, cardiovascular and pulmonary disease) that are themselves considered independent risk factors and predictors of COVID-19 severity(681, 688).

Another relevant issue is that the impaired immune response in patients with obesity may lead to an attenuated COVID-19 vaccine-specific antibody response, resulting in reduced long-term protection against re-infection(689).

To date, understanding of the immune response to COVID-19, as well as the development of immunity following appropriate vaccination, is still evolving, and the long-term effectiveness of COVID-19 vaccines, in general, remains uncertain(690).

Extracting available clinical evidence from large, multicentre, global randomized controlled trials evaluating the three FDA-approved SARS-CoV-2 vaccines (Pfizer-BioNTech, Moderna, and Johnson & Johnson), there appear to be no clinical differences in vaccine efficacy in individuals with versus without obesity(691, 692, 693). Based on these vaccine data and the generally-higher risk of more severe disease progression, two scientific societies in the field of obesity - *European Association for the Study of Obesity* (EASO)(694) and the *Obesity Society*(695) - suggest that patients with obesity should be prioritized for COVID-19 vaccination. They also have promoted studies to assess the long-term efficacy of vaccinations in this particular population.

In addition to the clinical impact that obesity appears to have on COVID-19, the COVID-19 pandemic has also a direct negative impact on the obesity pandemic itself, as extensive restrictive measures have been implemented to contain spread of the virus(696, 697). Reduced physical activity and changes in dietary habits — leading to increased hedonic and/or emotional eating (e.g., boredom or anxiety/depression enhanced eating, characterized by the consumption of sweets and processed foods) — during the various lockdowns, have led to increased weight gain(698).

In addition to addressing the SARS-COV2 pandemic, the prevention and treatment of obesity during the COVID-19 pandemic should not be neglected, as the interaction of these two diseases has even more deleterious consequences.

The relationship between obesity (especially visceral obesity) and COVID-19 severity is particularly relevant, because the former is a potentially-modifiable risk factor that should be addressed urgently. Vigorous action should be taken at the public health level to promote public health education on this issue, encourage healthy eating and physical activity, and ensure adequate safety measures to prevent the spread of infections, such as comprehensive and extensive vaccinations (697).

A temporary interruption in bariatric surgical programs worldwide was one of the immediate effects of the SARS-CoV-2 virus pandemic(699). Considering that obesity is a major negative prognostic factor in COVID-19 and that non-invasive approaches are unlikely to be sufficient to facilitate adequate weight loss, the resumption of elective bariatric interventions (surgical and endoscopic) seems to be mandatory, even during the SARS-COV2 pandemic(699). After bariatric surgery or endoscopy, patients should experience a decrease in their fat reservoirs, as well as improvements in existing comorbidities and, hence, become less susceptible to severe outcomes in case of SARS-Cov-2 infection(700).

To promote the safe resumption of bariatric procedures, the adoption of strict protocols is indispensable to ensure the protection of both patients and healthcare workers. A recent multicentre observational study from Italy(699) evaluated the safety of bariatric surgery during phase 2 (from May to September 2020, a period characterized by a decrease in COVID-19 incidence) and phase 3 (from October 2020 to January 2021, a time marked by a new wave of SARS-CoV-2 infections). All participating centres adopted strict protocols to enhance the protection of patients and healthcare workers. The pre-admission protocol included patients completing a COVID-19 questionnaire and undergoing PCR/antigenic swabs to test for SARS-Cov-2 24–48 hours before hospital admission. The operating room (OR) protocol included surgeons wearing standard personal protective equipment (PPE) plus N95 masks, while anaesthesiologists and any nurses who assisted in managing the patients' airways wore N99 masks and face shields. It also included employing a smoke evacuator system or filters connected to the insufflation system to minimize air-borne contamination. Access to the operating room was limited, and a sufficient time interval was maintained between consecutive operations to permit adequate air exchange in the room. Management of in-hospital patients included the use of standard PPE by staff and of surgical masks by patients and eventual caregivers. Social distances were maintained and, whenever possible, patients were accommodated in single-bed rooms. Visitors were not permitted. If the duration of hospitalization was longer than 48 hours, a SARS-CoV-2 test was performed again at the time of patient discharge. In the case of in-hospital contact with a SARS-CoV-2 positive patient or healthcare worker, a 14-day self-quarantine period after discharge was mandatory. Using this protocol, among 1258 patients who underwent bariatric surgery, only eight (0.6%) tested positive for SARS-CoV-2 after discharge, and none experienced COVID-19-related complications or mortality (all asymptomatic or having mild disease)(699), thereby suggesting that bariatric surgery can be resumed safely, if rigorous prevention protocols are adopted.

These protocols should also be applied in the setting of bariatric endoscopic procedures that conceptually resemble surgical ones.

Given the uncertainty about the evolution of the SARS-CoV-2 pandemic, the adoption of rigorous prevention protocols and vaccine prioritization for healthcare workers and individuals with obesity (as a particularly-fragile patient group) may ensure a safe standard of care in the field of bariatrics(699).

Data from several studies show that patients who underwent bariatric surgery immediately before or during the COVID-19 pandemic have experienced inferior weight loss outcomes than those treated in the pre-COVID-19 period, regardless of the surgical technique employed(701, 702, 703). The consequences of lockdowns on dietary habits, physical activity, and mental health and, thus, limited preparation of patients for the operation, are likely linked to these findings(701, 703). To the best of our knowledge, no published data on the impact of the COVID-19 pandemic on bariatric endoscopy outcomes yet exist, but we speculate that these outcomes could be similar.

Given the chronic-relapsing nature of obesity, long-term multidisciplinary support after a bariatric procedure is mandatory to promote proper lifestyle modifications that may be hindered by the above-mentioned effects of COVID-19-related restrictions. In these pandemic times when face-to-face visits are limited, the use of remote contacts may be particularly valuable to guide patients through their weight loss programs(704).

Table 6-1: Evidence-based KEY POINT statements on Obesity and COVID-19

<table>
<tr><td>1</td><td>Obesity has emerged as a significant and independent determinant of COVID-19 severity.</td></tr>
<tr><td>2</td><td>There is a linear dose-response association between BMI and both COVID-19 severity and mortality.</td></tr>
<tr><td>3</td><td>Visceral, but not subcutaneous adiposity is associated with enhanced COVID-19 severity; thus, excessive visceral adiposity has a crucial role in determining the risk of severe COVID-19.</td></tr>
<tr><td>4</td><td>Obesity-related leptin-resistance is enhanced by SARS-COV2 infection. Dysregulation of cytokine production and enhanced immune-suppression result in the host´s immunity incompetence, which can accelerate the course of infection.</td></tr>
<tr><td>5</td><td>Obesity is associated with comorbidities (e.g., diabetes, cardiovascular and pulmonary disease) that are themselves considered independent risk factors and predictors of COVID-19 severity.</td></tr>
<tr><td>6</td><td>Conversely, the COVID-19 pandemic has had a direct, adverse impact on the obesity pandemic. Isolation during lockdown periods have amplified negative behaviours like increased hedonic eating and reduced physical activity.</td></tr>
<tr><td>7</td><td>Vigorous actions to promote public health education on this issue are necessary. Comprehensive and extensive vaccinations are required with prioritization of patients with obesity.</td></tr>
<tr><td>8</td><td>Metabolic and bariatric surgery (MBS) can be performed safely during the SARS-Cov-2 pandemic if a strict safety protocol is implemented.
<table>
<tr><th colspan="2">Patients</th></tr>
<tr><td>1</td><td>Completion of a COVID questionnaire prior to admission</td></tr>
<tr><td>2</td><td>Testing for SARS-CoV-2 within 24-48 hours prior to admission</td></tr>
<tr><td>3</td><td>Accommodation of patients undergoing MBS in single rooms, whenever possible</td></tr>
<tr><td>4</td><td>SARS-CoV-2 testing upon discharge if hospitalized more than 48 hours</td></tr>
<tr><td>5</td><td>Social distancing</td></tr>
<tr><td>6</td><td>Restriction of all visitors</td></tr>
<tr><td>7</td><td>14-day self-quarantine if patient is exposed to anyone COVID-test-positive during hospitalization</td></tr>
</table>
</td></tr>
</table>

Healthcare personnel	
1	Appropriate PPE, including N95 masks for surgeons
2	N99 masks plus face shields for anaesthesiologists
3	Limited personnel access to the operating room
4	Smoke evacuators to minimize air-borne contaminants
5	Sufficient time interval between consecutive operations to permit adequate air exchange

PPE = personal protective equipment

5. AREAS OF CONSENSUS

In the two-round Delphi survey described in Chapter 1 of these guidelines, the following statements pertaining to pre-operative MBS patient assessment and preparation achieved consensus:

Table 6-2: Consensus reached on MBS patient evaluation and preparation

Statements	Most common choice	% consensus
General health		
A comprehensive medical and nutritional evaluation should be completed before bariatric surgery.	Agree	100.0%
Nutrient deficiencies should be evaluated and corrected in all candidates for bariatric surgery.	Agree	98.9%
Among smokers, smoking cessation is recommended before bariatric surgery.	Agree	96.8%
Sleep apnoea screening is recommended, with testing only necessary in patients in whom there is a high suspicion of sleep apnoea.	Agree	89.1%
Weight reduction decreases a person's future risk of developing cholangiocarcinoma.	Not yet known	86.1%
Computed tomography or magnetic resonance imaging should be used routinely to screen for hepatocellular carcinoma in patients with metabolic-associated fatty liver disease.	Disagree	81.6%
All antidiabetic drugs have an impact in reducing the risk of hepatocellular carcinoma in patients with metabolic-associated fatty liver disease.	Disagree	80.2%

Pre-operative endoscopy should be performed in every patient undergoing bariatric surgery.	Agree	76.5%
Screening for hepatocellular carcinoma should be performed in all patients with metabolic-associated fatty liver disease.	Agree	71.1%
COVID-19		
Due to the increased risk of severe symptoms from COVID in patients with obesity, until the spread of COVID-19 is well controlled, bariatric surgery procedures should be reduced to a minimum to reduce the risk of viral exposure.	Disagree	94.9%
Considering that patients with obesity are at higher risk of a severe COVID-19 course, more restrictive measures should generally be undertaken during hospitalisation for bariatric procedures or related pre-operative evaluations.	Agree	93.6%
Especially during the pandemic, metabolically sicker patients with obesity should be prioritized for bariatric surgery, since they are at greater risk from the pandemic and treatment decreases their risk.	Agree	91.1%
Unvaccinated, metabolically-sicker patients with obesity should be prioritized for vaccination against COVID-19.	Agree	87.6%
Unvaccinated or incompletely vaccinated patients scheduled for bariatric surgery who test negative for COVID-19 at admission can be placed in double rooms with other patients who have tested negative.	Agree	83.5%
Since diabetes mellitus places patients at increased risk of a severe COVID-19 course, patients with diabetes or who are otherwise metabolically-compromised warrant special protective measures during their care.	Agree	83.3%
Outpatients undergoing pre-operative evaluations should have an antigenic COVID swab test on the day of the planned procedure or investigation.	Agree	82.3%
Before gaining any kind of access to the hospital, all patients with obesity should be contacted by telephone and asked to report any recent potential COVID exposure or symptoms, as well as any situations or behaviours that might have placed them at particular risk of becoming infected.	Agree	81.5%
Since *vitamin D* is thought to be a protective factor, measurement of and/or treatment with vitamin D should be considered prior to treating patients with obesity.	Agree	80.0%

Since elevated interleukin-6 is considered a risk factor for a more severe COVID-19 course and is disproportionately elevated in patients with obesity, the level of IL-6 should be measured in all patients being treated for obesity, either before or at the beginning of their treatment.	Disagree	76.5%
More stringent anticoagulation after surgery/endoscopy should be considered for patients undergoing MBS because of the increased risk of thrombosis due to obesity *per se* and COVID.	Agree	76.3%
Patients scheduled for bariatric surgery who require hospitalization should have a PCR swab 24 hours before hospital admission and, if their hospitalization is longer than 48 hours, should have a second PSR swab at the time of hospital discharge.	Agree	74.7%
Due to the increased risk of a severe COVID-19 course in patients with obesity, during the COVID-19 pandemic, patients undergoing bariatric surgery should be provided a single room, both pre- and post-operatively, throughout their hospitalization for surgery.	Agree	70.5%

No consensus was reached on whether the different modes of weight reduction (calorie restriction, exercise, drugs, endoscopic and bariatric surgery) differ in terms of reducing the risk of hepatocellular carcinoma.

6. CONCLUSIONS AND RECOMMENDATIONS

Based upon our review of published scientific literature and the results of the IFSO/WGO Delphi survey, the following conclusions and recommendations pertaining to pre-operative patient evaluation and preparation are made:

Once a mutually agreed-upon decision is made for a given person with obesity to be considered for MBS, extensive patient evaluation is necessary involving a multi-disciplinary team.

Crucial areas of assessment include the patient's weight history and previous weight-loss attempts; nutrition history and current status; psychosocial history and current status; medical and surgical history; current level of health and fitness; and, in present times, COVID status. Such an evaluation helps to optimize the patient's preparation for surgery which, in turn, reduces the risk of peri-operative complications and enhances long-term outcomes.

Associated diseases – including type 2 diabetes (T2DM), obstructive sleep apnoea (OSA), hypertension and dyslipidaemia – should be evaluated and appropriate treatment initiated.

Obesity is a prevalent risk factor for 13 different types of cancer and screening should be reinforced, in accordance with national guidelines.

Upper gastrointestinal (GI) endoscopic evaluation is recommended in patients with a history of reflux disease and in patients undergoing gastric bypass surgery during the pre-operative period and every five years following surgery.

Patient preparation involves ensuring that patients have realistic goals and expectations regarding the benefits and potential problems that might arise from surgery, and that all psychosocial barriers to adherence are addressed.

Patients also must be alerted to any nutritional deficiencies and have such deficiencies corrected.

Cessation of tobacco, alcohol and drugs is mandatory and should be maintained lifelong.

Patients should be assessed for and instructed in an exercise program that they can realistically resume post-operatively.

After bariatric surgery, changes in the absorption of some medications may occur. Consequently, clear instructions on required post-operative changes should be communicated to primary care physicians and the patient prior to patient discharge.

During a life-threatening pandemic like COVID-19, suitable precautions must be taken to protect patients with obesity awaiting and undergoing MBS, because they are particularly vulnerable to severe COVID symptoms and mortality.

VII. Endoscopic metabolic and bariatric therapy (EMBT)

1. Role of EMBT in the management of obesity
2. General principles and modes of action
3. Specific procedures
4. Endoscopic management of non-alcoholic fatty liver disease (NAFLD)
5. Areas of consensus
6. Conclusions and recommendations

1. ROLE OF EMBT IN THE MANAGEMENT OF OBESITY

Starting in 1991, when the first National Health Institutes (NIH) guidelines on "Gastrointestinal Surgery for Severe Obesity" were published, bariatric surgery was for a long time the only available, sustainable therapy for severe obesity, though not ubiquitously available to all individuals in need(705). Since then, this chronic disease, along with its major comorbidities of type 2 diabetes mellitus and non-alcoholic fatty liver disease (NAFLD), has increasingly become a global public health issue of pandemic proportions(706, 707, 708, 709). It is estimated, however, that only a small proportion of the 1% of patients who are eligible for surgical weight loss actually undergo surgery; moreover, bariatric surgery on its own could never treat the immense number of affected individuals(707, 710). Therefore, new options that effectively treat the underlying chronic disease and its comorbidities are urgently needed.

Endoscopy has long been an integral part of visceral surgery and, thus, also of bariatric surgery, generally in the context of complication management(711). One particular challenge was that the endoscopist had to have knowledge of both the pathophysiology and altered functional anatomy of the postsurgical gastrointestinal (GI) tract. This eventually led to the development of a separate field of expertise – bariatric endoscopy. With the advancement of endoscopic techniques and the ever-increasing and urgent need for global obesity treatment - including treatment for lower BMI ranges like Class I and II obesity - stand-alone primary endoscopic bariatric procedures have evolved in recent years. These novel, less-invasive therapeutic options largely bridge the therapeutic gap between intensive lifestyle modification (as the least invasive intervention) and more invasive bariatric surgical procedures.

When to progress from employing lifestyle changes to EBMT and when to elect EBMT over metabolic and bariatric surgery are decisions to must be made on a patient-by-patient basis and be made by a patient and multi-disciplinary team working together. However, general guidelines do exist. In the USA, for example, the criterion for an EBMT is a BMI ≥ 30 kg/m^2.

For a new form of EBMT to be adopted as primary bariatric therapy, the American Society for Gastrointestinal Endoscopy (ASGE) and the American Society for Metabolic and Bariatric surgery (MBS) have defined acceptable thresholds of safety and efficacy as:

(1) A serious adverse event (SAE) rate $\leq 5\%$; and

(2) Mean weight loss of at least 25% EWL at 12 months; and

(3) A statistically-significant mean difference of at least 15% excess weight loss between the primary EBMT and control groups(712, 713).

Like all other weight-loss therapies, EBMTs should be offered in conjunction with lifestyle modification in a multidisciplinary approach. The therapeutic goal of any treatment for obesity, whether conservative lifestyle modification or invasive gastrointestinal modification, is weight loss that is sufficient to improve the underlying disease and its comorbidities. Relative to conservative therapy, invasive alterations of the GI tract generally lead to changes in the mediation of sensations of hunger and satiety/satiation, and thus play a crucial role in the sustainable success of bariatric surgery (Fig. 7-1), whereas lifestyle modification typically is associated with only modest weight reduction(714, 715).

Figure 7-1: Weight loss induced by reduced hunger and improved satiety and satiation

Figure borrowed, with permission, from (Stier, Chiappetta Langzeitbehandlung der Adipositas- und Metabolischen Chirurgie, Springer 2022).

These anatomic changes lead to the modification of nervous signals, altered stimulation of mechanical and chemo-receptors, and alterations in hormonal metabolic signaling within the gut-brain axis. Only these pathophysiological changes make sustained weight loss seemingly possible in the treatment of chronic obesity by addressing one underlying cause - the neuroendocrine uncoupling of the regulation of eating behavior. These principles have been adopted by bariatric endoscopy, which can reproduce some of the anatomic alterations to mimic the effects of surgery and, in some cases, induce unique mechanisms of action.

2. GENERAL PRINCIPALS AND MODES OF ACTION

Endoscopic bariatric and metabolic therapies (EMBT) can be divided into gastric and small bowel interventions(716, 717). In general, gastric interventions primarily induce weight loss, from which secondary effects may impact metabolic conditions. In contrast, small bowel interventions exert direct effects on metabolic conditions irrespective of whether significant weight loss occurs or not.

Endoscopic bariatric and metabolic therapies generally work via one of four general mechanisms.

One approach adopted by EBMTs, that specifically targets the stomach, is restricting (i.e., reducing) gastric capacity, either by using space-occupying devices or via the placement of endoscopic sutures/plications to reduce stomach size.

A second approach, which again targets the stomach, is to prolong a patient's sense of satiety by delaying gastric emptying.

A third approach that has most recently emerged and again targets the stomach is to reduce caloric uptake through postprandial emptying of ingested food from the stomach. In other words, patients are not restricted in the volume of food that they eat. Instead, after the food has been ingested, a proportion of it is removed from the stomach before it has a chance to enter the small bowel and any of its caloric content digested.

The fourth EMBT approach differs from the first three described here, in that it specifically targets the small bowel. It is, in fact, an approach that has been adopted from metabolic and bariatric surgery (MBS), its mechanism being to prevent food from passing through the duodenum, by diverting food around it. Causing food to bypass the duodenum prevents food from blending with biliopancreatic digestive juices in the upper part of the GI tract, a process that is associated with both incretin- and receptor-mediated metabolic effects. Endoscopically, this can be achieved by, for example, implanting an impermeable bypass-sleeve or duodenal mucosal resurfacing.

These four general approaches are summarized in Table 7-1, below.

Note that none of these approaches has yet been approved for use in non-adults, generally only approved for individuals who are 22-years-old or older.

Table 7-1: General principles and modes of action behind various EMBTs

Principle	***Mode of action***	***Effect***
Gastric restriction	Reducing gastric capacity	Early satiety
Gastric emptying	Prolonged gastric accommodation	Prolonged satiation
Transcutaneous aspiration of gastric contents	Removing ingested calories from the stomach	Reducing nutritional energy
Bypassing the duodenum and upper jejunum (duodenal exclusion)	Biliopancreatic diversion: sectional separation of chyme from digestive juices and small bowel mucosa by channeling food through a duodeno-jejunal bypass sleeve	Modified neuro-hormonal signaling Modified composition of bile acids (in bowel and blood) Modified composition of the microbiome

3. SPECIFIC PROCEDURES

Table 7-2, below, summarizes currently-available specific endoscopic procedures, starting with four different makes of intra-gastric balloon. As stated above, intra-gastric balloons primarily work by restricting gastric capacity. The table then summarizes two forms of gastroplasty, one form of gastric aspiration, and two forms of duodenal exclusion.

a. Restricting gastric capacity

The underlying premise behind restricting gastric capacity is that this will, in turn, hasten a patient's sense of satiety, thereby causing them to consume less food and, hence, fewer calories. In addition to being used as stand-alone interventions to facilitate weight loss, EBMTs that reduce gastric capacity may be applied as bridge therapy to surgery. This leads to decreases in visceral fat and liver volume, and to thickening of the omentum and abdominal wall, all these changes intended to additionally reduce the risk of a planned operation and make it technically easier, especially in patients with a BMI > 50kg/m^2.

The two main approaches to achieving gastric restriction are (1) by filling the stomach with a balloon and, by doing so, limiting the volume of space that is available for food(718, 719, 720); or (2) partitioning the stomach in such a way that food cannot access a sizeable percentage of it, again restricting the space available for food and, by doing so, inducing premature satiety and reduced caloric consumption(721, 722, 723, 724). This first objective has traditionally been achieved through the inserting of one or more fluid- or gas-filled balloons into the stomach(718, 719, 720); the latter by using sutures(721, 724) or some form of tissue plication (folding)(722, 723).

1. ***Intragastric Balloons (IGB)**:*

Table 7-2 summarizes four types of intra-gastric balloon (IGB), the Orbera, Obalon, Spatz3, and Elipse, each with different advantages and advantages.

Since the early 1990s, the former BioEnterics Intragastric Balloon (BIB, Allergan), currently known as the Orbera™ Intragastric Balloon (Apollo Endosurgery, Austin, TX), has been widely available internationally for clinical use. The Orbera is a silicon, globate, intragastric balloon (IGB) that can be filled with a fluid volume ranging from 450-700ml. The initial model was approved for a treatment period of six months, though a newer model (Orbera 365) can remain implanted for up to 12 months.

Many other types of IGB are currently available for clinical use. There are gas filled balloons that require endoscopy only for removal (Obalon Balloon System, ReShape Lifesciences, San Clemente, CA); adjustable balloons that can be made larger to improve efficacy or smaller to improve tolerability (Spatz3 Adjustable Balloon System, Spatz Medical, Great Neck, NY); balloons tethered to other balloons (Transpyloric Shuttle, BAROnova Inc, Goleta, CA); balloons that can be swallowed and then break down on their own over time, thereby not requiring endoscopy for either placement or removal (Elipse Balloon, Allurion Technologies, Wellesley, MA); and other versions of the typical single fluid-filled balloon.

Further distinctions between the different balloons include (a) the number of IGBs that are inserted (a single balloon with all but the Obalon system, with which up to three can be administered, by swallowing, over 9-12 weeks); balloon volume (as little as 300ml or as much as 800ml with the volume-adjustable Spatz3 system vs. up to 750ml with three Obalon IGB vs.

400-700ml with an Orbera IGB vs. 550ml with the Elipse); (c) how long they can be used, ranging from just four and six months with the Elipse and Obalon vs. up to 12 months with the newest model of Orbera IGB and the Spatz3; and (d) when and if currently approved, with approvals in 2015, 2016 and 2021 for the Orbera, Obalon, and Spatz3, but approval still pending for the Elipse.

Both randomized clinical trials and meta-analyses have been published examining the efficacy and safety of IGB devices, most demonstrating statistically-significant weight loss and relatively low rates of serious adverse events(725, 726, 727, 728, 729, 730). Nausea tends to be the most common side effect and reason for discontinuation, with fluid-filled balloons tending to be slightly less well tolerated in this regard(731). On the other hand, in one meta-analysis in which fluid-filled and gas-filled IGBs were compared, fluid-filled balloons were associated with statistically greater and more consistent weight loss than gas-filled balloons(726).

Further details regarding these different IGBs are provided in Table 7-2, including efficacy and adverse event rates and current approval status.

2. Gastric suturing and plication:

The objective of both gastric suturing and gastric plication procedures is akin to that of IGBs: to reduce the volume of stomach available for food. However, whereas IGBs achieve this by filling gastric space, gastroplasty and plication procedures accomplish this essentially by walling off part of the stomach, so it is inaccessible to food. Two currently-employed procedures to achieve this are endoscopic sleeve gastroplasty(721, 724) and the Incisionless Operating Platform plication approach (USGI Medical, San Clemente, CA)(722, 723). Both are summarized below in Table 7-2.

Endoscopic sleeve gastroplasty (ESG) involves endoscopic placement of full-thickness running sutures along the greater curvature of the stomach. This reduces stomach volume and might also alter gastric motility. The Overstitch Endoscopic Suturing System (Apollo Endosurgery, Austin, TX) is the device most commonly used to perform this procedure. This device is FDA-approved for tissue apposition and has CE (*conformité européenne*) mark approval. Full-thickness suture placement is aided by using a tissue helix that captures the gastric wall and retracts it into the suturing arm of the device. Several meta-analyses have been conducted comparing ESG against the more-invasive laparoscopic sleeve gastrectomy (LSG) and, generally, findings indicate that, though the percentage of weight-loss tends to be less with ESG, the rate of adverse events might also be slightly less, albeit typically non-statistically so(721, 732, 733, 734). One clear advantage of ESG over LSG is its reversibility(733). Meta-analysis authors have consistently suggested that its use should be restricted to patients with mild to moderate (class I or II) obesity(721, 724, 732, 733, 734).

The **Incisionless Operating Platform** (USGI Medical, San Clemente, CA), is used to place transmural, single-anchored suture plications in a similar attempt to reduce gastric volume and alter motility. The approach itself is referred to as the *Primary Obesity Surgery Endoluminal* (POSE) procedure, of which there are several versions, distinguished from each other by the pattern and number of gastric folds that are utilized.

b. Delayed gastric emptying

As with gastric restriction, earlier satiety is a primary objective of delayed gastric emptying(735). One such device, called the Transpyloric Shuttle (BAROnova Inc, Goleta, CA) is a spherical bulb that is tethered to a smaller cylindrical bulb that is positioned across the pylorus with the aim of creating intermittent obstruction. Like some intragastric balloons, it is both endoscopically placed and removed, the latter typically 12 months after its placement. It was approved for clinical use in 2019. The major risk is that the pyloric obstruction may cease being intermittent, which can lead to the life-threatening complications of oesophageal rupture and pneumothorax, as part of an overall 2.8% rate of serious adverse events (SAE).

c. Percutaneous gastric aspiration therapy

As stated above, the overriding objective of percutaneous gastric aspiration therapy is to remove caloric content from the stomach after food has been consumed. Food consumption is, hence, not specifically restricted(736, 737). What is restricted is the amount of food that is allowed to pass from the stomach into the duodenum for digestion. This therapeutic approach, which is predominantly used in the US, is less much less widespread in its use. Approved in the USA in 2016, the currently-available form of percutaneous aspiration therapy is the Aspire Assist® device (Aspire bariatrics). Via connection to a percutaneous gastrostomy tube, approximately 30% of ingested food can be aspirated(738).

d. Biliopancreatic diversion

Unlike the three previously-listed general approaches, biliopancreatic diversion targets not the stomach, but the small bowel and has the potential to positively impact obesity-associated metabolic disorders directly, and not just through weight loss. Also unlike the three above-listed approaches, biliopancreatic diversion has not yet been approved for clinical use, though pivotal clinical trials are currently underway. Two approaches that are currently being evaluated are (1) insertion of a duodenal-jejunal bypass-liner(739); and (2) duodenal mucosal resurfacing(740).

1. Duodenal-jejunal bypass-liner

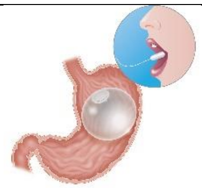
For three years (2013-2015), the duodenal-jejunal bypass-liner (DJBL) (GI Dynamics, Boston, MA) was available and in clinical use. It is currently unavailable. However, the device is presently undergoing a pivotal US trial and is also under review for CE marking. The liner is a 65cm-long Teflon sleeve secured with metal tissue anchors in the duodenal bulb, which is advanced throughout the duodenum and upper jejunum, thereby directing food passage within the sleeve. This ultimately results in food bypassing duodenal and upper jejunal mucosa and, concurrently, prevents food from mixing with biliopancreatic juices along this path. The DJBL mimics the duodenal exclusion that is a feature of gastric bypass procedures and, as such, has metabolic effects that directly target type 2 diabetes mellitus, in addition to inducing weight loss(741, 742, 743). As currently defined, treatment duration is up to one year.

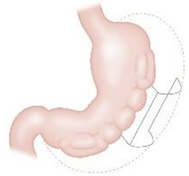
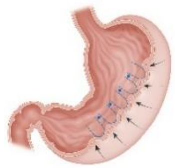
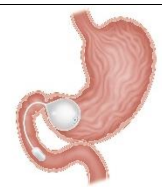
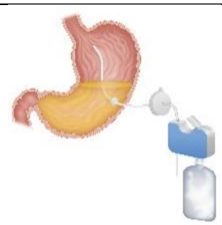
2. Duodenal Mucosal Resurfacing

Duodenal Mucosal Resurfacing (Fractyl, Lexington, MA) involves endoscopic thermal ablation of the duodenal mucosa using a balloon filled with heated water(740, 744). Though weight loss is usually fairly insubstantial, this approach has repeatedly been shown to have direct and significant effects on type 2 diabetes mellitus(745, 746, 747, 748, 749). The approach is currently undergoing a pivotal US trial, but already has CE mark approval.

Please see Table 7-2 for further descriptions of all these procedures, as well as for efficacy and serious adverse effect (SAE) rates, the most common SAEs observed, and current US FDA (Federal Drug Administration) approval and CE (Conformitè Europëenne) mark statuses.

Table 7-2: Specific endoscopic metabolic and bariatric therapy (EMBT) procedures

Primary EMBTs	Illustrations	Description	Efficacy	SAE Rate	FDA/CE Mark Status
Gastric volume restriction					
Orbera Gastric Balloon (Apollo Endosurgery, Austin, TX)		- Single fluid-filled balloon - Endoscopic placement and removal at 6-12 months - Filled with 400-700 ml of saline	11.3% TWL at 1 year	1.6% Migration, perforation, death	- FDA approved in 2015 - CE mark - BMI 30-40 kg/m^2 - Age 22 or older
Obalon Balloon System (ReShape Lifesciences, San Clemente, CA)		- Gas-filled balloon - Swallowable placement and endoscopic removal at 6 months - Three balloons administered over 9- to 12-week period - Each balloon filled with 250 ml of a nitrogen mix gas	10% TWL at 6 months	0.15% Severe pain, perforation	- FDA approved in 2016 - CE mark - BMI 30-40 kg/m^2 - Age 22 or older
Spatz3 Adjustable Balloon System (Spatz Medical, Great Neck, NY)		- Single fluid-filled balloon with a connecting tube for volume adjustment - Endoscopic placement and removal at 8-12 months - Filled with 400-550 ml of saline with methylene blue - Volume may be adjusted down to 300 ml or up to 800 ml	15.0% TWL at 8 months	4% Persistent accommodative GI symptoms	- FDA approved in 2021 - CE mark - BMI 30-40 kg/m^2 - Age 22 or older
Elipse Balloon (Allurion Technologies, Wellesley, MA)		- Single fluid-filled balloon - Swallowable with fluoroscopic guidance for placement and self-emptying mechanism at 4 months for removal - Filled with 550 ml of saline	Data pending pivotal trial	N/A	- Under FDA review - CE mark - Pivotal trial completed

Primary Obesity Surgery Endoluminal (POSE) (USGI Medical, San Clemente, CA)		- One of the applications of the Incisionless Operating Platform (IOP) - Endoscopic plications of the fundus (traditional) or gastric body (Distal POSE/POSE 2.0)	13.2% at 12-15 months (traditional) 15-17.5% TWL at 6-9 months (Distal POSE/POSE 2.0)	3.2% Chest pain, low-grade fever, extra-gastric bleeding, and hepatic abscess	- Cleared in 2006 for tissue apposition - CE mark - In U.S. clinical trial - Pending FDA approval
Endoscopic Sutured/Sleeve Gastroplasty (ESG) (Apollo Endosurgery, Austin, TX)		- One of the applications of the Overstitch Endoscopic Suturing System - Endoscopic suturing along the greater curvature of the stomach to create a sleeve-like structure	16.5% TWL at 1 year(721)	2.2% Severe pain, nausea, GI bleeding, leak, fluid collection	- Cleared in 2008 for tissue apposition - CE mark - FDA approved in 2022
Delayed gastric emptying					
Transpyloric Shuttle (BAROnova Inc, Goleta, CA)		- A spherical bulb tethered to a smaller cylindrical bulb - Endoscopic placement and removal at 12 months - Located across the pylorus creating intermittent obstruction	9.5% TWL at 1 year	2.8% Device impaction, oesophageal rupture, pneumothorax, pain, ulcer, vomiting	- FDA approved in 2019 - BMI 30-40 kg/m^2
Gastric aspiration					
Aspiration Therapy (Aspire Bariatrics, King of Prussia, PA)		- A 26-French gastrostomy tube with 15 cm internal fenestrated drainage catheter - Endoscopic placement and removal - Patients aspirate 25% to 30% of ingested calories 30 minutes after meals	17.8% TWL at 1 year	4.1% Buried bumper, peritonitis, severe pain, ulcer, product malfunction	- FDA approved in 2016 - CE mark - BMI 35-55 kg/m^2 - Age 22 or older
Small bowel bypass					

Duodenal-Jejunal Bypass Liner (GI Dynamics, Boston, MA)		- A 60 cm fluoropolymer liner anchored at the duodenal bulb and ending at the jejunum - Endoscopic placement and removal at 12 months	Data pending pivotal trial	N/A	- Not currently FDA approved - CE mark under review - In U.S. clinical trial
Duodenal Mucosal Resurfacing (Fractyl, Lexington, MA)		- Endoscopic thermal ablation of the duodenal mucosa using a balloon filled with heated water	Data pending pivotal trial	N/A	- Not currently FDA approved - CE mark - In U.S. clinical trial

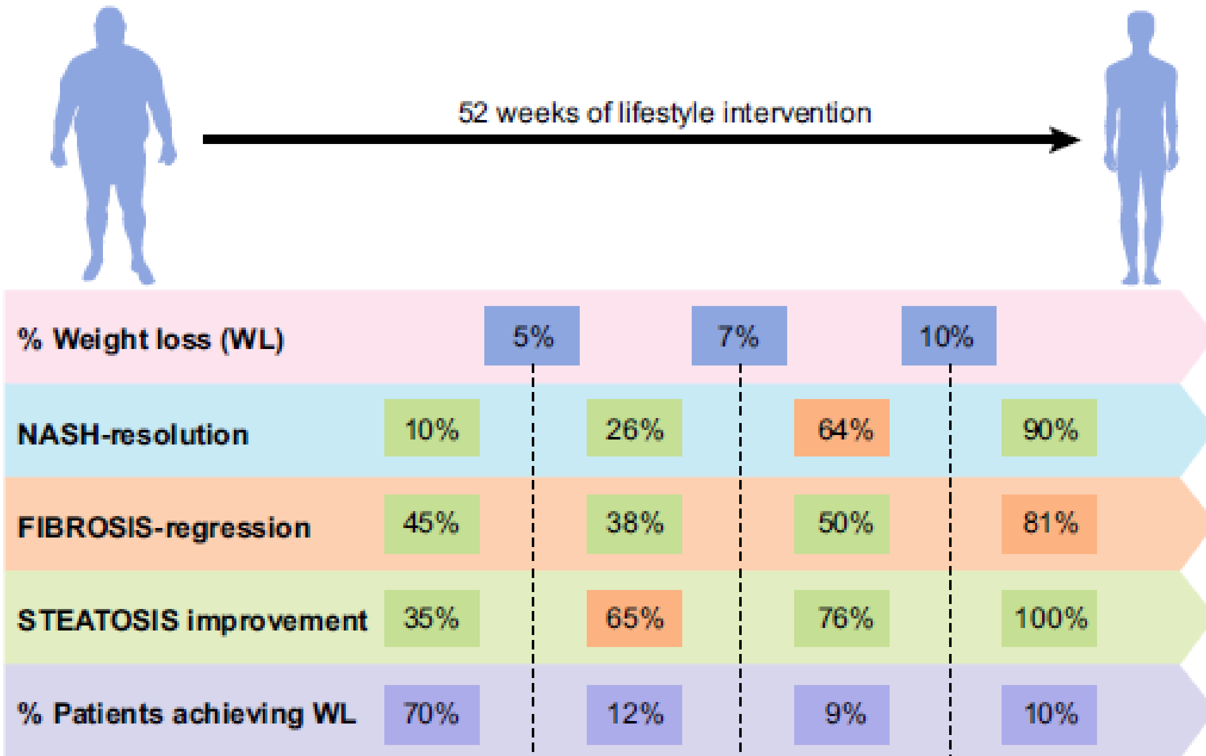
Source: Adapted from Jirapinyo P, Thompson CC. Obesity Primary for the Practicing Gastroenterologist. Am J Gastroenterol. 2021;116(5):918-9345(750). TWL = total weight loss; FDA = Federal Drug Administration (USA); CE = Conformitè Europëenne; BMI = body mass index; N/A = not available

4. ENDOSCOPIC MANAGEMENT OF NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

As stated in Section 3 of these guidelines, on obesity-associated co-morbid conditions, one of the hallmarks of NAFLD is an insulin-resistant state that is driven by increased body fat-promoting adipose tissue dysfunction, chronic inflammation, an altered gut mucosal barrier and microbiome, and permissive abnormal signaling between the central and enteric nervous system and peripheral metabolic organs. This results in the development of liver steatosis, due to increased fatty acid delivery from the adipose tissue and *de novo* hepatic lipogenesis. Excess liver fat leads to oxidative stress and organelle (mitochondria and endoplasmic reticulum) dysfunction that produces a chronic inflammatory state, within the liver, known as non-alcoholic steatohepatitis (NASH, a histopathological finding consisting of ballooning and lobular inflammation in the presence of fat). Ultimately, hepatocyte apoptosis and inflammation in the liver activate the fibrosis cascade, resulting in liver fibrosis and cirrhosis(751). Current treatment of NAFLD principally follows guidelines developed by the *American Association for the Study of Liver Diseases* (AASLD)(752). When appropriate, these guidelines recommend lifestyle modifications, weight loss, increased physical activity, and either pharmacotherapy or bariatric surgery.

The threshold for meaningful improvement in NASH is widely recognized by clinicians and in the literature as 7-10% total body weight loss (TBWL), with positive effects starting at 7% TBWL. With 10% TBWL, histologic abnormalities improve in most patients, including regression of steatosis, liver inflammation, and fibrosis(242, 753). Crucially important, however, is that patients are rarely able to achieve these requisite levels of weight loss with standard lifestyle modifications alone. Figure 7-3 depicts the improvements in NAFLD indicators that may be observed with increasing weight loss increments, along with the proportion of patients who can achieve these outcomes(754). This shortfall of lifestyle modifications on their own has resulted in an expanded armamentarium of interventional options that enable patients to reach the desired weight loss threshold and durably maintain it - combining lifestyle interventions, pharmacotherapies, endoscopic bariatric and metabolic therapies, and bariatric and metabolic surgery – all of which are needed to meet the largely unmet therapeutic needs of a sizeable proportion of NAFLD patients (Figure 7-4)(755). This section will focus on endoscopic bariatric and metabolic therapy (EBMT) approaches to treating NAFLD, with suitable metabolic bariatric surgery (MBS) approaches covered in Section 8.

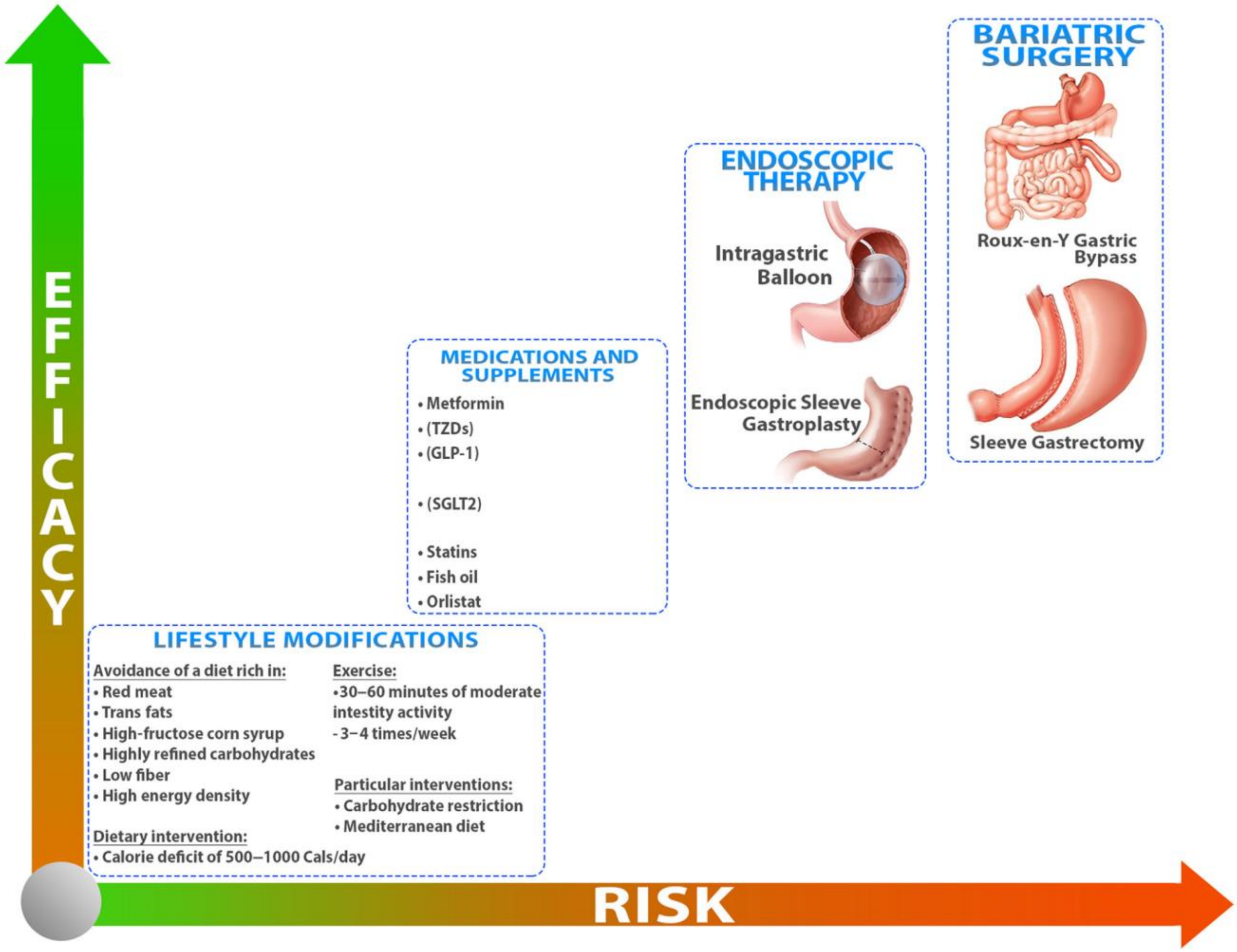
Figure 7-3: Probability of achieving resolution of non-alcoholic steatohepatitis, regression of fibrosis (≥1 stage), and improved steatosis in patients with NASH, per %TBWL, employing lifestyle interventions alone



Borrowed, with permission, from (754).

Capitalizing on the selective targeting of similar peripheral and central gastrointestinal pathways, EBMTs can reproduce the benefits of surgical interventions in a minimally-invasive and cost-effective manner, thereby allowing scalability to patients with mild to moderate obesity, and to those who choose not to pursue bariatric surgery(756). The gastrointestinal anatomical manipulations resulting from EBMTs produce weight-loss-dependent and weight-loss-independent physiological alterations that are conducive to improvements in both obesity and its metabolic consequences, such as type II diabetes and NAFLD.

Figure 7-4: Overview of currently-evaluated treatment options for NAFLD, including an expanded spectrum of therapeutics offering varying degrees of efficacy and invasiveness



Borrowed, with permission, from (755).

Endoscopic therapies with the potential to assist in NAFLD management are summarized and depicted in Figure 7-5, below.

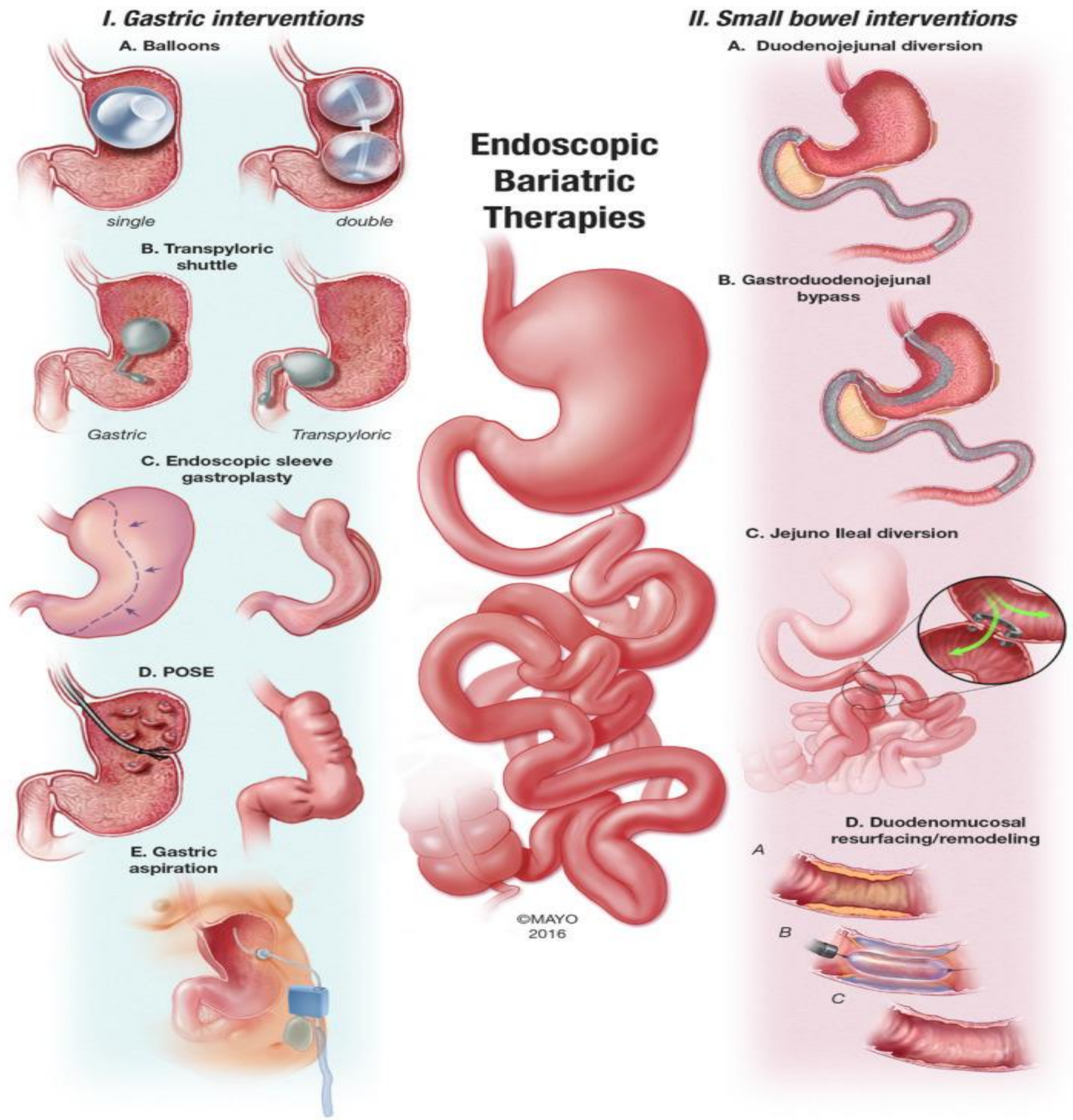
Gastric EBMTs include space-occupying devices that most commonly take the form of temporarily placed prostheses. These include intragastric balloons (A) and the TransPyloric Shuttle (BAROnova Inc, Goleta, CA) (B) (see Figure 7-5), which intermittently seals the pyloric channel and delays gastric emptying in the fed state to induce early satiation and prolonged satiety.

Another category of EBMT options includes gastric remodeling techniques that reduce the gastric reservoir by endoscopically creating a tubular sleeve along the greater curvature of the stomach. This can be achieved through either transoral suturing (Overstitch, Apollo Endosurgery, Austin, Tx) or plication (POSE, USGI Medical, San Clemente, CA) (Figure 7-5, C/D) to create an endoscopic sleeve gastroplasty (ESG). Finally, aspiration therapy (E) is a treatment approach for obesity that allows patients with obesity to dispose of a portion of each ingested meal via a specially-designed percutaneous gastrostomy tube, known as the ATube (Aspire Bariatrics, King of Prussia, PA).

Small intestinal EBMTs include impermeable polymer duodenojejunal bypass liners (Figure 7-5, A/B) (EndoBarrier, GI Dynamics, Lexington, MA) (Metamodix, Minneapolis, MN) that bypass the proximal intestines; self-assembling magnets for endoscopy (C) (GI Windows, Boston, MA) that create a dual-path enteral bypass between the proximal duodenum or jejunum and ileum to divert bile and enhance incretin function; and ablative duodenal resurfacing techniques that regenerate the proximal small intestinal mucosal barrier by thermal (Fractyl Laboratories, Cambridge, MA) or non-thermal electroporation methods (Endogenex, Plymouth, MN).

In one published meta-analysis of 18 studies encompassing 863 patients after EBMTs, the TBWL was 14.5% at 6-month follow-up. This improved liver fibrosis by a standardized mean difference of 0.7 (95% CI, 0.1, 1.3). Surrogates of NAFLD – including alanine aminotransferase (-9.0 U/L; 95% CI, -11.6, -6.4; $P < .0001$), hepatic steatosis index (SMD: -1.0; 95% CI, -1.2, -0.8; $P < .0001$), and the histologic NAFLD activity score (-2.50; 95% CI, -3.5, -1.5; $P < .0001$) – also improved(757). In a prospective study that assessed a single fluid-filled intragastric balloon in patients with NASH and early fibrosis who underwent paired liver biopsies - before and after therapy - histologic NASH activity scores (NAS) improved in 90% of patients with a median decrease of 3 points (range 1-4 points) and 80% of patients decreasing by ≥2 points. Fifty percent of patients achieved resolution of their steatohepatitis on overall histopathological reading, while none experienced worsening of their liver fibrosis(758).

Figure 3: Endoscopic bariatric and metabolic therapies (EBMTs) currently available or in the process of development that can be utilized to manage obesity and NAFLD.



Borrowed, with permission, from (756).

5. AREAS OF CONSENSUS

For IFSO/WGO Delphi survey statements on EMBT, voting was restricted to the 56 surgeons and gastroenterologists who performed EMBT procedures. For an EBMT to be included, at least 20% of the panel was required to have had prior experience with the procedure. Greater than a third of the panel had experience performing intragastric balloon placement and removal (63.6%) and endoscopic sleeve gastroplasty (36.4%), meeting the *a-priori* 20% threshold for inclusion in this document. Since the expert panel was international, including many less-developed countries, many lacked adequate exposure or experience with all EBMT technologies. Consequently, some procedures that are commonly performed in certain countries, but not yet used globally, are not summarized here.

The following three tables (Tables 7-6 – 7-8) summarize areas where consensus was reached and where it was not with respect to general principles of EMBT, intra-gastric balloons, and endoscopic sleeve gastroplasty.

With respect to general principles, there was strong consensus regarding the value of EMBT in obesity management, but also that physicians need to specifically train in how to perform them and that a comprehensive care plan needs to be communicated both to patients and their primary healthcare providers. No consensus was reached regarding whether all EMBT procedures are efficacious (though more disagreed – 55.6% - than agreed) or on their role for purely aesthetic reasons.

Table 7-6: General statements on EMBT

GENERAL STATEMENTS **Statements**	Most common selection	% consensus
Endoscopic bariatric and metabolic therapies include a diverse set of minimally-invasive procedures that play unique and important roles in the treatment of obesity and related metabolic diseases and should be included as part of a multidisciplinary approach to managing these patients.	Agree	98.3%
A prerequisite for any bariatric endoscopist should be endoscopic bariatric training, a curriculum still undefined, but which should include learning about the various surgical procedures, the physiology of obesity, and endoscopic skills.	Agree	98.3%
	Agree	98.2%

Bariatric surgical centres should communicate a comprehensive care plan, both to patients and their primary care providers, including details about the surgical procedure, blood tests, required long-term vitamin supplements, and when patients need to be referred back.		
There is currently inadequate empirical evidence to support the use of ANY bariatric endoscopic procedure as an option in multidisciplinary weight loss programs.	Disagree	55.6%
No bariatric endoscopic procedure is justified in patients with obesity whose only reason for weight loss is to look better.	Neither	50.0%

With respect to intragastric balloons (IGBs), there was consistent consensus in their efficacy and safety, including their use as bridge therapy pending other treatment (e.g., surgery) and for purely aesthetic reasons. With respect to the former use, though IGBs are traditionally offered just to patients with class I or II obesity, their use in patients with class III obesity was deemed justified as a form of bridge therapy. However, no consensus was reached regarding whether the use of IGBs alone can generate enough weight loss to induce improvements in obesity-associated comorbid conditions like type 2 diabetes.

Table 7-7: Intragastric Balloons (IGB)

INTRAGASTRIC BALLOONS **Statements**	Most common selection	% consensus
With intragastric balloons, adjunctive weight loss medications or repeat balloon placements may be necessary to achieve adequate long-term weight loss in many patients.	Agree	87.9%
The ability to induce meaningful weight loss and an acceptable risk profile are characteristics of intragastric balloons.	Agree	85.2%
Intragastric balloons should be/should not be considered for patients with Class 1 or 2 obesity.	Should be	82.8%
As an available option in multidisciplinary weight loss programs, there is currently enough empirical evidence to support the use of intragastric balloons.	Agree	81.0%
Intragastric balloons should be/should not be considered bridge therapies for patients with Class 2 or 3 obesity in need of weight loss to improve outcomes for a specific surgery or medical	Should be	81.0%

treatment/procedure (e.g., orthopedic surgery, organ transplant, fertility, bariatric surgery).		
Intragastric balloons should be/should not be considered for patients who are in the overweight category and have obesity-related comorbidities.	Should be	80.7%
In patients with obesity whose only real reason for weight loss is to look better, it is reasonable to carefully consider intragastric balloons.	Agree	72.2%
Generating enough weight loss to induce improvement in obesity-related comorbidities is achievable with intragastric balloons.	Agree	62.3%

Traditionally, endoscopic sleeve gastroplasty (ESG) is offered to patients with class I or II obesity. Long-term data on endoscopic sleeve gastroplasty show that most patients can maintain an average of 15.9% TWL five years following the procedure(724). As for intragastric balloons, ESG was felt to be both efficacious and safe enough to be used in patients with obesity-associated comorbid conditions, though adjunct weight-loss medications and repeat procedures may be necessary to achieve adequate long-term weight loss. It also was considered justified in patients with class III obesity for whom MBS is either deemed unsuitable or declined. No consensus was reached on if or how often it can be repeated.

Table 7-8: Endoscopic Sleeve Gastroplasty (ESG)

ENDOSCOPIC SLEEVE GASTROPLASTY (ESG) Statements	Most common selection	% consensus
With endoscopic gastric suturing procedures, adjunctive weight loss medications or repeat procedures may be necessary to achieve adequate long-term weight loss in some patients.	Agree	88.9%
Endoscopic gastric suturing procedures should be/should not be considered for patients who are in the overweight category and have obesity-related comorbidities.	Should be	85.2%
Endoscopic gastric suturing procedures should be/should not be considered in patients with Class 3 obesity when they are not good surgical candidates or have declined surgery.	Should be	72.7%
In patients with unsatisfactory weight loss after an endoscopic sleeve gastroplasty (ESG) procedure, endoscopic treatment can be repeated at most once, more than once, or not at all (in lieu of surgical revision).	Not at all	57.4%

Though too few experts performed the other EMBT procedures – aspiration therapy, endoscopic duodenal bypass procedures, endoscopic gastric bypass revision, endoscopic gastric plication – for their votes to be considered valid, less enthusiasm generally was expressed regarding their proven efficacy and/or safety and current role in obesity management.

6. CONCLUSIONS AND RECOMMENDATIONS

Considerable evidence has been published documenting the effectiveness of a range of EMBTs in the treatment of both obesity and certain obesity-associated comorbidities, like type-2 diabetes. Though their efficacy appears to generally be slightly less than that of metabolic and bariatric surgery, they have the advantages of being perhaps slightly safer, and certainly both less invasive and more reversible. Though not all approaches have yet been approved for clinical use, pivotal studies are underway and past results are encouraging. Both the literature and our expert panel recommend the use of intragastric balloons and endoscopic sleeve gastroplasty for type I and II diabetes. Our experts also experts agreed that intragastric balloons should be considered for patients with class II or class III obesity as bridge therapy to improve the safety profile of patients undergoing specific medical or surgical therapy, such as fertility therapy, orthopedic surgery, bariatric surgery, and transplant surgery. Below is a list of specific evidence-based guidelines.

Evidence-based guidelines for endoscopic metabolic & bariatric therapy (EMBT)

- **Statement 1: Principles of action**

Applicable principles of action by EBMTs are **restriction** (reduction of gastric capacity), **biliopancreatic diversion** (sectional separation from duodenal and upper jejunal mucosa, as well as of food from digestive juices), and **percutaneous aspiration** of already-ingested gastric contents, with the aim of achieving weight loss by influencing the sensation of hunger and satiety.

- **Statement 2: Applicability**

Globally, EBMTs that reduce gastric capacity, like ***intragastric balloons*** (various models) and endoscopic ***sleeve gastroplasty (ESG),*** are used regularly in everyday clinical practice.

- **Statement 3: Indication**

The indication spectrum of EBMTs is the BMI range of >30 kg/m^2 to < 40 kg/m^2 or BMI > 27 kg/m^2 with concomitant comorbidities.

- **Statement 4: Procedure safety**

EBMTs are effective and safe. They also can be used repeatedly.

- **Statement 5: Weight Loss**

EMBTs have a reported total weight loss (TWL) range from 10% (Obalon) to 17.8% (ESG).

- **Statement 6: Improvement of comorbidities**

The Orbera® Intragastric Balloon has received a Breakthrough Device Designation for the treatment of non-alcoholic fatty liver disease from the FDA.

VIII. Metabolic and bariatric surgery (MBS)

1. Introduction - past and current MBS procedures
2. Patient selection and preparation
3. Peri-operative patient care
4. Impact of MBS on obesity-associated co-morbid conditions
5. Metabolic and bariatric surgery for non-alcoholic fatty liver disease (NAFLD)
6. Impact of MBS on patient quality of life
7. Areas of consensus
8. Conclusions and recommendations

1. INTRODUCTION – PAST AND CURRENT MBS PROCEDURES

Despite dramatic advances and improving results being published for pharmacological and endoscopic treatments for severe obesity, surgery remains the most successful option for achieving meaningful and sustainable weight loss. Originally, the field was referred to only as "weight loss surgery." However, shortly thereafter, it was renamed "Bariatric Surgery." Recently, the term "Metabolic Surgery," has been increasing in popularity. This reflects the observation that, in addition to weight loss, these procedures result in dramatic improvements in obesity-associated medical conditions such as type 2 diabetes mellitus (see Section 3 below for more details)(759, 760, 761) and other metabolic diseases such as sleep apnoea, hypertension, and high cholesterol. Currently, it is becoming increasingly popular to combine the two names noted above and refer to this field of procedures as either *metabolic and bariatric surgery (MBS)* or *bariatric and metabolic surgery* (BMS).

Metabolic and bariatric surgery (MBS) procedures have always been described by the primary mechanism, or mechanisms, by which they achieve weight loss. Generally, they are considered restrictive if they reduce the stomach's capacity to store consumed food (e.g., laparoscopic adjustable gastric band) or malabsorptive if they limit intestinal absorptive capacity (e.g., intestinal bypass). Procedures like the gastric bypass have been considered to have both restrictive and malabsorptive processes and, thereby, deemed restrictive/malabsorptive. However, recent evaluations of these procedures have determined that the mechanisms of action are not so simplistic. Other factors, like hormonal and neuronal effects, might also contribute to the actions of these procedures.

Metabolic and bariatric surgery began in earnest in the early 1950's with the intestinal bypass procedures(591). In these procedures, the proximal intestine was connected to the distal small intestine, thereby "bypassing" about 80% of the small intestine's absorptive capacity. The malabsorption of nutrients and calories resulted in significant weight loss. However, it also put patients at great risk for the development of side effects such as arthralgias, myalgias, diarrhoea, steatorrhea, and vitamin, mineral, and protein deficiencies. In addition, some patients developed cirrhosis of the liver.

In the late 1960's, intestinal bypasses were replaced by gastric procedures, such as the gastric bypass (GB). Mason et al(762) developed the first GB. He divided the stomach horizontally and then attached a loop of jejunum to it. The loop GB was successful for weight loss and was considered to be a combined restrictive and malabsorptive procedure. However, the procedure also was technically difficult, resulting in an unacceptably high incidence of perioperative complications such as bleeding, leakage, thromboemboli, intestinal obstructions, deep wound infections, and even death.

It was Mason et al and others who followed who developed a group of procedures called gastroplasties(763). These procedures involved restricting nutrient intake by partitioning the stomach, creating a small pouch to accept the swallowed food while cordoning off the rest. There were no manipulations of the intestines. A second major effort was to make gastric bypass procedures safer and more efficacious. As a result of several technical changes, gastric bypass procedures evolved from a horizontal pouch and loop connection to a vertically-oriented pouch on the lesser curvature of the stomach connected to a single limb of intestine (Roux limb). An additional intestine-to-intestine connection was created between the Roux limb and the small intestine just distal to the ligament of Treitz (jejuno-jejunostomy). The procedure was then named the "Roux-en-Y Gastric Bypass" (RYGB)(764) (Figure 8-1). The RYGB became the most commonly performed MBS procedure in the world for several decades, as gastroplasties fell from favour and essentially became obsolete, secondary to inferior results.

The use of malabsorptive procedures to achieve meaningful weight loss was revisited in the late 1970s when Nicola Scopinaro(765) developed the biliopancreatic diversion (BPD) (Figure 8-2).

In this procedure, a large gastric pouch was created by performing a distal gastrectomy. The pouch was then connected to the distal ileum. While this procedure had similarities to the abandoned intestinal bypasses, its construction reduced the likelihood of nutritional and metabolic complications. The BPD procedure was deemed best for patients with a particularly high body mass index (BMI > 50kg/m^2). In the 1990s, Picard Marceau and Douglas Hess, working independently(766, 767), improved the procedure by creating a lesser curvature, tubular-shaped longitudinal pouch (called a 'sleeve') instead of the large proximal gastric pouch. The distal ileum was then connected to the first portion of the duodenum, instead of to a gastric pouch. The procedure was called biliopancreatic diversion with duodenal switch (BPD/DS) or just duodenal switch (DS) (Figure 8-3). Compared to the classic BPD, the BPD/DS dramatically reduced the risk of marginal ulcers and dumping syndrome.

While the BPD/DS quickly proved to be the most efficacious procedure for weight loss and controlling co-morbid conditions, it was a challenging operative procedure, particularly in the early days of laparoscopic surgery. Regan et al demonstrated that performing the DS in two stages reduced the incidence of perioperative complications(768). The first stage entailed performing a sleeve gastrectomy (237) along the lesser curvature of the stomach. The second stage, performed months later after significant weight loss was achieved with the SG, was an intestinal bypass.

By serendipity, Gagner noted that several patients did not want to proceed with the second stage as they were doing very well after the sleeve gastrectomy (See Figure 8-4). Thus, the SG became viewed as a primary, stand-alone procedure(769). The SG has demonstrated itself to be a formidable procedure. It is simpler and safer than the gastric bypass, but achieves similar weight loss and control of comorbid conditions. These characteristics have resulted in the SG replacing the RYGB as the most commonly-performed MBS procedure in the world. However, the SG has one major concern: it can exacerbate pre-existing acid reflux or cause reflux in patients who did not have reflux preoperatively.

Any discussion of current MBS procedures would be incomplete without mentioning a variant of the gastric bypass procedure called the one anastomosis gastric bypass (OAGB) (Figure 8-5). This procedure, then called the mini-gastric bypass (MGB), was first reported by Robert Rutledge in 1997(770). It involves creation of a gastric pouch similar to a sleeve, followed by an anastomosis of the sleeve to a loop of small intestine. The procedure has a long afferent limb (150-250cm) that can cause malabsorption. The long gastric sleeve pouch and the single anastomosis result in fewer perioperative complications and shorter operative times than the RYGB. The OAGB achieves great weight loss, as well as control of obesity-associated conditions, similar to or mildly superior to the RYGB. It is popular and its popularity is increasing as it is considered to be superior to the previously-described GB procedures. However, it remains a controversial procedure, as there is concern that the OAGB can cause chronic bile reflux that could result in Barrett's oesophagus or even gastroesophageal cancer.

2. PATIENT SELECTION AND PREPARATION

Patients with class 2 obesity or greater cannot have MBS just because they desire to. There is a universal set of criteria that must be satisfied before any patient with class 2 or greater obesity is offered surgery. These criteria were first established by the U.S. *National Institutes of Health* (NIH) in 1991(771). The NIH guidelines use BMI as the focal point. Patients qualify for surgery if their BMI is 40kg/m^2 or greater. This is regardless of whether or not the patients have any associative health issues, such as type 2 diabetes mellitus (T2DM), hypertension, sleep apnoea, or several others. Patients with any of these comorbid conditions qualify if their BMI is 35kg/m^2 or greater. Recent-published evidence would suggest that patients with comorbid conditions, like T2DM, should be considered for surgery at even lower BMIs (30kg/m^2). However, this has not been universally accepted.

Patients who meet the BMI criterion for surgery must then undergo a comprehensive program of screening and education. While this process may vary from program to program, it generally includes a thorough history and physical examination, as well as patient interactions with bariatric dietitians, behavioural therapists, and surgeons. In addition, a battery of screening blood work is done that includes haemoglobin-A1c (HgA1c), liver function tests, thyroid function tests, and serum vitamin levels, with patients provided supplements for any micronutrient deficiencies that are uncovered prior to surgery. Most MBS programs will also obtain radiographic studies and, possibly, require an upper endoscopy. Patients with health issues may undergo more extensive evaluations and even specialty consultations. For example, patients with a past history of deep vein thrombosis or pulmonary embolism may require an evaluation to identify any hypercoagulable condition that would require greater perioperative and postoperative thromboprophylaxis. In addition, some degree of weight loss may be required prior to proceeding with surgery.

This entire process may take several months to complete. It varies between countries and hospital programs, based on funding and education before operations. Generally, there is agreement that MBS is such a life-changing procedure, patients need to be empowered to use this 'tool' properly. Throughout their preparation, patients are educated extensively on many issues, including postoperative diet, exercise, surgical complications, eating habits, and nutrient supplementation, as well as on certain, pertinent behavioural topics. It is advisable to only perform MBS on patients who have a good understanding of both its short- and long-term impacts.

3. PERI-OPERATIVE PATIENT CARE

a. Just prior to surgery

Currently, few patients are admitted to the hospital on the day before their surgery, most patients admitted on the morning of surgery. After intravenous access is obtained, the patient is placed on an operating table and anesthetized. Special operating room tables and instruments are often used for these patients. Compression sleeves are placed on the lower extremities to minimize the risk of thromboembolism. Foley catheters, abdominal drains, and nasogastric tubes are now rarely used. Preoperative antibiotics and either subcutaneous heparin or low-molecular-weight heparin are administered. The abdomen is widely prepped with an antiseptic solution. Prior to making the first skin incision, a surgical time out is taken. This is a brief period of time when everyone stops what they are doing to discuss the patient and the operative procedure that will be done. This simple procedure reduces intraoperative complications by getting all members of the operating team to communicate with one another.

b. Just after surgery

Most programs now follow patient-care pathways that include early ambulation and minimal narcotic use. Patient pain is treated with combinations of non-opioid medications. Liquids are generally given to patients to drink that afternoon or evening. Some programs obtain a fluoroscopic imaging series to rule out any leaks or obstruction. Patients are usually discharged to their home the following day (post-operative day #1), provided they can tolerate oral liquids and their pain is adequately controlled. Some programs have been sending selected patients home the same day as their surgery.

4. IMPACT OF MBS ON OBESITY-ASSOCIATED CO-MORBID CONDITIONS

From their first use in the 1950's, it was clear that the early bariatric surgeries were successful at achieving significant weight loss. That weight loss resulted in better mobility, reduced joint pain, less dyspnoea on exertion, etc. However, the metabolic benefits of these procedures were not yet recognized, despite the evidence being there. Since then, however, MBS has been repeatedly shown to exert beneficial long-term effects on a number of obesity-associated conditions including, among many others, type 2 diabetes, with total resolution of diabetes observed in from a majority(759) to over 90% of patients(760). Such conditions for which meaningful improvements in disease status have been documented following MBS further include obstructive sleep apnoea, hypertension, other cardiovascular disease, liver disease, kidney disease, gastro-oesophageal reflux disease (GERD), cancer, and others. Mortality rate, which has consistently been shown to be markedly elevated in patients with overweight or obesity relative to individuals of normal weight (772), also declines, both from all causes and secondary to specific obesity-associated comorbid conditions. The high rate of resolution of obesity-related comorbidities is one reason that bariatric surgery has become the standard of care for treating not only obesity itself, but several of its metabolic complications(26, 27, 28).

a. Type 2 diabetes mellitus (T2DM)

As early as 1955, Friedman et al observed that T2DM completely resolved in three diabetic patients after they underwent subtotal gastrectomies for duodenal ulcers(773). This finding had the potential to radically change the management of T2DM, but instead was essentially ignored until 1995, when Pories et al published their series of 298 patients with severe obesity and T2DM who underwent open RYGB surgery and demonstrated resolution of the diabetes in 91% of their diabetic patients(760). Currently, there is overwhelming data, including the results of several randomized controlled trials (RCTs), that have unanimously concluded that MBS results in greater control and potentially higher rates of remission of T2DM than even optimal medical therapy(180, 182, 759). Additionally, other studies have shown that MBS reduces the risk of developing T2DM and slows the progression of this disease. In the randomized STAMPEDE Trial, Schauer et al randomized 150 patients with T2DM and severe obesity to receive either (a) best medical therapy, (b) laparoscopic SG, or (c) laparoscopic RYGB(182, 761). The primary endpoint was a serum haemoglobin A1c level less than 6.0% while off all anti-diabetes medications. After 12 months, significantly more patients in both surgical groups reached the primary endpoint than those who received best medical therapy(761), with just 12% of the medical patients reaching a HgA1c < 6.0% versus 42% of the RYGB patients, ($p=0.002$) and 37% of the GS patients ($p<0.008$). There were also statistically-significant differences in weight loss, as well as statistically-significant reductions in serum triglyceride and C-reactive protein levels. At five years of follow up, only 5% of the medical patients still met the primary endpoint, versus 9% of the RYGB patients and 23% of the SG patients (both $p=0.03$)(182).

Similar findings can be demonstrated for several other obesity-associated medical conditions.

b. Obstructive sleep apnoea (OSA)

Obstructive sleep apnoea (OSA) is relatively uncommon in the general population (2-4%), but is seen in nearly 80% of patients who suffer from either overweight or obesity (BMI $\geq$ 25kg/m^2)(774). Patients who have OSA are at greater risk of hypertension, pulmonary hypertension, myocardial infarction, respiratory failure, and even sudden death(775). In multiple publications, including meta-analyses, MBS has been shown to result in improved OSA symptoms, including their total resolution(776).

A large body of literature has documented that OSA improves, and often even resolves after MBS. In fact, MBS is currently considered the treatment of choice for patients with a BMI $\geq$ 35kg/m^2 who suffer from OSA. This recommendation is supported by the *American Society for Metabolic and Bariatric surgery (MBS)*, based on a review of the existing literature by their clinical issues committee(1).

c. Cancer

Patients who suffer from obesity are at greater risk of developing cancer than patients without excess adiposity(266, 777). Thirteen cancers that are hormonally-sensitive are even more closely associated with obesity(266, 267). These cancers include adenocarcinoma of the esophagus, postmenopausal breast malignancies, renal cell carcinoma, cancers of the endometrium, gallbladder, stomach, ovary, thyroid, and colorectum, meningioma, and multiple myeloma(267). Currently, 40% of all new cancers diagnosed are associated with obesity, accounting for 55% of cancers in women and 24% of cancers in men(267). Obesity also has an adverse effect on cancer treatment. Women with obesity and breast cancer have been found to have larger primary tumours, higher rates of lymphatic spread, and lower survival rates(19, 267). One pathophysiological explanation behind the carcinogenic effect of excess adiposity relates to the induction of metabolic and endocrine abnormalities, which include increases in inflammatory markers, insulin, sex hormones, and insulin-like growth factor(268).

The weight reduction achieved after MBS has been observed to reduce someone's likelihood of acquiring cancer and has been shown to improve outcomes and increase the life expectancy of patients afflicted with cancer. Adams et al. reviewed a database generated for a previous retrospective cohort mortality study(284), comparing 9,949 patients who had undergone gastric bypass surgery between 1984 and 2002 against a matched control group of 9,628 participants with obesity who did not undergo MBS. Follow-up sometimes exceeded 24 years (mean = 12.5 years). The investigators found that the incidence of cancer was 24% lower in those patients who had undergone gastric bypass (p= 0.0006). However, this difference only was evident in women. In another systematic review and meta-analysis that evaluated the incidence of cancer following bariatric surgery in 52,257 patients, among controlled studies MBS was found to lower the incidence of cancer by 1.1 cases per 1000 person-years(274). Additional meta-regression analysis identified an inverse relationship between patients' presurgical body mass index (BMI) and cancer incidence following surgery (beta coefficient = -0.2, $p<0.05$)(274).

Other studies have spurred a range of conclusions on the effects of weight loss on cancer risk reduction after bariatric surgery. One retrospective case-control study of 18,355 patients undergoing bariatric surgery was conducted to determine the association between post-operative weight loss and the risk of cancer(265). In these patients, the average amount of weight loss one year postoperatively was 27% among patients who had undergone MBS versus 1% in matched nonsurgical patients. Percent weight loss at one year was, in turn, significantly associated with a significantly-reduced overall risk of cancer in an adjusted model (hazard ratio, HR = 0.897, p=0.005), though bariatric surgery itself was not a significant independent predictor of cancer incidence(265). In another large multisite case-control study, also conducted by Schauer and associates at five sites within the Kaiser Permanente Healthcare System, 22,198 patients who underwent MBS were compared to 66,427 nonsurgical subjects matched for sex, age, study site, BMI and Elixhauser comorbidity index score(275). After a mean follow-up of 3.5 years, 2543 incident cancers were identified; but when MBS and non-surgical patients were compared, the former had experienced a 33% reduction in the hazard of developing any cancer ($p<0.001$), and this reduction was even greater when analysis was restricted to obesity-associated cancers ($p<0.001$). When sub-classified into obesity-associated cancers, the isolated risks of postmenopausal breast cancer, colon cancer, endometrial cancer, and pancreatic cancer were each significantly lower among those who underwent bariatric surgery ($p<0.001$; 0.04; 0.001; and 0.0.04, respectively)(275).

There is virtually no residual doubt that the weight loss achieved from MBS significantly decreases individuals' subsequent risk of cancer(276, 277, 278, 279, 280, 281, 282, 283). Why such reductions in cancer incidence and mortality occur remains an issue of ongoing investigation. However, an empirically-documented direct correlation between weight loss and telomere length — with greater degrees of weight loss linked to greater increases in telomere length(287), combined with evidence that telomere lengthening after bariatric surgery lasts for up to three to five years after the procedure(288) have led many to speculate that the telomere lengthening observed with rapid weight loss following bariatric interventions is one feasible explanation for the reduced cancer risk that patients experience after bariatric surgery.

The well-documented link between weight loss post MBS and reduced rates of cancer and cancer mortality should also serve as a call to healthcare providers and policy makers and the general public to become aware both of the link between obesity and cancer, and how cancer risk is lessened by weight loss, whether such weight reduction are achieved by dietary interventions and lifestyle changes, by using medications, or through the provision of endoscopic metabolic and bariatric therapy or metabolic and bariatric surgery. If more people start losing weight, by any of these means, this could prevent the development of cancer in many patients already at higher risk because of their excess weight.

d. Kidney Disease

Obesity has been shown to be a risk factor for the development of chronic kidney disease, associated with a nearly 25% increase in the risk of acquiring chronic kidney disease(778). For patients with a BMI above 40kg/m^2, there is seven-fold elevated risk of developing ESRD than in normal weight individuals(778). Obesity also contributes to the progression to end-stage renal disease and even negatively affects outcomes after renal transplantation. Furthermore, many patients who suffer from severe obesity will not be considered candidates for renal transplantation, because of the increased perioperative risk secondary to their weight.

On the other hand, MBS and the weight loss that results from it have several beneficial effects in this population. Firstly, it slows the progression of kidney dysfunction to end-stage disease. In one study, relative to matched, non-surgical controls, patients with a BMI above 35kg/m^2 and stage 4 or 5 chronic kidney disease who underwent MBS achieved a 3-year improvement in their estimated glomerular filtration rate (eGFR) of nearly 10mL/min/1.73m^2(779). This improvement was correlated with the degree of weight loss: for every 10 pounds lost, eGFR increased by 0.21 mL/min/1.73 m^2(779).

Metabolic and bariatric surgery also improves the success rate in patients who undergo renal transplantation. Thirdly, it enables some patients whose weight previously prevented them from being considered for a renal transplant, to be reassessed and placed on a waiting list. Lastly, it reduces the mortality rate among patients on the transplant waiting list(780).

e. Hypertension

Obesity and hypertension are closely associated with one another. Several published studies have demonstrated that obesity contributes to hypertension directly by increasing sympathetic drive and indirectly by raising blood pressure through renal mechanisms(781). There is also increased sodium and fluid reabsorption in renal glomeruli, which raises intravascular fluid volume and arterial blood pressure.

Even modest weight loss can result in significant improvements in blood pressure(91). Several published studies have confirmed that MBS and the resultant weight loss reduces the likelihood of a patient developing hypertension and improves blood pressure in those already with hypertension(782). Based upon the results of a multicentre RCT comparing RYGB and medical management of patients with metabolic syndrome, Ikramuddin et al reported that patients who underwent RYGB were much more likely to reach the composite end point consisting of a serum haemoglobin A1c (HbA1c) level less than 7%, a serum low-density lipoprotein level less than 100mg/dL, and a systolic blood pressure less than 130mmHg, with 28% of RYGB patients achieving these three milestones versus just 11% of controls(178). Five-year follow-up data essentially showed the same, with 23% of those who had undergone RYGB maintaining the composite outcome versus just 4% of controls(783).

f. Cardiovascular disease

Patients who are either overweight or have severe obesity are at increased risk of developing cardiovascular disease (CVD) and having cardiovascular events, including coronary artery disease, myocardial infarction(784), congestive heart failure(772) and atrial fibrillation(785). Additionally, with excess adiposity there is unfavourable remodelling of the heart itself. Compared to normal-weight adults, those with severe obesity have an earlier onset of CVD, suffer more cardiac events, and have an overall shorter life expectancy(786). Additionally, like end-stage renal failure patients, patients with end-stage heart failure and obesity might not be considered for life-saving heart transplantation.

Several publications now document that MBS improves cardiac function due to multiple metabolic changes. In the Utah Obesity study, Owan et al demonstrated that patients undergoing MBS achieved significant reductions in systolic blood pressure and hyperlipidaemia, improvements in serum glucose homeostasis, and reversal of the obesity-induced cardiac remodelling seen with obesity(787). They also observed reductions in left ventricular mass index, right ventricular cavity area, interventricular septal thickness, posterior wall thickness, and relative wall thickness. These morphologic changes result in improved cardiac function(787). Additionally, some patients with end-stage heart disease previously considered unfit for consideration for heart transplantation might be reassessed after MBS and considered appropriate for heart transplantation.

g. Liver disease

Studies have shown that 90% of adults with severe obesity will ultimately develop nonalcoholic fatty liver disease (NAFLD) (186, 788). Twenty-five percent of these patients will progress to nonalcoholic steatohepatitis (NASH), while a third will progress to cirrhosis(789). Nonalcoholic steatohepatitis is rapidly becoming a leading indication for liver transplantation(790). In a review of one large insurance administrative claims database, 2942 patients with NAFLD who underwent MBS were compared to 5884 matched controls who did not undergo MBS(788). At

24 months, the relative risk of cirrhosis in the surgical arm was just 0.31 (95 CI, 0.19 – 0.52) relative to controls.

Further details regarding the management of NAFLD with MBS are provided in subsection VIII-5.

h. Gastro-oesophageal reflux disease (GERD)

Obesity has been shown to be an independent risk factor for gastro-oesophageal reflux disease (101). In individuals with obesity, there also are greater risks of developing erosive esophagitis, Barrett's oesophagus, and adenocarcinoma of the oesophagus than among normal-weight patients(336, 791). Moreover, persons with obesity are over three times more likely to have a hiatal hernia than non-obese individuals(792). Gastroesophageal reflux disease (GERD), with or without a hiatal hernia, manifests in a variety of ways at endoscopy. It can occur with no visible oesophageal injury (non-erosive reflux disease). It can also present as erosive reflux disease with or without mucosal metaplasia, and even as Barrett's oesophagus(793). It is not clear if these manifestations are part of a continuous spectrum of disease or if they are distinct phenotypes of GERD(794). However, this wide range of clinical conditions increases the need for more preoperative investigations and influences the choice of MBS procedure, as stated in the recent IFSO 2020 Position Statement on Barrett's Esophagus(795).

Classically, the preoperative diagnosis of a hiatal hernia relies on its presence during endoscopy or a barium swallow study, although both of these techniques have several limitations(796, 797). High-resolution manometry has recently been proposed for the preoperative work-up to improve the hiatal hernia detection rate(798).

The effects of MBS on GERD can vary, based upon the type of surgical procedure performed. While RYGB is associated with good control of GERD(799), data on SG are conflicting. While some studies have demonstrated a high GERD remission rate after SG, an increasing number of studies have documented a negative impact of SG on GERD(800). Furthermore, a higher prevalence of Barrett's oesophagus has been reported in patients after SG, usually three or more years after surgery(801, 802).

The role of hiatal hernia repair during MBS is an important consideration for patients with GERD. In several studies, performing SG plus concomitant hiatal hernia repair has been reported to improve GERD at both short-and mid-term follow-up(803). However, at long-term follow-up, a significant rate of hiatal hernia recurrence was described, consistently linked to the presence of GERD symptoms. Additionally, high rates of oesophagitis and Barrett's oesophagus were detected(804). To overcome the problem of GERD related to SG, some anti-reflux operations have recently been introduced. Nissen-sleeve, Rossetti-sleeve, and Dor-sleeve gastrectomies have all been assessed in clinical trials, with encouraging early results. However, the long-term effects of these procedures on GERD are not yet known(805, 806, 807).

i. Miscellaneous

Numerous other diseases and conditions have been shown to benefit from MBS, both in terms of quality of life and economic savings. They are detailed later in this chapter. Some studies also have tracked the long-term outcomes of patients who have undergone MBS relative to patients who have received medical treatment for their obesity. All these studies have documented superiority of surgery over nonsurgical medical management. The most-often quoted papers are those reporting on the various outcomes of the Swedish Obesity Surgery (SOS) study. For over 15 years, the SOS study has been collecting data on a cohort of patients who have had bariatric surgery and a matched control group of patients with obesity treated medically. Numerous publications reporting these results, some with up to 15 years of follow up, have been published(580, 808, 809, 810, 811, 812).

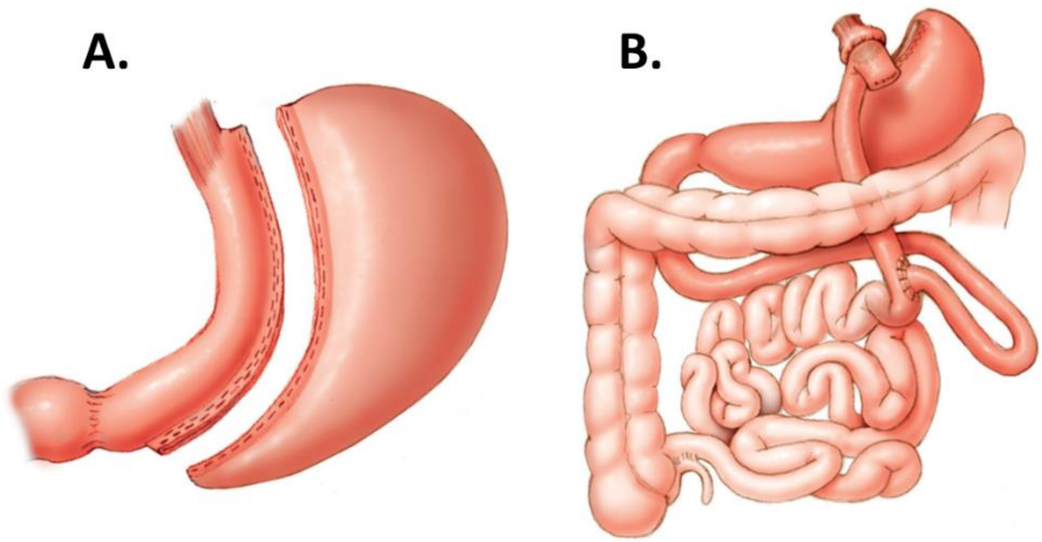
j. Mortality

Metabolic and bariatric surgery and the weight loss that follows have been convincingly shown to mitigate, and even “cure”, the vast majority of obesity-associated health conditions. Furthermore, reduced body weight enables patients to be more active, further improving their overall health. Therefore, it is not surprising that MBS has been observed to increase life expectancy, a finding reported in numerous publications(813, 814, 815, 816, 817, 818, 819). To date, no publications have demonstrated the opposite effect.

5. MBS FOR NON-ALCOHOLIC FATTY LIVER DISEASE (NAFLD)

Bariatric surgery is the most effective method of producing sustained weight loss for patients with obesity(820). The most performed metabolic bariatric surgeries include laparoscopic sleeve gastrectomy (LSG) and Roux-en-Y gastric bypass (RYGB) (Figure 8-1). Use of an adjustable gastric band (AGB) is another less common bariatric surgical option.

Figure 8-1: Most common bariatric and metabolic surgical options for NAFLD



A. Laparoscopic sleeve gastrectomy surgery. B. Roux-en-Y gastric bypass surgery. Borrowed, with permission, from (755).

Laparoscopic sleeve gastrectomy (LSG) is a restrictive surgery that reduces gastric capacity by 80% and generates both neurohormonal and bile signaling alterations that yield metabolic benefits(821). Roux-en-Y gastric bypass excludes a portion of the stomach, as well as part of the proximal intestine, and rearranges the distal end of the intestine into a Y-configuration, through which food can flow from the upper stomach pouch through the Roux limb, resulting in weight loss dependent and independent metabolic benefits(822). One meta-analysis of 32 studies (15 retrospective and 17 prospective cohort studies) that encapsulated over 2649 biopsies performed at follow-up, showed a mean %TBWL of 25%, accompanied by resolution of steatosis in 66% of patients, of inflammation in 50%, of ballooning degeneration in 76%, and of fibrosis in 40%(823). However, in a small subset of patients (12%) the rapid weight loss resulted in worsened liver fibrosis, which is more common with malabsorptive procedures that bypass the small intestines, such as jejunoileal bypass surgery(823, 824, 825). In a landmark prospective study of 180 patients with obesity and biopsy-proven NASH who underwent bariatric surgery (66% RYGB, 22% adjustable gastric band, 12% LSG), liver biopsies performed after one and five years revealed NASH resolution without worsening fibrosis in 84% of patients(826); fibrosis actually decreased, relative to baseline, in 70% of patients (95% CI, 56.6%-81.6%). Meanwhile, fibrosis had resolved in 56% (95% CI, 42.4%-69.3%) of patients at five years, first noted to have begun decreasing within one year of surgery and continuing to decrease through to five years of follow-up ($p < 0.001$). Of note, patients who experienced decreases in body mass index (BMI) of 0-5, 5-10, and >10 kg/m² achieved 60%, 80%, and 90.5% resolution of their NASH without worsening fibrosis at five years, respectively, indicating that even a modest 5 kg/m² decrease in BMI can exert significant benefits on long-term NAFLD outcomes. Three patients died over the course of five years of follow-up, including two deaths from surgical complications that occurred within the first month after surgery and one from cardiac dysfunction four years after surgery(826).

6. IMPACT OF MBS ON PATIENT QUALITY OF LIFE

a. Introduction

Obesity is associated with several comorbidities that increase costs associated with the disease, including conditions like hypertension, coronary artery disease, metabolic liver disease, sleep apnoea, diabetes, and certain forms of cancer(827). In recent years, MBS has become the gold standard treatment for obesity in patients with a BMI greater than 35kg/m^2 who have been unsuccessful with non-operative management(771) It also has become established as the most effective treatment for a number of obesity-associated conditions like type 2 diabetes(26, 27, 28).

b. Quality-adjusted life-year benefits from MBS

The quality-adjusted life year (QALY) is a single outcome measure that encompasses both the duration and quality of life. It has been established as a reference standard in cost-effective analyses as a means of guiding decision-making for the allocation of limited resources to achieve the greatest benefit(828). For MBS, this is an important outcome measure, as it allows one to determine the cost-effectiveness of any given MBS procedure in its ability to treat obesity and improve quality of life. In one Delphi consensus study recently conducted by WGO-IFSO — in which bariatric surgeons, bariatric endoscopists, and other healthcare providers specialized in obesity management from around the globe participated — consensus was reached that obesity is a major contributor to the global burden of chronic disease, disability, and healthcare costs, and that global rates of obesity are increasing in children and adolescents. These adolescents with obesity are then placed at increased risk of obesity-related comorbidities, such as hypertension and type 2 diabetes mellitus (T2DM). In this survey, 98.9% of these intercontinental experts agreed that MBS can improve overall quality of life, and that short-term studies indicate that MBS improves obesity-related medical problems and quality of life. Furthermore, almost unanimous consensus was reached that substantial net health and economic benefits may be anticipated on a societal level from the wider use of bariatric procedures in patients with severe obesity, and that bariatric surgery has the potential to reduce obesity-related health inequalities.

A microsimulation model developed in the United States found that bariatric surgery is cost-effective relative to no surgery(829). The most cost-effective MBS procedure was laparoscopic Roux-en-Y gastric bypass (LRYGB), when compared to laparoscopic sleeve gastrectomy (LSG) and laparoscopic gastric banding (LAGB). The LRYGB procedure yielded 17.07 QALYs, which exceeded the 16.56, 16.10, and 15.17 QALYs attained from LSG, LAGB, and non-surgical management, respectively. On the other hand, of these procedures, LSG was found to be the most cost-effective choice when patients' preoperative BMI was between 35.0 and 39.9kg/m^2, though LRYGB was the most cost-effective choice if the patient's BMI exceeded 40kg/m^2(829).

A cost-utility analysis conducted in England found that bariatric surgery was cost-saving to the healthcare system, saving an average of €2742 (£1944) per patient(662). It also yielded a 4.0 QALY gain relative to no surgery (10.1 vs 6.0, respectively)(662). These results were similar to those of a cohort study conducted in 2016, which was published as part of the Health Technology Assessment programme at the National Institute of Health Research(174). Using individual patient-level data from the hospital records of hospitals in the United Kingdom (UK), the model estimated that bariatric surgery provided a gain of 2.142 in incremental QALYs and that the cost per QALY gained was £7129. In Spain, another cost analysis also supported these results, concluding that bariatric surgery led to an additional 4.4 QALYs over conservative management over the average patient's lifetime(830). Over a ten-year time period, the cost of each additional QALY was €5966.

Other studies have yielded similar results on the incremental cost-effectiveness ratio (ICER). Picot et al. found that the ICER for bariatric surgery ranged from €1833 (£1300) to €5640 (£4000) per QALY(661). Ackroyd et al. reported that gastric bypass and adjustable gastric banding (AGB) had

ICERs of €2139 (£1517) and €2720 (£1929) per QALY, respectively(831), while Pollock et al. found an ICER of €5079 (£3602) per QALY for AGB(832). These results were further supported by separate studies conducted in Thailand(833) and Korea(834). In Thailand, the authors found that the incremental cost per QALY of bariatric surgery, relative to medication, was 26,907.76 Thai Baht ($USD803) (833). In Korea, the ICER was US$1,771 per QALY, the cost-utility analysis indicating that bariatric surgery added 0.86 incremental QALYs(819).

Increased QALYs following MBS are largely due to the substantial increase in the number of life-years lived free of comorbidities. Gulliford et al. found that patients who had undergone MBS lived more life-years free of diabetes mellitus than patients who received conservative management(174). Thus, by facilitating long-term weight loss and alleviating comorbid obesity-related conditions, MBS increases both quality of life and life-years.

In 2015, the Second Diabetes Surgery Summit (DSSII) was held, in collaboration with leading diabetes organizations and endorsed by several international professional societies, including IFSO. At this conference, a multidisciplinary group of clinicians and scholars convened and, after appraising the evidence surrounding metabolic surgery for T2DM, participated in three Delphi rounds of voting. Based on this Delphi survey, conference attendees concluded that MBS should be recommended as the treatment of choice for patients with T2DM and class III obesity and for patients with T2DM and class II obesity if hyperglycaemia is inadequately controlled with conservative therapy(175). Metabolic surgery may also be considered in patients with T2DM and class I obesity if hyperglycaemia is inadequately controlled conservatively(175).

The second Diabetes Surgery Summit (DSSII) guidelines were established based on current evidence supporting the superiority of MBS for obesity management. There is a growing body of literature, which includes several high-quality randomized controlled trials (RCTs), which has consistently demonstrated the superiority of MBS at achieving sustained weight loss and reducing glycaemia and insulin resistance versus both medical and dietary modifications(176, 177, 178, 179, 180, 181, 761). Analysis of the available literature revealed a median HbA1c reduction of 2.0% for surgery compared to 0.5% for conservative management(175). Furthermore, metabolic improvement following bariatric surgery in patients with T2DM is correlated with a shorter diabetes duration, possibly reflecting preservation of patients' B-cell function(183, 835). Therefore, given the DSSII guidelines recommending surgical management of T2DM in certain patients with obesity, the potential for bariatric surgery to improve quality of life by reducing comorbid conditions has been recognized. This is especially true in patients with T2DM, as the cost-effectiveness of bariatric procedures appears to be greater in patients with T2DM than those without(184). The average cost per QALY gained from bariatric surgery ranges from approximately $USD5,000 to $USD10,0008(184). Comparatively, intensive glycaemic control using conservative interventions costs approximately $USD41,384 per QALY(185). Thus, the initial cost of bariatric surgery is repaid early on from the medications that are discontinued, hospitalisations avoided, and complications not suffered. As such, these guidelines further demonstrate the improvement in QALYs from MBS that is due its effect on T2DM.

Metabolic and bariatric surgery has also been shown to be cost-effective and to provide more QALYs than no surgery in adolescents. In one study conducted in the United States, after three years, bariatric surgery had led to a gain of 0.199 QALYs when patients who underwent MBS were compared to patients who did not undergo surgery(836). Surgery also proved cost-effective at five years, with an ICER of $91 032 per QALY. Thus, over a 5-year period, bariatric surgery led to gains in QALYs and was cost-effective(836). A further example is a meta-analysis conducted in 2011 found that the estimated cost per surgery for LAGB placement was $AU31553, while the net cost savings per disability-adjusted life year (DALY) were $AU44,400(837). The authors concluded that LAGB was cost-effective, although they expressed some concerns regarding postoperative complications, non-compliance, and brevity of follow-up, especially given the relative paucity of longer-term data in adolescents(837). For these reasons, further studies are recommended to assess the long-term outcomes of MBS, especially in adolescent patients.

In a lifetime analysis of adolescents with obesity, RYGB was found to add 5.57-5.66 QALYs relative to no surgery, while LSG gained 5.50-5.64 QALYs versus no surgery(838). The authors also found that the incremental cost per QALY gained from RYGB versus no surgery was £2,005-£2,018, while the mean incremental cost per QALY gained from SG versus no surgery was £1,941-£1,978. Thus, they concluded that bariatric surgery in adolescents is both cost-effective and improves QALYs relative to no surgery(838). The higher costs of surgery were due to the costs associated with the bariatric procedure itself, including the costs of pre- and post-operative care. However, these high initial costs were offset by reducing the costs required to treat co-morbidities, which were found to be lower among patients who had undergone surgery.

These results were similar to those of a separate study which found that, although MBS was not cost-effective over the first three years, it became so in the fourth year and remained so afterwards(839). In this study, the authors found that MBS cost $80,065/QALY after the fourth year and $36,570/QALY after seven years, which highlights the long-term economic gains achieved with MBS(824). Its cost-effectiveness may be partly explained by the remission of obesity-associated comorbidities. This is particularly true in adolescents, where a Teen-Longitudinal Assessment of Bariatric Surgery study found that diabetes and hypertension resolved in 95% and 80% of patients, respectively(840). These improvements in comorbidities lead to reduced healthcare resource use and, thus, can even be cost saving for healthcare systems.

Cost analyses of MBS have also found that it is cost-effective with greater gains in QALYs for certain population groups, such as patients with diabetes, women, and patients with a higher preoperative BMI(662, 829, 841). Additionally, older patients incur lower total costs and fewer total QALYs, consistent with their shorter life expectancy. However, their incremental costs and QALYs are higher, due to the higher absolute risk reductions in their demographic, which has a higher baseline risk compared to the general "at risk" population.

The results of landmark studies examining the cost-effectiveness of MBS and its impact on quality of life are summarized in Table 8-1, below. From these results and others, it is clear that MBS has already been well established not only as the gold-standard for treating severe obesity, but also as a highly cost-effective approach that generates increased QALYs relative to non-surgical treatment options, much of which may be due to the resolution of obesity-linked comorbid conditions.

The next chapter – Chapter 9: Outcomes and Follow-up – details the essentials of both short-term and long-term follow-up; identifies both common and serious problems that can arise, including weight regain; and describes the steps necessary for their management. It begins by providing a practical definition of MBS success.

Table 8-1: Summary of the literature

Author	Year	Method	Population	QALY	$/QALY
Alsumali et al.	2018	Microsimulation model over a lifetime horizon	Adults	RYGB: 17.07 LSG: 16.56 LAGB: 16.10 No surgery: 15.17	RYGB: $USD5446 LSG: $USD7655 LAGB: $USD8214
Borisenko et al.	2018	State-transition Markov model	Adults	Bariatric surgery: 10.1 No surgery: 6.0	Bariatric surgery saves the healthcare system €2742 (£1944)
Klebanoff et al.	2017	Markov model, using TreeAge Pro 2015 (TreeAge)	Adolescents	After 3 years, surgery led to a gain of 0.199 QALYs versus no surgery	Bariatric surgery had an incremental cost-effectiveness ratio of $USD91 032 per QALY over 5 years
Panca et al.	2018	Markov cohort model	Adolescents	RYGB: gained 5.57-5.66 QALYs versus no surgery LSG gained 5.50-5.64 QALYs versus no surgery	RYGB versus no surgery: incremental cost/QALY was £2,005 to £2,018 LSG versus no surgery: £1,941 to £1,978
Bairdain and Samnaliev	2015	Markov cohort model	Adolescents	Not analysed	Bariatric surgery was not cost-effective in the first three years, but became cost-effective after that ($80,065/QALY in year four and $36,570/QALY in year seven)
Gulliford et al.	2016	Probabilistic Markov model populated with empirical data from electronic health records.	Adults	Incremental QALYs were 2.142 per participant	Cost per QALY gained was £7129
Sanchez-Santos et al.	2017	Probabilistic Markov model	Adults	Bariatric surgery led to a gain of 4.4 QALYs over conservative management	€5966/QALY over a ten-year time horizon

Viratanapanu et al.	2018	Combined decision tree and Markov model for analysis	Adults	Bariatric surgery: 13.57 Conservative management: 10.75	Incremental cost per QALY of bariatric surgery relative to medication was 26,907.76 Thai Baht/QALY
Song et al.	2013	Markov model	Adults	Bariatric surgery: 16.29 Conservative management: 15.43	Incremental cost-effectiveness ratio was US$1,771/QALY

RYBG = Roux-en-Y gastric bypass; LSG = laparoscopic sleeve gastrectomy; LAGB = laparoscopic gastric banding; QALY = quality-adjusted life year; $USD = United States dollars

7. AREAS OF CONSENSUS

For IFSO/WGO Delphi survey statements on MBS, since all the statements pertained to the efficacy and to the health benefits and risks of surgery, with no statements on the technical aspects of surgery, all N=94 experts were encouraged to vote, if they felt comfortable doing so. The number of experts who voted on individual statements ranged from 79 to 91, all percentages greater than the a-priori 80% participation criterion that decided the validity of results for each given statement. Hence, all the results summarized in Table 8-2, below, are considered valid, from a consensus perspective.

Table 8-2: Consensus achieved on metabolic and bariatric surgery (MBS)

Statements	Most common selection	% consensus
Substantial net health benefits may be anticipated, on a societal level, from the wider use of bariatric surgical procedures in patients with severe obesity.	Agree	98.9%
Since severe obesity shows strong socioeconomic patterning, bariatric surgery has the potential to reduce obesity-related inequalities in health, as long as there is equitable patient selection.	Agree	98.9%
Relative to medical therapy, in patients with obesity and type 2 diabetes, bariatric surgery is generally, in the long run...	More effective	95.5%
Substantial net economic benefits may be anticipated, on a societal level, from the wider use of bariatric surgical procedures in patients with severe obesity.	Agree	95.4%
The cost benefit of bariatric surgery is greater in patients with obesity-related comorbidity, greater in patients with no obesity-related comorbidity, or about the same on these two populations.	Greater with comorbidity	86.4%
Similar cost-effectiveness may be anticipated in diverse groups undergoing MBS, including men & women, patients across a wide range of ages, & patients with different levels of social deprivation.	Agree	85.9%
Increasing patient selection for bariatric surgery to include patients who are less obese will increase the overall societal health benefits of bariatric surgery.	Agree	85.9%
Due to the increased risks of surgery in those who are more obese, in patients who are very obese, bariatric surgery is less cost effective than in those who are less obese.	Disagree	80.7%

The cost benefit of bariatric surgery is greater in younger than older patients, greater in older than younger patients, or about the same in youths and seniors.	Greater in younger	79.7%
All forms of bariatric surgery are effective, overall, at improving patients' quality of life.	Agree	77.8%
Patients with a BMI between 40 and 50 kg/m^2 experience the greatest cost benefit from bariatric surgery.	Agree	77.6%
Weight regain depends on the type of MBS performed.	Agree	72.7%

8. CONCLUSIONS AND RECOMMENDATIONS

The following conclusions and recommendations are based both upon a thorough review of the published scientific literature and the consensus opinions of the IFSO/WGO expert panel.

Over the past few decades, metabolic and bariatric surgery has become firmly, empirically established as the most effective treatment for obesity, in terms of reducing weight loss, managing the numerous comorbid conditions that have been empirically linked to BMI, enhancing overall patient quality of life, and reducing patient mortality.

Sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB) are currently the most commonly performed MBS procedures worldwide, though newer procedures, like one-anastomosis gastric bypass (OAGB) show promise.

Which procedure is employed should largely be decided on a patient-by-patient basis, that decision influenced by various patient characteristics – for example, evidence favours utilizing RYGB in patients with GERD – as well as by the operating surgeon's level of experience with each surgical approach.

Regardless of which operation is elected for use, patients must be thoroughly assessed by a multi-disciplinary team pre-operatively to determine their suitability for surgery and identify any issues that may require addressing.

Patients also must be monitored closely throughout the peri-operative period for peri-operative complications; then followed, essentially for the rest of their life by the multi-disciplinary obesity-management team.

IX. Post-operative outcomes and follow-up

1. Introduction: defining treatment response and non-response
2. Importance of post-operative follow-up
3. Monitoring post-operative medical status and medications
4. Nutrition status
5. Areas of consensus
6. Conclusions and recommendations

1. INTRODUCTION: DEFINING TREATMENT RESPONSE AND NON-RESPONSE

There is no longer any reason to debate whether metabolic and bariatric surgery (MBS) results in significant weight loss and numerous other positive outcomes, including the prolongation of life(813, 814, 815, 816, 817, 818, 819), or that published evidence unequivocally supports MBS being the current gold-standard treatment for obesity(763). This said, there is no consistent degree of weight loss that every patient experiences(842, 843, 844), and not all patients observe complete or even meaningful resolution of obesity-associated comorbid conditions like type 2 diabetes(761). Also, over time, some beneficial effects, including the degree of weight loss, may diminish(51, 843, 845, 846). And, psychologically, many patients – including most women – will continue to identify themselves as living with obesity even after they achieve sizeable losses of weight(847).

Being able to decide whether MBS has been adequately or inadequately successful is an important determination because it also determines whether further therapy is necessary and, if so, which kind. Are, for example, anti-obesity medications or further surgery worth considering? Is weight regain enough to justify further treatment? If so, how much weight regain, and which metric (e.g., % excess weight loss [%EWL] vs. % total weight loss [%TWL]) should be used to measure it(844)?

Weight regain after MBS is multi-factorial, potentially including nutritional non-adherence, physical inactivity, mental health issues, and anatomical issues encountered during MBS; and such issues warrant investigation. This said, some degree of weight regain after MBS is normal between two and ten years after MBS(427). One common problem that arises, however, is that many patients perceive any weight regain as personal failure, and such a negative perception can exert appreciable adverse psychosocial impacts upon their overall outlook on life; their satisfaction and, hence, continued adherence with treatment; and, ultimately, their health(425, 428). One thing that healthcare practitioners can do to reduce patients' perception of "failure" is to personally stop using this word all together, replacing it with much less emotionally-charged words like "sub-optimal response". Among other potential effects, referring to response and non-response instead of success and failure shifts the burden from the patient to the treatment. The healthcare provider can then work with the patient to improve the treatment program, primarily focussing on those components that patients have control over, like their diet and activity level.

The quantity of weight that a patient might regain depends on several patient- or procedure-related factors(848). For example, patients whose pre-operative BMI is 50kg/m^2 or greater have a higher rate of weight regain than patients with less severe obesity (BMI <50 kg/m^2)(849). Similarly, adjustable gastric banding (AGB) and sleeve gastrectomy are generally associated with more weight regain than Roux-en-Y gastric bypass and biliopancreatic diversion(848).

There is no uniformly-recognized definition for what constitutes surgical success after MBS. Different definitions of success include achieving >50% reduction in excess weight (%EWL), a BMI <35kg/m^2, and >10% reduction in total body weight (%TWL). However, the most commonly used definition for significant weight regain after MBS is achieving less than 50% EWL(842).

Regardless of how it is defined, weight regain after MBS must <u>never</u> be considered failure. Instead, it must be treated like a recurrence of disease, in the same way that cancer or rheumatoid arthritis recurrence is viewed. Like patients presenting with recurrence after cancer therapy, patients presenting with significant weight regain after MBS require an extensive evaluation, including anatomical studies – upper endoscopy [EGD], upper gastrointestinal barium studies [UGI] – and evaluation by the multidisciplinary team(848, 850). Moreover, weight regain is not the only clinical outcome that can warrant investigation. For example, patients presenting with GERD symptoms, with or without weight regain after MBS, also require an objective assessment to identify or rule out GERD, including pH studies with or without manometry(851).

Patients with significant weight regain after MBS require both an evaluation by the multi-disciplinary team and supplementary medical treatment (e.g., a glucagon-like peptide-1 agonist)(848). In addition, significant weight regain after MBS, as well as the presence of obesity-related medical problems, may require further medical, endoscopic, or surgical treatment. Hence, MBS centres should work jointly with primary care providers to provide follow-up and access to appropriate healthcare professionals, as clinically indicated, because patients need annual life-long follow-up after MBS(848). Similarly, follow-up after endoscopic bariatric treatment must always involve a complete multidisciplinary team [MDT] (e.g., dietitian or nutritionist, psychologist, exercise therapist)(852). Throughout this process, however, it is crucial that all members of the MDT avoid calling weight regain, in itself, evidence of treatment non-response. It must never be considered so. Though no uniformly-accepted definitions presently exist for either treatment response or treatment non-response, what is certain is that stigmatizing either less-than-expected weight loss or weight regain as failure can have serious psychological and, ultimately, physical consequences. Given the past focus of obesity interventions on weight loss as the primary outcome and pervasive social bias against people with obesity, patient's expectations of both short-term and long-term weight loss often exceed what obesity management interventions can realistically achieve(425). It is essential that obesity management professionals work together to reduce the stigma of obesity and weight regain after MBS, in the same way that it is crucial to always provide patients undergoing MBS with an empathic and non-judgmental clinical environment throughout the duration of patient follow-up(434).

2. IMPORTANCE OF POST-OPERATIVE FOLLOW-UP

Patients who undergo MBS, irrespective of their age, must typically be followed by a multi-disciplinary term for the remainder of their lives. This even includes patients who have MBS during adolescence. There are several reasons for this.

First, long-term weight loss and control of obesity-associated comorbidities relies upon patients remaining adherent with all the other non-surgical facets of their care, including their diet, exercise, any nutritional supplements and/or medications that they have been prescribed; and behavioural counselling, especially for patients with recognized disordered eating patterns or conditions or a history of substance or behavioural addiction. Adherence with treatment has been empirically linked to enhanced weight loss and cardiometabolic outcomes(355, 356, 357). Attendance at follow-up sessions is particularly important, since the number of intervention sessions attended is directly correlated with the degree of weight loss achieved(357, 358). Data from one recently-published meta-analysis further suggest that higher levels of adherence occur with interventions that incorporate social support (e.g., group sessions, peer coaching, participation of friends/family members), attendance monitoring, and supervised (vs. self-directed) programming(359).

Second, all patients who undergo MBS are at marked risk of nutritional deficiencies due to alterations in their GI pathway and resultant reductions in the absorption of certain nutrients. This is especially true of patients who have a nutrient deficiency diagnosed preoperatively, who also are at risk of developing more severe and other nutrient deficiencies post-operatively(33, 509, 512, 513). In the short-term, nutritional deficiencies also may occur secondary to the physiological stress of surgery(514, 515). Twelve micronutrients – seven vitamins (A, C, D, E, B6, B12, folate) and five minerals (iron, zinc, copper, magnesium, selenium) are now known to be involved in every stage of a fully functioning immune system, which includes maintaining physiological barriers and innate, inflammatory, and adaptive immune responses(516, 517), and many of these micronutrients are commonly deficient after MBS(33, 446, 508, 509, 518). Nutritional deficiencies also can lead to such dire consequences as central nervous system disease and peripheral neuropathies(853, 854), anaemia(855, 856), severe protein malnutrition(36, 857), and an increased risk of osteoporotic fractures. (858, 859, 860, 861).

A third reason for life-long post-operative monitoring is the risk of other relatively common post-operative complications, some of which may not be life-threatening – e.g., post-prandial abdominal pain, nausea, and/or vomiting; and GERD – but which can significantly diminish patients' quality of life, lead to psychological issues like anxiety and depression, and potentially lead to further problems like addiction transfer – whereby a person's "addiction" to food is replaced by addiction to some other substance or behaviour(43) – or even suicide(862, 863, 864), with successful suicides estimated, in one meta-analysis, to occur in roughly three out of every 1000 patients who undergo MBS(815).

Fourth, persons with obesity generally have two- to three-fold the risk of at least thirteen different forms of cancer, relative to individuals with a normal weight(46, 266, 777); and, although considerable evidence has been published showing that MBS reduces a person with obesity's cancer risk(265, 274, 275, 281, 284), such reductions appear to be site-specific(865), meaning that the MBS patient's overall cancer risk likely remains elevated, even after substantial weight loss.

Fifth, the anatomical and physiological changes that occur from the surgical procedure itself and the weight loss that usually follows can have numerous other effects on a patient's health. This includes improvements or lowered risk of other health conditions (like type 2 diabetes), but also potentially increased risks or severity of others, like gallstones(866, 867, 868, 869), gout(870, 871, 872, 873), and nephrolithiasis(874, 875, 876, 877).

Finally, similar to the impact of the anatomical and physiological changes that occur with MBS on various health conditions, patients may experience clinically-significant changes in their body's absorption of and response to various medications.

3. MONITORING POST-OP MEDICAL STATUS & MEDICATIONS

a. Medical conditions

As explained above, managing MBS patients after their surgery requires monitoring for a number of different health conditions, some of which may improve or completely resolve; others of which might worsen or even present for the first time. Especially among patients who experience rapid reductions in weight, the presence and clinical severity of gallstones(866, 867, 868, 869), gout(870, 871, 872, 873), and nephrolithiasis(874, 875, 876, 877) may become significant issues, though these risks appear to differ between different procedures.

Several studies have shown that the risk of gouty attacks is significantly elevated early in the post-MBS period, with acute attack rates as high as 30-40% among patients diagnosed with gout pre-operatively(870, 871), most of these early attacks occurring within the first month(870, 871, 872, 873). These attacks can be polyarticular(871). Patients who undergo gastric bypass and patients with severe obesity may be at particularly high risk of these attacks(870, 871). Patients with pre-existing gout should be made aware of this elevated risk by the obesity-management team and assured access to immediate treatment should an attack arise. Steps also can be taken peri-operatively to ensure adequate hydration, early mobilization, and the use of urate lowering drugs and nonsteroidal anti-inflammatory drugs (NSAIDs), or colchicine and corticosteroids if NSAIDs are ineffective or not tolerated(873).

The risks of both gallstones and of symptomatic cholecystitis seem to be both acutely and chronically elevated following MBS, and this may be especially true in patients who undergo either RYGB or a gastric sleeve procedure(868, 869). In one meta-analysis of eleven randomized controlled trials, the prophylactic use of ursodeoxycholic acid was associated with statistically-reduced rates of gallstone formation (OR = 0.25, 95% CI = 0.21-0.31), symptomatic cholecystitis (OR = 0.29, 95% CI = 0.20-0.42) and cholecystectomy (OR = 0.33, 95% CI = 0.20-0.55)(867).

As for gallstones, the risks of kidney stones and symptomatic kidney stones both seem to be elevated, though this is largely observed later in the post-operative period(874, 875, 876, 877). Also like gallstones, nephrolithiasis appears especially common in patients who undergo RYGB(874, 877).

Obstructive sleep apnoea is a condition that typically improves or even resolves after MBS. However, neither the STOP-Bang nor Berlin Questionnaire are effective tools for detecting patients undergoing MBS who are at either moderate or high risk of obstructive sleep apnoea (OSA). Consequently, clinicians managing patients who either have had or are awaiting MBS should have both (a) a high index of clinical suspicion for OSA, and (b) a low threshold for screening for sleep-disordered breathing.

With progressive weight loss, individuals diagnosed with obstructive sleep apnoea may experience improvements in their sleep-disordered breathing(878). Alterations in the level of continuous positive air pressure (CPAP) that is required to treat their obstructive apnoeic episodes also may decrease over time. Similarly, individual optimal CPAP pressures and how well a patient's mask fits his or her face can change as they lose weight, both requiring monitoring and potential adjustments. Moreover, even with significant weight loss postoperatively, moderate to severe obstructive sleep apnoea may persist(879). It also may resolve post-operatively but then recur several years later, independent of weight regain(880, 881).

Appreciable bone loss also can occur after MBS, a phenomenon that has been attributed to nutritional factors, skeletal unfolding, calcium hormone abnormalities, changes within the bone marrow and body fat, and changes within the hormones of the GI tract, thereby requiring systematic surveillance with bone density evaluations(882).

b. Medication changes

How and if several medications are used is another consideration following MBS. For example, chronic nonsteroidal anti-inflammatory drug (NSAID) use should be avoided in patients who undergo RYGB, among whom vitamin K antagonists generally are preferred oral agents for anticoagulation over direct oral anticoagulants, as the latter's absorption may be affected(608).

Extended and long-acting release medications also might need to be converted to short-acting preparations to enhance post-operatively reduced absorption. Medications which are pH dependent may similarly need to be re-evaluated and other medications may require crushing or liquid preparations to enhance absorption(610, 883, 884).

For contraception, alternatives to oral birth control pills may be required.

Diabetic medications associated with a high risk of either hypoglycaemia or diabetic ketoacidosis – like SGLT2 (sodium-glucose transport-2) inhibitors – should be avoided after MBS(885). Insulin requirements also may need to be adjusted shortly postoperatively and then episodically thereafter as a patient's caloric intake and weight change.

4. NUTRITIONAL STATUS

a. Importance of nutritional follow-up

Nutritional deficits are among the most common complications of MBS, with Italian investigators reporting nutritional deficiencies in 28%, 70%, and 87% of patients who underwent adjustable gastric banding (AGB), sleeve gastrectomy (SG), and Roux-en-Y gastric bypass (RYGB), respectively, five years after their surgery(886). As stated earlier, they also can have severe consequencies, including central and peripheral nervous system disorders(853, 854), iron-deficiency anaemia(855, 856), severe protein malnutrition(36, 857), osteoporosis and osteomalacia secondary to both rapid weight loss and vitamin D deficiency(858, 859, 860, 861), and immunocompromise(517), among many others.

The mechanisms behind these nutritional deficiencies can be best understood by understanding where each nutrient is absorbed along the gastrointestinal tract.

- **Macronutrients and micronutrients, associated calories, and the site/mechanism of absorption along the gastrointestinal tract**

The majority of macro- and micro-nutrients are absorbed in the small intestine, where the duodenum and jejunum both contain an especially large amount of transport proteins for vitamins and electrolytes. Most **electrolytes** (Na^+, Cl^-, etc.) are either absorbed by specific transport mechanisms or diffuse passively from the intestine into the blood. The absorption of carbohydrates is performed by specific sugar transporters of mono- and disaccharides across the entire gastrointestinal tract. Proteins are cleaved into amino acids and peptides by pepsin and other enzymes and then are absorbed by specific transporters (887).

The uptake of **fat/lipids** mainly takes place in the duodenum, where pancreatic lipase is released. Monoglycerides, long-chain fatty acids, and fat-soluble vitamins (A, D, E, K) are resorbed into enterocytes by creating micelles with bile salts. These components then are released as chylomicrons into the thoracic duct. The uptake of vitamin D is closely connected to parathyroid hormone (PTH) levels.

The exogenic uptake of **water-soluble vitamins** is essential, as humans cannot synthesize the majority of vitamins. Vitamin C, biotin, folic acid, thiamine, and vitamins B2, B3, and B6 are absorbed via specific transport mechanisms. Vitamin B12 (cobalamin), which is obtained from animal products and colonic macrobacteria, requires gastric intrinsic factors to be absorbed as a complex via a transport mechanism within enterocytes (887).

In terms of minerals, **calcium** (Ca^{2+}) uptake is mainly located in the duodenum and jejunum. Its main sources are dairy products and vegetables. Calcium uptake has two complementary mechanisms — passive diffusion, and active transport through calcium channels — both determined by bodily calcium levels. **Parathyroid hormone** (PTH) mainly regulates circulating Ca^{2+} levels in the blood. Parathyroid hormone is also tightly linked to vitamin D; as such, patients with vitamin D deficiency may also suffer from secondary hyperparathyroidism (888).

Iron (Fe^{3+}) is reduced to Fe^{2+} in the duodenum and absorbed via a transporter. Its uptake is its only form of regulation, since there is no natural mechanism to excrete iron from the body. Further micronutrients that are essential for bodily homeostasis are **phosphate, zinc, copper, cadmium, and selenium**, all of which depend on specific transport mechanisms mainly in the duodenum and jejunum (887).

Broadly speaking, the daily requirement of calories ranges between 1600 and 2000kcal/day for women and from 2000 – 2500kcal/day for men, though research shows that those with higher body weights have higher energy requirements(889, 890). Chronic calorie intake in excess of adequate energy use causes calories to be stored, thereby increasing body weight, just as chronic energy usage in excess of calorie intake leads to weight loss (891).

b. Basics of nutritional follow-up

For MBS patients to understand how necessary long-term, regular follow up of their nutrition status is, it is crucial that this is the message they receive clearly, regularly, and from all members of the multi-disciplinary team. Such nutrition status follow-up should include regular appointments, laboratory examinations, and anthropometric measurements, along with recurring clinical evaluations to check for signs and symptoms of potential nutritional deficiencies.

Moreover, research has linked regular postoperative dietary counselling by a dietitian/nutritionist to greater weight loss at both four and 24 months than no such counselling(892, 893). One of these studies also revealed improved eating behaviours among those receiving dietary counselling. Visits are thus recommended to occur with either a dietitian or nutritionist preoperatively, at one month, three months, six months and one year postoperatively, and then annually(446, 892).

In one study by Mitchell et al., patients who lost adequate amounts of weight generally were those who weighed themselves weekly, saw their nutritionist/dietitian regularly, practiced exercises, and kept a register of their food intake as self-monitoring strategies(894). Adherence to follow-up also is associated with fewer postoperative adverse events, greater excess body weight loss, and fewer comorbidities. A recent study revealed that complete follow-up over the first year after Roux-en-Y gastric bypass (RYGB) was independently associated with a higher rate of improvement in or remission of comorbid conditions(895). Other studies have identified an association between excess weight loss and adherence to follow-up visits(892). Consistent with this, in another study, Weichman et al. found that fewer than seven follow-up visits per year was associated with less excess weight loss than with seven or more follow-up visits(896).

As obesity is a chronic disease, both nutritional and psychological follow up are crucial to keeping patients on track and focused on achieving and maintaining healthier habits and good nutritional status. However, the extent of nutritional follow-up after MBS depends upon several factors, most notably the surgical procedure performed, the bodily changes anticipated, and the presence and severity of any pre-existing comorbidities. Such follow-up should be conducted continuously by a dietitian/nutritionist on the patient’s multidisciplinary team at an outpatient level, and can be done individually and/or in group sessions, in accordance with the institution's lifelong monitoring protocol for patients with obesity(33, 446, 508, 897).

The primary objectives of post-operative nutritional treatment should be to minimize any potential adverse nutritional effects from bariatric surgery, in both the short and long term, as well as to continue the process of nutrition education initiated in the preoperative period. Achieving these two goals requires:

- Introducing patients to their postoperative diet
- Ensuring caloric and nutritional adequacy
- Monitoring for nutritional deficiencies long-term
- Advising regarding nutritional supplementation, which varies from patient to patient, depending on both the bariatric procedure performed and the patient's personal nutritional status.

c. Introducing the postoperative diet

Introduction to the postoperative diet may start after the first 24 hours following the surgical procedure. The diet must initially have a liquid consistency and its nutritional composition should be of low sugar content, as prescribed by the clinical nutritionist/ dietitian and/or bariatric surgeon(898). Progression of the diet should be orchestrated by the dietitian, during the first post-operative consultation, again depending on the surgical procedure performed. Over time, diets usually evolve, in successive stages, from a clear liquid to a full liquid, then a puree, then a soft and, finally, a normal diet, often transitioning from one to the next dietary stage roughly every two weeks. The five dietary forms included in transition, in their order of introduction, are:

Clear liquid diet: This diet is usually initiated on the first day after surgery, It consists of sugar-free or low-sugar clear liquids (e.g., gelatine, teas, and broths), and is initiated when the patient is still in the hospital.

Full liquids: Patients usually transition from clear to full liquids after discharge from the hospital. This diet includes milk, yogurt, bottled protein drinks, fortified soups, and protein supplements.

Pureed diet: Pureed diets consist of foods that have been blended or liquified, like pureed fruits and/or vegetables, scrambled eggs, and canned fish (a spoonful).

Soft food: Soft food includes anything that can be kneaded with a fork, including vegetable purees, peeled fruits, eggs, and finely diced or ground lean meats.

Regular diet: The final, usually-prescribed stage is a regular diet, which encompasses tougher-to-digest meats, raw fruits and vegetables, and so on.

The rate of progression through the various stages is largely determined by the surgical procedure performed and by local practices., but also depends on and is tailored to the individual patient(446). Post-operative protein recommendations range from 1.2 to 1.5 g/kg/day, based upon both the patient's body weight goal and the surgical procedure performed, including a minimum of 60 grams of protein per day after a sleeve gastrectomy or RYGB, but 80–120g/day after a duodenal switch procedure(360, 899). There also is a need to routinely include vitamin and mineral supplementation, which in the first month should be in liquid or chewable form(898).

Over the long term, patients are encouraged to follow a structured diet that involves three balanced meals and one to two healthy snacks each day. This scheduled meal and snack frequency is intended to help patients avoid the temptation to snack or graze between meals. Such snacking or grazing may hinder weight loss and/or lead to weight regain in the long term. A low-fat, moderate-carbohydrate, and high-protein diet is recommended.

Patients are advised not to eat and drink at the same time, especially over the first post-operative year. This includes avoiding any consumption of fluids 30 minutes prior to eating, during meals, and for 30 minutes after eating. All carbonated beverages and caffeinated drinks should be avoided. Alcohol intake should either be minimised, or alcohol avoided entirely due to increased absorption.

d. Ensuring caloric and nutritional adequacy

Dietary and nutritional follow up must be appropriate for the bariatric procedure performed. By design, every bariatric procedure should reduce food intake. The impact on absorption of macronutrients and micronutrients, however, depends on the procedure. The manner in which the new gastrointestinal tract will function — resulting from its revised gastric capacity, the anatomy of the small intestine, and the length of a common channel — may or may not influence the absorption process, depending on the procedure being performed(900). However, post-operative nutritional deficiencies still may occur. For example, the absorption of micronutrients does not change after adjustable gastric banding (AGB), after which any nutritional deficiencies that transpire typically are linked to decreased food intake and/or food intolerances that patients might develop. In contrast, biliopancreatic diversion (BPD) with or without duodenal switch (DS), DS on its own, one-anastomosis gastric bypass (OAGB), and single anastomosis duodenal-ileal (SADI) bypass introduce anatomical changes that interfere with the absorption of both macro- and micro-nutrients. Further contrasting are sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB), which can lead to certain nutritional deficiencies due to decreased food intake, alterations in the gastrointestinal tract, and both reduced contact with and briefer exposure of food to digestive enzymes. Table 9-1 summarizes these procedures and possible nutrient deficiencies.

Table 9-1 - The impact of bariatric surgery on nutritional absorption

Procedure / Nutrient	SG	RYGB	OAGB	DS	SADI
Protein	No	No	Yes	Yes	Yes
Fat	No	No	Yes	Yes	Yes
Vitamin D	Yes	Yes	Yes	Yes	Yes
Vitamins A, E, and K	No	Vitamin A	Yes	Yes	Yes
Iron, folate, vitamin B12	Yes	Yes	Yes	Yes	Yes
Zinc, copper, selenium	Yes	Yes	Yes, (High risk)	Yes (High risk)	Yes (High risk)
Thiamine	Yes	Yes	Yes	Yes	Yes

Borrowed, with permission, from O'Kane et al, 2021(900)
SG = sleeve gastrectomy; RYGB = Roux-en-Y gastric bypass; OAGB = one-anastomosis gastric bypass; DS = duodenal switch; SADI = single anastomosis duodenal-ileal bypass

e. Monitoring for specific nutritional deficiencies long-term

Reduced food intake, rerouting of nutrient flow, and changes in gastrointestinal anatomy and physiology resulting in malabsorption are among several potential mechanisms that often lead to nutritional deficiencies. Another widely-recognized critical cause of nutritional deficiency after bariatric surgery is patient nonadherence with recommendations regarding nutritional supplementation(33, 508, 901, 902). It is possible that, in addition, the deficiency of certain nutrients — like protein, vitamins and minerals — may occur due to potential food intolerances and maladaptive eating with subsequent gastrointestinal symptoms(36).

Keeping MBS patients on track by performing an appropriate preoperative assessment, providing thorough patient education and preparation, offering dietetic support, maintaining them on adequate nutritional supplementation, and monitoring their dietary and nutritional status lifelong can lead to the prevention and proper management of numerous potential nutritional deficiencies(900).

Thiamine: Besides being an elevated preoperative risk, thiamine deficiency may likewise occur within one to three weeks after surgery(854). Patients have a higher risk of thiamine deficiency during the early post-operative period due to their rapid weight loss, decreased caloric intake, and possible GI tract symptoms, like nausea and vomiting(900).

Given the potential consequences of thiamine deficiency — which can include potentially catastrophic consequences like ataxia, confusion, coma, Beriberi, Wernicke's encephalopathy, neuropathy and neuritis — all centres involved in post-bariatric follow-up should be aware of the potential risk of this severe deficiency, especially if patients have suffered from prolonged vomiting, rapid weight loss, alcohol abuse, poor nutritional intake, or possible small intestine bacterial overgrowth(33, 508, 855, 903). General multivitamins and mineral supplements may not have the adequate amount of thiamine to prevent deficiencies. Parrot et al recommend a minimum of 12mg/d to 50mg/d, given in the form of a once or twice per day complex B supplement(33). Certain signs and symptoms — like oedema, ataxia, forgetfulness, neuropathy, and abnormal visual changes — may be related to thiamine deficiency and must be treated immediately.

In any suspected cases of thiamine deficiency, immediate oral or intravenous treatment is recommended, even without biochemical confirmation of the deficiency(446, 508, 509, 903). See Table 9-2, below, for more details.

Protein: After any bariatric procedure, there is the risk of protein deficiency, mainly due to gastric capacity reduction(360, 509, 902, 904). Furthermore, in addition to changes in the digestive tract that interfere with protein intake, prolonged vomiting, diarrhoea, food intolerance, depression, fear of weight regain, alcohol consumption, inadequate financial resources, inadequate chewing, and low-calorie diets all may contribute to reduced protein consumption. Inadequate calorie and protein intake is also often associated with anaemia, as well as with zinc, vitamin B6 and B12, folic acid and copper deficiencies(902, 903).

Research has shown that protein-calorie malnutrition is not particularly prevalent after either a SG or RYGB procedure. However, most studies that have looked at this were limited to short-term follow-up and primarily evaluated albumin and total protein levels, which certainly could result in underestimating actual protein deficiency prevalence(446, 508, 902, 904) It is important to emphasize that, in patients undergoing malabsorptive surgeries — like BPD-DS, OAGB, and SADI — malnutrition occurs in 7-21% of patients. In these patients, there is an even greater need for protein supplementation to compensate for losses (an average of 30g/day) that result from marked malabsorption(902, 904, 905).

Oedema is one possible indicator of protein-energy malnutrition. However, it also can mask weight loss and muscle mass loss. Thus, besides obtaining a detailed dietary history, clinical/anthropometric assessments are necessary for proper diagnosis.

To properly assess protein intake among AGB, SG and RYGB patients, clinical practice recommendations are currently for at least 60g to 120g/day or 1.5g/kg/day of ideal body weight (IBW). Prescribing higher amounts of daily protein - up to 2.1g⁄kg⁄day of IBW – requires a personalized assessment. The malabsorptive procedures BPD-DS, OAGB, and SADI are associated with higher risks of protein malnutrition. Therefore, protein intake of at least 90g/day or as much as 2.1g/kg of IBW is needed. Whey protein, casein, and protein drinks are recommended as additional supplementation, especially in the initial stages and up to the point when patients can consume the appropriate amount of protein in their diet(900).

Iron, Vitamin B12 and Folic Acid: Due to the lower intake of food sources, hypochlorhydria, the surgical exclusion of the site of intestinal absorption in the small intestine (RYGB), and the hastened passage of food in the first segment of the small intestine, there is a high incidence of iron deficiency anaemia in patients undergoing either a RYGB or SG procedure. The same is observed after malabsorptive surgeries (BPD-DS, OAGB and SADI). Especially high-risk populations are females at a fertile age, adolescents, and athletes(33, 446, 508, 509, 855).

Vitamin B12 absorption is also affected after bariatric surgery (RYGB, SG, BPD, and DS), as it requires an acidic environment and the presence of an intrinsic factor produced by parietal cells in the stomach(446, 508, 902). In addition, the absorption of B12 requires an ideal ileal pH for absorption, which can also be altered after bariatric procedures. As vitamin B12 is stored in the liver, B12 stores can last for a long period of time. Consequently, continuous, long-term monitoring is recommended, since deficiency can appear years after the index surgery(508). This said, neurological manifestations of B12 deficiency can also sometimes present shortly after surgery(853).

Since vitamin B12 is necessary for both erythropoiesis and the nervous system, inadequate concentrations can lead to both megaloblastic anaemia and irreversible neuropathy – therefore, if there is any suspicion of deficiency, immediate treatment is recommended(508).

It is important to emphasize that measuring serum B12 levels is inadequate as a means to confirm deficiency, because of the low sensitivity and specificity of such measurements. In patients undergoing bariatric surgery, methylmalonic acid has been proposed as a more sensitive indicator, since it can help to diagnose this deficiency early. This is because vitamin B12 is a coenzyme that accelerates the conversion of methylmalonyl-coenzyme A to succinyl-coenzyme A. When there is insufficient vitamin B12 for this conversion to take place, methylmalonyl-coenzyme A accumulates and is converted to methylmalonic acid, which accumulates in the blood and ultimately is excreted in urine, elevating urine levels.

The absorption of folic acid, which occurs in the small intestine, also can be affected, especially after RYGB, BPD-DS, OAGB and SADI. This deficiency, however, may likewise occur after SG. It is believed that folic acid deficiency is more connected to reduced food intake and lack of adherence to supplementation, rather than to any decrease in absorption itself(508). One important point to consider is that the megaloblastic and macrocytic anaemia associated with vitamin B12 deficiency can be masked by folic acid(33, 508, 902, 903, 906).

Vitamin D, Calcium, and Parathyroid Hormone (PTH): Vitamin D, among other functions, is fundamental to skeletal muscle health and essential for calcium absorption and bone mineralization. The optimal concentrations of 25-OH vitamin D for maintaining bone health and preventing secondary hyperparathyroidism have not yet been determined among patients undergoing MBS. Consensus surveys of field experts and other, more methodologically robust clinical studies have generated recommended ideal serum levels of >75nmol/L and >50nmol/L, respectively. However, more studies are needed to confirm these levels(446, 508, 907, 908).

In the presence of increased calcium concentrations and persistently-elevated PTH, it is important to check PTH at baseline, so as to exclude the diagnosis of primary hyperparathyroidism(446, 508). After bariatric surgery, the risk of developing vitamin D deficiency is high. However, in those with more malabsorptive procedures, the risk is even greater. Thus, after the surgery, vitamin D, as well as serum calcium, should be monitored periodically, including after any adjustments to supplements are made, to ensure adequate intake(33, 350, 446, 508, 902).

Vitamins A, E and K: Vitamin A deficiency is more prevalent after BPD-DS, OAGB when the biliopancreatic BP limb is >150cm, and SADI procedures and should be routinely monitored postoperatively(33, 446, 902). However, there are reports of vitamin A deficiency in the long term after RYGB and, therefore, monitoring the nutritional status of RYGB patients for vitamin A deficiency should also be considered, as well as in cases of protein-calorie malnutrition, night blindness, and dry eyes. Adolescents are also more susceptible to developing vitamin A deficiency after all bariatric procedures(909).

Deficiency of the fat-soluble vitamins E and K is more frequently reported after malabsorptive surgeries, so there should especially be periodic monitoring after these procedures(446, 508, 910). It is recommended that the evaluation of vitamin E be performed by measuring serum α-tocopherol levels. Meanwhile, the nutritional status of vitamin K should be assessed by measuring levels of both serum K1 and a protein induced by vitamin K, called PIVKA-II(508).

In clinical practice, vitamin K levels are still not easily available, mainly due to difficulties with methodological analysis and high costs. It also is important to emphasize that coagulation tests are unreliable for evaluating the nutritional status of this vitamin.

Although routine monitoring of vitamin E and K is not recommended in individuals undergoing RYGB, SG, or adjustable gastric banding (AGB), in any such patients who develop unexplained anaemia, neuropathy, or haematomas, their evaluation should be considered similarly to how they are periodically measured after other, malabsorptive procedures(446, 508).

Zinc, Copper, Selenium and Magnesium: The most common trace mineral deficiency among bariatric surgery patients is zinc deficiency, affecting 42% of patients one year after RYGB and 25% one year after SG. After a BPD-DS, OAGB, or SADI bypass, the prevalence of zinc deficiency is even higher, potentially as high as 91.7% one year after surgery. Moderate levels of zinc deficiency are associated with hypogeusia, hyposmia, anorexia, eczema, somnolence, and reduced dark adaptation, while severe forms are associated with acrodermatitis enteropathica, bullous or pustular dermatitis, diarrhoea, balding, mental abnormalities including depression, and recurrent infections due to impaired immune function(911).

It is recommended that zinc concentrations in plasma/serum be monitored if patients develop altered taste, anaemia, delayed wound healing, hair loss and/or glossitis. Additionally, it is recommended that post-operative monitoring be continued, after all procedures, at least once per year(508).

The highest prevalence of copper deficiency also occurs after malabsorptive surgeries. However, there are reports in the literature of its occurrence after RYGB. Thus, it is recommended that serum copper be monitored after a RYGB, SG, BPD-DS, OAGB or SADI bypass, as well as in individuals using supplementation with high doses of zinc and in patients with anaemia, leukopenia, thrombocytopaenia, or neuromuscular abnormalities(508).

Although serum selenium levels are measured uncommonly after bariatric surgery, studies have been published demonstrating selenium deficiency after SG, RYGB, and malabsorptive procedures(446, 508, 887, 906).

In cases of chronic diarrhoea, metabolic bone disease, unexplained anaemia, or unexplained cardiomyopathy, selenium should be monitored(508).

In the case of magnesium, more data are needed to recommend its routine evaluation. However, in cases of hypocalcaemia and hypomagnesaemia, investigations should be performed and treatment administered prior to calcium supplementation(508).

Supplementation: Per recent guidelines, as nutritional needs and adherence to supplementation may vary over time, it is recommended that supplements be reviewed and adjusted regularly, reiterating the need for regular, multi-disciplinary, professional follow-up after bariatric surgery(508, 509).

The use of general multivitamins and multi-minerals in the postoperative period is recommended. However, the composition of vitamins and minerals must be carefully checked to ensure that the amounts of each nutrient are sufficient to avoid the effects of malabsorption from bariatric surgery, with additional supplements often necessary. In general, multivitamin and multimineral supplementation should achieve a level equal to 200% dietary reference intake (DRI) levels(33, 898). However, due to the altered GI tract, some vitamins and minerals may be needed in even higher doses.

Table 9-2 summarizes current postoperative nutritional supplementation recommendations for patients who have undergone bariatric surgery.

Table 9-2: Nutritional recommendations for patients after bariatric surgery

Vitamins and minerals	Prevention of deficiencies	Treatment of deficiencies
Thiamine	Complete multivitamin and mineral (MVI & M) supplementation, including 12-50mg thiamine daily. Consider additional oral thiamine for the first 3 to 4 months after surgery.	Treat immediately if the risk or suspicion of thiamine deficiency exists. Oral 200-300mg daily or a strong complex B vitamin (1 to 2 tabs. TID) For persistent nausea and vomiting: 100 mg daily IV or IM for at least 3 days, followed by 100mg QD until symptoms resolve.
Vitamin B_{12}	Three monthly IM injections (1000mcg/month) 350-500mcg/d orally or 1000mcg IM monthly	1000mcg/d IM until symptoms resolve, followed by 1000mcg IM every 2 months
Folic Acid	MVI & M containing 400-800mcg/d (women) or 400mcg (men) folic acid. Additional need for women planning pregnancy.	Check vitamin B12 first. Folic acid 5mg orally daily for 4 months. Further investigation if malabsorption is suspected.

Iron	Daily MVI & M containing 18-45mg/d of iron. Woman at a fertile age: add 200mg ferrous sulphate, 200mg ferrous fumarate or 300mg ferrous gluconate/d (twice daily in women of fertile age)	Consider investigating all cases of deficiency. 65mg elemental iron (ferrous sulphate 200mg) up to 150-300mg (split into 2-3 doses/day) IV should be used
Vitamin D	Complete MVI & M to maintain 25OH vitamin D level >75ng/mL After SG or RYBP - 2000-4000UI oral vitamin D3 daily. Higher dose after BPD/DS, OAGB, or SADIs	6000 IU/d or 50,000UI 1 to 3 times/week Refer to a specialist if levels unresponsive to treatment.
Calcium	Ensure dietary calcium intake. After SG, RYGB, BPD-DS, OAGB, or SADI, an additional 500-1500mg/d should be prescribed.	If the intact parathyroid hormone (iPTH) level is elevated in the presence of normal levels of vitamin D and calcium, consider additional calcium supplements.
Vitamin A	Complete MVI & M daily After BPD-DS, OAGB, or SADI, consider starting supplementation at a dose of 10,000IU/d and adjusting, if necessary	10,000-25,000 IU/d and reassess every 3 months For vit A deficiency that is unresponsive to treatment, refer to a specialist for an assessment for and consideration of IM injections of vitamin A
Vitamin E	15mg/d Consider starting with 100 IU daily	Oral doses 100-400IU/d Check every 3 months
Vitamin K	90-120mg/d After SADI, OAGB, or BPD-DS, consider starting supplementation at a dose of 300mcg/d	Treat with 1-2 mg of oral vitamin K daily. Recheck every 3 months. If levels fail to improve, consider referral to a specialist for 10mg parenterally.
Zinc	After RYGB or SG: 15 mg/d After SADI, OAGB, or BPD-DS : 30mg/d (split into two doses)	Upper Level: 40 mg/d or more Maintain a zinc/copper ratio of 8-15mg of zinc to 1mg of copper

Copper	Complete MVI & M daily, including 2mg/d of copper.	3–8mg/d - consider referral to a specialist Maintain a zinc/copper ratio of 8-15mg of zinc to 1mg of copper Monitor zinc if giving high doses of copper.
Selenium	Complete MVI & M daily After SADI, OAGB or BPD-DS, additional selenium may be needed	Additional supplement and recheck after 3 months
Protein	Diet + supplement = 80g total daily intake	Diet + supplement = 120g total daily intake

MVI = multivitamin; MVI & M = multivitamin and mineral; IU = international units; RYGB = Roux-en-Y gastric bypass; SG = sleeve gastrectomy; SADI = single-anastomosis duodenal ileal bypass; OAGD = one-anastomosis gastric bypass; BDP-DS = biliopancreatic diversion with duodenal switch

f. Nutritional management and follow-up

Even if a patient is adhering to adequate vitamin and mineral supplementation, both laboratory and clinical exams will remain necessary to evaluate that patient's nutritional status. Many patients will require additional micronutrient supplementation, in addition to two daily multivitamins(446, 892).

Due to the importance of nutrition, patients should have continuous access to a dietitian or nutritionist who specializes in MBS. Patients should receive support with dietary and lifestyle changes to address practical issues related to these changes and to ensure adherence with vitamin and mineral supplementation(900).

Patients who undergo malabsorptive procedures should receive more frequent follow-up evaluations. Anthropometric evaluations and laboratory exams should be done frequently (see Table 9-4). Signs and symptoms of possible nutritional deficiencies should be evaluated by a dietitian. Neurological symptoms, ataxia, and night blindness should be properly investigated and treated by the multidisciplinary team. Malabsorptive procedures can lead to steatorrhea and bowel changes, and strategies to deal with these consequences should be discussed.

In terms of caloric and macronutrient intake, research has shown that decreases in energy intake are very important over the long term. Kanerva et al. found that lower energy intake over the first six months is linked to greater excess weight loss long term (10 years post-op)(912). These investigators also found that increasing protein and carbohydrate over lipid intake generated better weight loss long term. Meanwhile, Schoemacher et al. similarly found that decreased energy intake is very important for weight loss and that patients whose protein intake exceeds 0.8g/kg IBW experience better excess weight loss and lower energy intake(913).

In the long term, the diet should contain all essential nutrients at doses that might be altered, depending on the type of MBS procedure performed and the presence versus absence of specific at-risk features or evidence of deficiency. Such doses are listed in Table 9-3, below.

Also recommended are small meals that are rich in protein, whole grains, vegetables, fruits, and other foods that are a rich source of omega-3, in addition to avoiding sweets. Regarding hydration, consumption of > 1500ml of water per day is recommended, or 35ml per kg of body weight/day(914).

Besides all this, patients' postoperative eating behaviours must be refined to ensure that good dietary practices are maintained(509, 899, 902, 915). Such practices should include:

- Being conscious of eating (avoiding mindless eating out of habit)
- Taking time to properly chew one's food
- Not eating past a point of satiety, aided by eating slowly enough (e.g., chewing one's food adequately) to allow satiety to be achieved prior to excess intake
- Consuming adequate quantities of low-to-no-calory liquids and not drinking right around meals
- Eating meals of appropriate size and content
- Restricting the consumption of simple sugars, carbonated drinks, and alcohol
- Avoiding snacking and grazing, which also is crucial to maintaining control of eating, as both behaviours can seriously hinder weight loss and maintenance

Table 9-3: Specific nutritional supplement recommendations

Supplement	Usual daily dose	Special circumstances
VITAMINS		
Iron	18 mg	At risk patients: 45-100 mg Anaemia: up to 300 mg IV
Vitamin B1	12-50 mg	Early beriberi: 20-30 mg/day Vomiting: 100-150 mg IV daily for 7 days
Vitamin B12	500-1000 mcg	EV 1000mcg/month Deficiency: 1000 mcg IM for 8 weeks
Folate	400-800 mcg	Pregnancy: 800-1000 mcg/day
Vitamin D	3000-6000 IU (to achieve serum vit 25(OH)D levels ≥ 30 ng/ml)	
Vitamin A	Depends on surgery	RYGB/SG: 5000-10,000 IU/day AGB: 5000 IU/day BPD: 10,000 IU/day
Vitamin E	15 mg	
Vitamin K	Depends on surgery	AGB/SG/RYGB: 90-120 mcg/day BPD: 300 mcg/day
MINERALS		
Calcium	Depends on surgery	BPD/DS: 1800-2400 mg/day RYGB/SG/AGB: 1200-1500 mg/day
Zinc	Depends on surgery	RYGB: 8-22 mg/day SG/AGB: 8-11 mg/day BPD: 16-22 mg/day
Copper	Depends on surgery	RYGB/BPD: 2 mg/day SG/AGB: 1 mg/day
OTHER		
Protein	60 grams minimum 1.2-1.5 g/IBW	SG/RYGB: 60 grams/day minimum BPD/DS: 80-120 grams/day minimum

IU = international units; IV = intravenously; AGB = adjustable gastric banding; RYGB = Roux-en-Y gastric bypass; SG = sleeve gastrectomy; BPD = biliopancreatic diversion; DS = duodenal switch; BPD/DS = biliopancreatic diversion with duodenal switch; IBW = ideal body weight

For long-term nutritional follow-up, in addition to guiding adequate nutritional supplementation, the patient’s dietitian/nutritionist needs to develop an individualized, overall nutritional plan for each and every patient. In the postoperative period, this orientation is reinforced with consultations, wherein nutritional, metabolic and body composition assessments must be performed individually, yet systematically following a set monitoring protocol.

Dietitians/nutritionists are vital to the MBS process. In this role, they are the ones primarily responsible for the patient's nutritional care from the time of their preoperative evaluation, through the peri-operative and immediate post-operative period, and then long-term as the patient's course evolves and long-term monitoring becomes necessary to allow for whatever adjustments might become necessary for them to maintain a favourable weight and health trajectory(33, 446, 508, 901).

Table 9-4: Suggested postoperative nutritional evaluations and their timing

	1M	3M	6M	9M	1 Y	1½ Y	2Y	2 ½ Y	3Y	4Y	5Y
DXA							X		X		X
Hemoglobin, CBC	X	X	X	X	X	X	X	X	X	X	X
Calcium					X		x		X		X
Creatine	X		X		X		X		X		X
BUN	X		X		X		X		X		X
Iron					X		X		X		X
Transferrin	X	X	X	X	X	X	X	X	X	X	X
Ferritin + TS		X	X	X	X	X	X	X	X	X	X
Zinc/Copper		X	X		X		X		X	X	X
Glucose		X	X		X	X	X	X	X	X	X
Transferrin		X	X		X		X		X	X	X
Vit A/E/K*			X		X		X		X		X
25 OH D3		X	X		X		X		X		X
Vitamin B12			X		X		X		X		X
Folic acid			X		X		X		X		X
Parathormone			X		X		X		X		X

MMA			**X**		**X**		**X**		**X**		**X**
Vitamin B1	**X**	**X**	**X**		**X**		**X**		**X**		**X**
Vitamin B6	**X**		**X**		**X**		**X**		**X**		**X**
Body composition		**X**	**X**		**X**		**X**		**X**		**X**

M = month; Y = year; DXA – Dual-energy X-ray absorptiometry; TS – transferrin saturation; MMA - methylmalonic acid; BUN – blood urea nitrogen * For malabsorptive procedures or if deficiency is suspected.

5. AREAS OF CONSENSUS

In the two-round Delphi survey described in Chapter 1 of these guidelines, the following statements pertaining to MBS post-operative follow-up and outcomes achieved consensus:

Table 9-5: Consensus reached on post-operative follow-up and outcomes

Statements	Most common choice	% consensus
Some degree of weight regain is normal between 2 and 10 years after MBS.	Agree	100.0%
Significant weight regain, or the presence of obesity-related medical problems, may require further medical, endoscopic, or surgical treatment after MBS.	Agree	100.0%
After MBS, annual follow-up is recommended life-long.	Agree	100.0%
MBS centres should work jointly with primary care providers to provide follow-up and access to appropriate healthcare professionals, as clinically indicated.	Agree	100.0%
After MBS, if a patient still has severe obesity with obesity-related medical problems two years after MBS, additional therapy may be indicated (medical, endoscopic, or surgical).	Agree	98.9%
Follow-up after endoscopic bariatric treatment must always include nutrition counselling.	Agree	98.9%
	Agree	98.9%

Bone health should be evaluated post-op, especially in patients considered at high risk for osteoporosis.		
Patients presenting with significant weight regain after MBS require an extensive evaluation, including anatomic studies (EGD, UGI) and evaluation by the multidisciplinary team.	Agree	97.8%
Weight regain after MBS is multi-factorial, potentially including nutritional non-adherence, physical inactivity, mental health issues, and anatomical issues encountered during surgery.	Agree	96.7%
Patients presenting with GERD symptoms, with or without weight regain after MBS, require an objective assessment for GERD, including pH studies with or without manometry.	Agree	95.4%
In patients undergoing MBS who experience unsatisfactory post-op weight loss, supplementary medical treatment (e.g., glucagon-like peptide-1 agonist) should be added as combination therapy.	Agree	93.3%
There is no uniformly-recognized definition of "significant weight regain" after MBS.	Agree	88.9%
Follow-up after endoscopic bariatric treatment must always involve a complete multidisciplinary team.	Agree	88.8%
There is no uniformly-recognized definition for what constitutes surgical success after MBS.	Agree	80.9%
All forms of bariatric surgery are effective, overall, at improving patients' quality of life.	Agree	77.8%
Patients with a BMI from 40-50 kg/m^2 experience the greatest cost benefit from bariatric surgery.	Agree	77.6%
Weight regain tends to be greater in patients with super obesity (BMI >50kg/m^2).	Agree	76.2%
Weight regain depends on the type of MBS performed.	Agree	72.7%

Weight regain after MBS, even when significant, should never be called failure.	Agree	71.9%

EGD = upper gastrointestinal endoscopy; UGI = upper gastrointestinal; MBS = metabolic and bariatric surgery; GERD = gastroesophageal reflux disease

No consensus was reached on the frequency of patient visits to at least one member of the obesity management multi-disciplinary team over the first year after their surgery, though more than half of the 78 experts who voted recommended "at least monthly" visits.

6. CONCLUSIONS AND RECOMMENDATIONS

Based upon our review of published scientific literature and the results of the IFSO/WGO Delphi survey, the following conclusions and recommendations pertaining to post-operative follow-up and outcomes are made:

A comprehensive pre-operative nutritional, physical and mental health evaluation is necessary, followed by routine post-operative evaluations by the multidisciplinary team for the remainder of the MBS patient's life.

Cessation of tobacco, alcohol and all recreational drugs is mandatory and should be maintained lifelong.

Bariatric and metabolic surgery often leads to improvements in obesity-associated diseases like type 2 diabetes, obstructive sleep apnoea (OSA), hypertension and dyslipidaemia, but patients must continue to be monitored for these conditions life-long.

After MBS, changes in the absorption of some medications may occur and clear instructions on required post-operative changes should be communicated to primary care physicians and patients.

Upper gastrointestinal (UGI) endoscopic evaluation is recommended in patients with a history of reflux disease and in patients undergoing gastric bypass surgery during the pre-operative period and every five years following surgery.

Since obesity is a prevalent risk factor for 13 different types of cancer, MBS patients must continue to be screened for cancer post-operatively, in accordance with national guidelines.

Bariatric surgery centres should communicate a comprehensive post-operative care plan to primary care providers, including procedures, blood tests, required long-term vitamin supplements, and when they should refer patients back to the bariatric surgery centre.

Nutritional intake, activity, adherence with multivitamin and mineral supplements and weight, as well as comorbidity assessments and blood tests should be done annually.

Patients should be referred back to the bariatric surgical centre or to a local specialist for GI symptoms, nutritional issues, pregnancy, psychological support, weight regain or other medical issues requiring bariatric care.

X. Conclusions and final recommendations

Obesity is a chronic disease, caused by abnormal or excess body fat accumulation that impairs health and is associated with increased risks of premature morbidity and mortality, and overall reduced quality of life. It is also a condition that is becoming increasingly more common globally, having become a leading cause of chronic disease, disability, and healthcare costs worldwide. That said, though the overall rates of overweight and obesity are rising globally, their rates and how those rates have been changing over the past decade vary geographically. Consequently, geographical origins and ethnicity are important factors in the pathophysiology of obesity and associated diseases, and interventions must take these specifics into consideration.

Much of the reduction in general health and quality of life that individuals living with obesity experience stems from the broad range of co-morbid health conditions that commonly accompany obesity, conditions that appear to influence every organ system and both physical and psychological health. These conditions include life-altering and life-threatening conditions like type 2 diabetes, chronic liver disease, cancer, cardiovascular disease, sleep apnoea, venous thromboemboli, urinary stress incontinence, chronic renal insufficiency, idiopathic intracranial hypertension, other gastrointestinal disorders, osteoarthritis, and psychiatric disorders like depression and anxiety, sometimes leading to suicide. Such conditions are essential to recognize for several reasons that include their potential for severe and even life-threatening consequences; how they might influence decisions regarding whether surgical therapy is indicated and safe for a given patient, and which surgical procedures to consider. Many of these conditions, including diabetes and cardiovascular disease, have been documented to improve or even abate altogether following successful metabolic and bariatric surgery (MBS). However, other conditions, like the risk of certain cancers, may or may not decline after MBS. Diagnosing, managing, and monitoring comorbid conditions are among many good arguments for healthcare practitioners to adopt a multi-disciplinary team approach to managing patients with obesity.

Such a multidisciplinary approach should begin with a comprehensive assessment of each patient's physical health and fitness, psychological health, nutritional health, and dietary practices

A trained psychotherapist, preferably with considerable expertise managing patients with obesity, should perform this initial assessment. Purposes of the psychological assessment include identifying dysfunctional eating behaviours — like binge-eating disorder, emotional eating, and food addiction — that could undermine the effectiveness of any obesity treatment modality. Though the concept of ‘food addiction’ remains unproven and controversial, since obesity manifests many of the same symptoms, it also is important to assess for behavioural factors that might place patients at higher risk of developing problems associated with alcohol and other substance abuse over the course of treatment, especially if a more invasive approach like MBS is being considered.

Patients with severe psychiatric disorders, like schizophrenia and bipolar disorder, must have it controlled prior to undergoing MBS, though the presence of such conditions is not an absolute contraindication to MBS, in itself. Psychological assessments also should examine each individual’s perceptions of their obesity and how stigmatized they feel because of it. All members of the treatment team need to treat obesity as the chronic disease that it is now known to be, both to counter many patients’ perceptions that it is merely the result of weak willpower, and to reinforce the importance of regular life-long follow-up and adherence to treatment. Healthcare providers who work with patients living with obesity need to be especially vigilant regarding their own potential weight bias and recognize that patients with obesity typically have suffered from such bias long-term, including bias exhibited by other healthcare providers that might adversely impact their adherence with follow-up and the overall treatment plan. It is also important to help patients establish realistic goals so they do not become severely discouraged later on, lest the degree of weight loss they experience is appreciably less than they had anticipated.

Obesity management also requires a detailed nutritional assessment and prolonged nutritional follow-up, even if surgery is elected as the cornerstone of therapy. This is because, as adjunctive therapy, dietary measures enhance surgical outcomes and because potentially life-threatening dietary complications, like severe nutritional deficiencies, may occur in patients who either elect for or against MBS. Obesity management should, therefore, begin with a thorough assessment of every patient’s nutritional status and dietary practices. Any nutritional deficits that are identified must then be corrected.

Exercise is another essential component of therapy, even if MBS is undertaken. Moreover, like patients’ psychological and nutritional status, their current level of fitness, exercise interests, and capacity for different exercise regimes must be assessed, and such exercises tailored to each individual patient.

Thereafter, irrespective of whether surgery is elected for or rejected, all aspects of non-surgical management must be tailored to each individual patient, as no one diet, exercise program, or medication will be accepted by or effective in all patients, and none has been documented as first-line or superior to all others. Long-term and often life-long monitoring of all non-operative components of obesity management is required to continuously assess the effects of treatment, identify treatment non-response and/or intolerance, and detect any adverse effects that might have arisen from the treatments chosen.

Associated diseases – including type 2 diabetes (T2DM), obstructive sleep apnoea (OSA), hypertension and dyslipidaemia – also must be identified, evaluated for severity, and appropriate treatment initiated pre-operatively. Since obesity is a common risk factor for 13 different types of cancer, the importance of cancer screening should be reinforced, in accordance with national guidelines. A pre-operative upper gastrointestinal (GI) endoscopic evaluation also is recommended in patients with a history of reflux disease and in those undergoing gastric bypass surgery. In present times, a patient's COVID status also is considered important.

One alternative to surgery that may be considered in select patients is endoscopic metabolic and bariatric therapy (EMBT), which includes a range of procedural therapies that rely on one of three predominant mechanisms of action. These mechanisms are **restriction** (reducing gastric capacity), **biliopancreatic diversion** (sectionally separating duodenal and upper jejunal mucosa and preventing the exposure of food to digestive juices), and the **percutaneous aspiration** of already-ingested gastric contents. Forms of EMBT also can be categorized as either gastric or small intestinal. Currently, they are those EBMTs that reduce gastric capacity, like various models of ***intragastric balloon*** **(IGB)** and endoscopic ***sleeve gastroplasty (ESG),*** that are being used regularly in everyday clinical practice. The current indication spectrum for EBMTs is a body mass index (BMI) ranging from 30 kg/m^2 up to just under 40 kg/m^2; or a BMI > 27 kg/m^2 in patients with one or more concomitant, obesity-associated comorbidities.

In general, EMBTs are considered as safe, if not safer than MBS, though data remain inclusive. Advantages that EMBTs do have over MBS is that they can both be repeated and reversed easily.

Many are, by their very nature (e.g., intra-gastric balloons), transient. Reported weight loss with EMBT generally ranges from 10.0 to roughly 20% of total body weight.

Despite the emergence of EMBT, over the past few decades, a growing body of evidence has established MBS as the most effective treatment for obesity, with respect to reducing weight, improving numerous comorbid conditions that have been empirically linked to BMI, enhancing overall patient quality of life, and decreasing patient mortality. Among the various surgical approaches that are currently in use, sleeve gastrectomy (SG) and Roux-en-Y gastric bypass (RYGB) are currently the most commonly performed worldwide, though newer procedures, like one-anastomosis gastric bypass (OAGB) show promise. Which procedure is employed should largely be decided on a patient-by-patient basis, that decision influenced by various patient characteristics – for example, evidence favours utilizing RYGB in patients with GERD – as well as by the operating surgeon's level of experience with each surgical approach. Regardless of which operation is chosen, patients must be thoroughly assessed by a multi-disciplinary team pre-operatively to determine their suitability for surgery and identify any issues that may require addressing.

Pre-operative patient preparation for MBS involves ensuring that the patient has realistic goals and expectations regarding the benefits and potential problems that might arise from surgery, and that all psychosocial barriers to adherence are addressed. Patients also must be alerted to any nutritional deficiencies and have such deficiencies corrected. Cessation of tobacco, alcohol and drugs is mandatory and should be maintained lifelong. Patients should be assessed for and instructed in an exercise program that they can realistically resume post-operatively. During a life-threatening pandemic like COVID-19, suitable precautions also must be taken to protect patients with obesity awaiting and undergoing MBS, because they are particularly vulnerable to severe COVID symptoms and mortality.

After MBS, since changes in the absorption of some medications may occur, clear instructions on required post-operative medication changes should be communicated to both primary care physicians and patients prior to their discharge from the hospital.

For post-operative follow-up, patients must be monitored closely throughout the peri-operative period for peri-operative complications; then followed, essentially for the remainder of their life, preferably by the multi-disciplinary obesity-management team thus far involved in their assessment and treatment.

Other specifics of post-operative follow-up include ensuring adherence with nutritional guidelines and vitamin and mineral supplements, as indicated, and reinforcing continued abstinence from tobacco, alcohol, and all recreational drugs; such abstinence should be maintained lifelong. As stated earlier in this summary, the anatomical changes induced by both MBS and EMBT also can alter the absorption of some medications, and such medications must be identified and both primary care physicians and patients provided with clear instructions regarding any changes that might be required.

Changes also may be necessary in the management of certain obesity-associated conditions – like type 2 diabetes, obstructive sleep apnoea (OSA), hypertension and dyslipidaemia – like reduced or the elimination of insulin requirements and changes in night-time CPAP settings. This said, patients must also continue to be monitored for these conditions life-long, even if they appear to resolve, because disease recurrence may occur, sometimes independent of the patient's weight loss trajectory.

Also as stated above, UGI endoscopic evaluation is recommended in patients with a history of reflux disease and in those undergoing gastric bypass surgery, both pre-operatively and every five years post-operatively. Since obesity is a risk factor for 13 different types of cancer, MBS patients also must continue to be screened for cancer post-operatively, in accordance with national guidelines. Nutritional intake, activity levels, adherence with multivitamin and mineral supplements, current weight, and both comorbidity assessments and blood tests should be done annually by the obesity management team.

Once a patient has undergone MBS, the centre where the surgery was conducted also needs to relay a comprehensive post-operative health management plan to primary care providers, which must include which procedures, blood tests, and long-term vitamin supplements are required, any medication changes that may be necessary, and when MBS patients should be referred back to the MBS centre. Reasons for referral back to the MBS centre or to a local specialist include persistent GI symptoms, nutritional issues, pregnancy, a need for psychological support, weight regain, and other medical issues requiring bariatric care.

Obesity has been called the world’s most extensive pandemic, and its prevalence, distribution, and costs continue to rise. To stem this rising tide of obesity and its numerous complications and costs, healthcare providers, insurers, and public officials must now work together, systematically, to increase public awareness both about the adverse health risks associated with obesity and the potential amelioration of such risks with combined non-operative and operative therapy. They also must work to remove the stigma associated with obesity, since such stigmatization can prevent individuals from seeking appropriate treatment and from adhering to such treatment if sought. This requires that everyone recognizes and treats obesity as the chronic disease it is now known to be, using a multidisciplinary team approach like that used for other chronic diseases, like diabetes, heart disease, and cancer. It is only through such concerted effort that the worsening obesity pandemic can be reversed.

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APPENDIX

Methodology and full results of the Delphi survey of 94 international experts in obesity management

I. INTRODUCTION

In October 2020, the IFSO-WGO Obesity Guidelines Steering Committee met through an online meeting platform, along with an international, PhD-level population epidemiologist (KPW) with specific expertise in Delphi surveys. One primary purpose of the meeting was to initiate the development of a survey of international, interdisciplinary experts in obesity management to identify areas of consensus and non-consensus spanning a range of topics in the management of obesity, the results of which could then be used to assist in the drafting of obesity management guidelines. The panel itself was both international and inter-disciplinary, consisting of non-surgeons (e.g., hepatology, endocrinology, general medicine), surgeons, endoscopists, nutritionists/dieticians, and other counsellors, all having internationally-recognized expertise and extensive experience in obesity management.

During this meeting, a decision was made to conduct a two-round, on-line, modified Delphi survey of a sizeable number of experts who encompass all the areas expertise listed above. Development of the on-line survey was facilitated by the Delphi expert (KPW), in close co-operation with Dr. Lilian Kow and other members of the steering committee.

II. SURVEY DEVELOPMENT

Survey development began by asking each member of the advisory committee to generate a list of issues/questions of major interest, particularly within their own discipline. To be considered for survey inclusion, the issue had to (a) not yet be considered firmly-established, universal standard of care, based upon published empirical evidence; and (b) nonetheless be considered of appreciable importance to the management of overweight or obesity. Such issues could pertain to (a) the epidemiology, clinical and physiological characteristics of obesity; (b) both the patient and societal impacts of obesity; (c) diagnosing obesity; (d) diagnosing, managing and monitoring obesity-associated co-morbidities and risks; (e) the overall impact and risks of obesity-associated comorbidities; (f) patient monitoring; (g) patient selection and preparation for both nonprocedural and procedural treatment; (h) treatment; (i) peri-procedural care; (j) and both short-term and long-term follow-up, both post-procedural and with conservative management.

Such lists then were sent to the Delphi survey expert for editing, consolidation into a single survey, and reformatting to ensure comprehensibility and consistency of presentation. Also part of survey development were several developmental procedures intended to reduce the risk of any bias that might be induced by the survey itself. Steps taken to reduce survey instrument bias included (a) primarily using non-judgmental statements (e.g., neither favoring nor opposing a particular treatment approach); (b) altering the order of response options to minimize the risk of order bias (e.g., sometimes listing the most favorable response option first, sometimes last, and sometimes in the middle – when the number of response options was three or greater); and (c) conducting a pilot survey of a small number of experts (n=10) to identify concerns and any language, factual, or conceptual errors.

Prior to the pilot survey, the survey's first full draft was sent to all steering committee members for feedback and potential modification. After several iterations, a penultimate Round 1 survey was generated which then was sent, via an online link, to a small core group of ten experts – including experts in each field of expertise (bariatric surgery, bariatric endoscopy, non-surgical medicine, nutrition, psychology) for a pilot run. As stated above, these 10 experts also were asked to comment on the survey, identify errors, areas of confusion and other issues, and submit these comments as part of survey completion (i.e., before clicking the SEND icon).

The pilot survey results and comments then were reviewed by KPW and a smaller core of four steering committee members towards generating a final Round 1 survey, which again was sent to all steering committee members for final approval. Pilot study results were NOT included in the analysis of data to determine consensus (i.e., Round 1 or 2).

III. SURVEY METHODS

In June 2021, an email was sent to 100 experts who had previously agreed to participate in the survey, along with a link to the above-mentioned, committee-approved Round 1 survey on the online platform Survey Monkey. These experts spanned Africa, Asia, Europe, Latin America, the Middle East, North America, and Oceania and the fields of bariatric endoscopy, bariatric surgery, general medicine, hepatology, psychology, and nutrition. Among the 100 experts who were invited to participate in the survey, 94 completed it within the 30-day window of time allotted for Round 1 survey completion and were included in consensus analysis. Practice characteristics of these 94 experts are summarized in Table A-1. Further practice characteristics of the n=37 bariatric surgeons and the n=55 who practiced either bariatric surgery or bariatric endoscopy (or both) are summarized in Table A-2.

Table A-1: Characteristics of the sample

Continent	N =	Percentage of total
Africa	2	2.1%
Asia	15	16.0%
Europe	26	27.7%
Latin America	10	10.6%
Middle East	7	7.4%
North America	28	29.8%
Oceania	6	6.4%
Total	94	100.0%
Specialty	N =	Percentage of total
Bariatric endoscopy	18	19.1%
Bariatric surgery	37	39.4%
General medicine	6	6.4%
Hepatology	15	16.0%
Psychology	4	4.3%
Nutrition	14	14.9%
Total	94	100.0%
Nature of clinical practice	N =	Percentage of total
Primarily university based	59	62.8%
Some university affiliation	25	26.6%
Non-academic	10	10.6%
Total	94	100.0%
Member of obesity care team	N =	Percentage of total
Yes	85	90.4%
No	9	9.6%
Total	94	100.0%
% Time managing patients with obesity	N =	Percentage of total
< 25%	21	22.3%
25-50%	26	27.7%
> 50%	47	50.0%
Total	94	100.0%

Years managing patients with obesity	N =	Percentage of total
< 5 years	5	5.3%
5-10 years	18	19.1%
> 10 years	71	75.5%
Total	94	100.0%
Years performing bariatric procedures	N =	Percentage of total
< 5 years	7	12.7%
5-10 years	10	18.2%
> 10 years	38	69.1%
Total	55	100.0%

Table A-2: Bariatric surgical & endoscopic procedures performed by the expert panel

Surgeons only (N = 37)		
Minimally-invasive surgery only	27	73.0%
Open surgery	0	0.0%
Both	10	27.0%
Total (Surgeons only)	37	100.0%
Surgeons and endoscopists (N = 55)		
Roux-en-Y bypass	41	74.5%
Sleeve gastrectomy	42	76.4%
MGB-OAGB	18	32.7%
Other	39	70.9%
Balloon	35	63.6%
ESG	20	36.4%
POSE	5	9.1%
Aspiration	7	12.7%
Other	14	25.5%

MGB-OAGB = mini gastric bypass, also called one anastomosis gastric bypass; ESG = endoscopic sleeve gastroplasty; POSE = primary obesity surgery using an endoluminal approach

The final Round 1 survey consisted of 157 statements upon which each expert was asked to vote. The survey was subdivided into six modules: Epidemiology & risk factors (20 statements); Module 2 – Patient selection for metabolic and bariatric surgery (MBS) (29 statements); Module 3 - Psychological issues (14 statements); Module 4 - Patient preparation for MBS (23 statements); Module 5 - Bariatric endoscopy (39 statements, to be voted on by surgeons and endoscopists only); and Module 6 – Outcomes and follow-up (32 statements). Hence, the Round 1 survey consisted of 157 statements upon which experts were asked to vote. All 157 statements were analyzed for degree of consensus and voter participation, with statement achieving < 70%

consensus included in a second-round survey. Also asked at both the start and end of each of the six modules was how comfortable each expert was voting on the area of focus of that module, with the following five available response options: very uncomfortable, somewhat uncomfortable, neither uncomfortable nor comfortable, somewhat comfortable, very comfortable. This was done (a) as a reminder to discourage voters from voting on statements on which they felt uncomfortable voting; and (b) to allow for the exclusion of votes from uncomfortable voters during data analysis. In other words, only votes from experts who felt either somewhat or very comfortable in a particular area were included in analysis. Note that *a-priori* decisions had been made, by the steering committee, to (a) define consensus with any particular statement as ≥ 70% agreement on the most commonly selected response option; and (b) require at least 80% voting participation (≥ 80% of eligible voters) on any statement for the final vote tally for that statement to be considered a valid result.

IV. SURVEY RESULTS

Among the five modules that were open to all experts (i.e., only surgeons and endoscopists were eligible to vote in Module 5, on bariatric endoscopy), the number of voters ranged from n=80 (85.1%) to n=94 (100%) out of 94, meaning that no statement in any of the five Round 1 modules open to all experts failed to achieve the minimum 80% allowable to be considered a valid vote. For Module 5, which was restricted to bariatric surgeons and endoscopists only, the number of voters on statements ranged from n=54 (94.7%) to n=57 (100%), again indicating valid voting results for every statement.

After the Round 1 results were analyzed, six statements were excluded due to ambiguity expressed by voters, while 29 statements – Module 2 (Part B), on the Relative importance of pre-operative patient factors – were added to the Round 2 survey. The final, two-round analysis was, therefore, of 180 statements (157 + 29 – 6).

Among the 180 statements ultimate voted upon and included in final analysis, only 17 (9.4%) were deemed by the core panel as favorable to a particular bariatric intervention, 19 unfavorable (10.6%), and 144 (80.0%) non-judgmental. Among these 180 statements, 134 (74.4%) had the binary response options of agree versus disagree, while 46 (75.6%) had other and potentially more than two response options (e.g., more, less, about the same). At least 70% consensus was achieved on 158 statements (87.8%) – 114 in the first round, and 44 in the second round.

An abbreviated third round of voting was conducted for the eight of 29 statements added to the Round 2 survey for which no consensus was achieved, thereby permitting two rounds of voting on all statements for which no consensus was achieved the first time voted upon.

An overall summary of the above-noted results is provided in Table A-3.

Results for each of the six modules are summarized individually in Tables A-4 through A-10, with Module 2 – on patient selection for MBS – subdivided into Part A (Table 5) and Part B (Table 6, the 29 statements added to Round 2, based upon responses to an open-ended question in Round 1). Each of these seven tables lists each statement individually, along with the number of experts who voted on it during the definitive round (whether Round 1 or 2), the number of rounds required, the response option (e.g., agree vs. disagree) selected by the largest percentage of voters, the percentage of consensus ultimately achieved; and whether or not consensus of at least 70% was reached. In these tables, statements are listed based upon the final level of consensus achieved, in decreasing order, with statements failing to achieve 70% consensus shaded to facilitate recognition.

These results also are listed, sometimes accompanied by discussion, in Sections 2-9 of these guidelines.

Table A-3: Overall summary of results over two rounds of voting

Statements	N =	% =
Total number of statements	180	100%
Consensus reached	158	87.8%
No consensus reached	22	12.2%
Consensus reached in 1st round	114	72.2%
Consensus reached in 2nd round	44	27.8%
% Statements consensus reached - Epidemiology & risk factors (20 statements)	18	90.0%
% Statements consensus reached - Patient selection (29 statements)	24	82.8%
% Statements consensus reached - Relative importance of pre-op factors (23 factors)	21	91.3%
% Statements consensus reached - Psychological issues (14 statements)	12	85.7%
% Statements consensus reached - Patient preparation -general (10 statements)	9	90.0%
% Statements consensus reached - Patient preparation - COVID-19 (13 statements)	13	100.0%
% Statements consensus reached - Bariatric endoscopy (39 statements)	31	79.5%
% Statements consensus reached - Outcomes & follow-up (32 statements)	30	93.8%
100% consensus reached	12	7.6%
90-99% consensus reached	43	27.2%
80-89% consensus reached	68	43.0%
70-79% consensus reached	35	22.2%
Statements agreed with (total)	104	57.8%
Statements disagreed with (total)	30	16.7%
Statements agreed with (consensus)	96	60.8%
Statements disagreed with (consensus)	24	15.2%
Statements worded favorably to bariatric interventions	17	9.4%
Statements worded unfavorably to bariatric interventions	19	10.6%
Non-judgemental statements	144	80.0%
Average consensus - Epidemiology & risk factors	84.7%	
Average consensus - Patient selection	84.3%	
Average consensus - Relative importance of pre-op factors	86.5%	
Average consensus - Psychological issues	81.3%	
Average consensus - Patient preparation -general	84.6%	
Average consensus - Patient preparation - COVID-19	82.8%	
Average consensus - Bariatric endoscopy	78.0%	
Average consensus - Outcomes & follow-up	87.9%	
Average consensus - OVERALL	83.6%	
Minimum/Maximum level of consensus on a statement	50%/100%	
Min. when consensus reached	70.5%	

Table A-4: Module 1 - Epidemiology & risk factors (N = 94 voters in round 1; 79 in round 2)

Statements (N = 20)	N*	Rounds required	Most common selection	Percent consensus	Consensus achieved
Since obesity is a major contributor to the global burden of chronic disease, disability, and healthcare costs, all medical societies should cooperate to address this problem systematically.	94	1	Agree	100.0%	Yes
Longitudinal national and regional surveillance of obesity, with measured data, should be conducted on a regular basis.	94	1	Agree	100.0%	Yes
Obesity is a chronic disease, caused by abnormal or excess body fat accumulation that impairs health and increases the risk of premature morbidity and mortality.	94	1	Agree	97.9%	Yes
Emotional eating is a common feature of obesity.	94	1	Agree	97.9%	Yes
Ethnicity and geographical origins are important factors in the pathophysiology of obesity and metabolic diseases.	94	1	Agree	91.5%	Yes
Interventions for obesity and metabolic diseases should take the patient's ethnicity and geographic location into consideration.	94	1	Agree	90.4%	Yes
There are individuals who, despite being severely obese, never experience eating binges.	94	1	Agree	90.4%	Yes
Food addiction cannot exist, since food contains no substances capable of acting directly on brain areas related to reward processing.	91	1	Disagree	87.9%	Yes
All individuals with obesity have eating binges.	94	1	Disagree	85.1%	Yes
Emotional eating and food addiction are the most common causes of eating binges in candidates for bariatric surgery.	79	2	Agree	84.8%	Yes
Some patients with problematic alcohol use pre-operatively exhibit less problematic alcohol use after they undergo bariatric surgery.	79	2	Disagree	84.8%	Yes
Patients addicted to food develop alcohol or other substance abuse after bariatric surgery...	79	2	In a minority of cases	83.5%	Yes
Candidates for bariatric surgery with a history of binge eating are more prone to experience undesirable behavioral outcomes after bariatric surgery than candidates with no history of binge eating.	94	1	Agree	81.9%	Yes
Food addiction is a common feature of obesity.	79	2	Agree	81.0%	Yes
Sufficient empirical evidence exists to consider "food addiction" a valid clinical entity.	79	2	Agree	79.7%	Yes
Food addiction is more common in candidates for bariatric surgery who exhibit problematic use of alcohol or other mood-altering substances.	75	2	Agree	78.7%	Yes
Candidates for bariatric surgery with a history of binge eating are more prone to suicide or suicidal behaviors after bariatric surgery than candidates with no history of binge eating.	79	2	Disagree	77.2%	Yes
Candidates for bariatric surgery with a history of binge eating are more prone to regain weight after bariatric surgery than candidates with no history of binge eating.	93	1	Agree	76.3%	Yes
Emotional eating is more common in candidates for bariatric surgery than in other people who are obese.	79	2	Disagree	68.4%	No
The great majority of candidates for bariatric surgery have an addiction to food.	79	2	Disagree	55.7%	No

N* = number of voters in the final/definitive round of voting on the statement

Table A-5: Module 2 (Part A) - Patient selection (N = 94 voters in round 1; 79 in round 2)

Statements (N = 29)	N*	Rounds required	Most common selection	Percent consensus	Consensus achieved
Global rates of obesity are currently increasing in children and adolescents.	94	1	Agree	100.0%	Yes
Most children and adolescents with obesity grow up to have obesity in adulthood.	93	1	Agree	100.0%	Yes
Children and adolescents with severe obesity are at risk of significant obesity-related comorbidities, like type 2 diabetes mellitus, hypertension, etc.	94	1	Agree	100.0%	Yes
Metabolic and bariatric surgery in adolescents requires a multidisciplinary team [e.g., paediatric psychologists & endocrinologists] with experience dealing with children & adolescents & their families.	93	1	Agree	100.0%	Yes
Lack of physician and public knowledge, as well as the lack of long-term results of MBS in adolescents, represent some of the potential barriers for referral of adolescents for MBS.	92	1	Agree	100.0%	Yes
Life-long follow up is needed in adolescents who undergo metabolic bariatric surgery (MBS).	92	1	Agree	98.9%	Yes
Bariatric surgery in the elderly improves their overall quality of life (QoL).	90	1	Agree	96.7%	Yes
In adolescents, MBS should be performed by experienced bariatric surgeons with a proven track record performing MBS in adults.	91	1	Agree	95.6%	Yes
Short-term studies show that MBS in adolescents is safe and leads to excellent outcomes, including durable weight loss and improvements in obesity-related medical problems and quality of life.	89	1	Agree	95.5%	Yes
Life span expectations should be taken into account when considering bariatric surgery for elderly patients.	92	1	Agree	90.2%	Yes
Sleeve gastrectomy is the most common procedure performed in adolescents, followed by Roux-en-Y gastric bypass.	87	1	Agree	89.7%	Yes
The choice between sleeve gastrectomy and Roux-en-Y gastric bypass in adolescents should be based on BMI, and the presence versus absence of comorbidities like GERD and diabetes.	87	1	Agree	88.5%	Yes
Besides the extent of obesity and the patient's consent, a patient's age should be the only consideration when surgeons are planning bariatric surgery in an elderly	94	1	Disagree	87.2%	Yes
Laparoscopic Roux-en-Y Gastric Bypass (LRYGB) should be considered a viable option for patients who are elderly.	91	1	Agree	86.8%	Yes
The 30-day post-operative mortality risk of 0.4% in patients over 65 years (versus 0.1% in younger patients) contraindicates bariatric surgery in this patient group.	89	1	Disagree	86.5%	Yes
The amount of weight loss achieved should <u>not</u> be the primary indicator of treatment success in patients who are elderly.	94	1	Agree	86.2%	Yes
Short-term studies show that MBS in adolescents is similar to MBS in adults, in terms of major complications, readmissions, and mortality.	86	1	Agree	86.0%	Yes
Biliopancreatic diversion [duodenal switch] and one anastomosis gastric bypass are not recommended in adolescents.	87	1	Agree	85.1%	Yes
Operating time directly impacts the rate of complications in the elderly.	86	1	Agree	83.7%	Yes
Only high-volume bariatric services and experienced bariatric surgeons should operate on patients who are elderly.	91	1	Agree	82.4%	Yes
Enough empirical evidence has been published to affirm that metabolic and bariatric surgery (MBS) is the most effective therapy for severe obesity in adolescents.	92	1	Agree	79.3%	Yes
The overall risk of bariatric surgery may be prohibitive in patients who are elderly.	79	2	Disagree	77.2%	Yes

The rate of obesity in adolescents is increasing without a similar increase in the rate of adolescent MBS.	90	1	Agree	71.1%	Yes
Peri-operative risk in the elderly is comparable to that of younger patients.	93	1	Disagree	71.0%	Yes
Patients who are elderly can undergo hypo-absorptive procedures.	79	2	Agree	69.6%	No
In terms of weight loss, patients who are elderly tend to respond more, less, or about the same to a laparoscopic Roux-en-Y gastric bypass (LRYGB) than patients who are younger.	79	2	About the same	65.8%	No
In terms of weight loss, patients who are elderly tend to respond more, less, or about the same to a laparoscopic sleeve gastrectomy (LSG) than patients who are younger.	79	2	About the same	60.8%	No
For elderly patients with metabolic syndrome, the gold standard procedure should be… (LRYGB, LSG, other)	78	2	LRYGB	60.3%	No
In terms of bariatric surgery, a patient should start to be considered elderly…	79	2	Based on physiological age	51.3%	No

N* = number of voters in the final/definitive round of voting on the statement
MBS = metabolic and bariatric surgery; LRYGB = laparoscopic Roux-en-Y gastric bypass

Table A-6: Module 2 (Part B) – Relative importance of pre-operative patient factors (N = 79 voters in round 2)*

Statements (N = 29)	N	Level of importance	Percentage consensus	Consensus achieved
Patient's levels of general health and fitness	79	Very	98.7%	Yes
The presence and/or nature of comorbid illness	79	Very	97.5%	Yes
Ability to understand/cognitive level	79	Very	96.2%	Yes
Alcohol or other substance abuse	79	Very	96.2%	Yes
Psychological health and illness	79	Very	94.9%	Yes
Cardiovascular health	79	Very	94.9%	Yes
Liver health (including cirrhosis and portal hypertension)	78	Very	94.9%	Yes
Patient's level of compliance	79	Very	92.4%	Yes
Obesity's impact on patient's quality of life	79	Very	92.4%	Yes
Patient's nutritional status	79	Very	91.1%	Yes
Physiological more than chronological age	79	Very	89.9%	Yes
Kidney function	78	Very	89.7%	Yes
Respiratory health	79	Very	88.6%	Yes
Social and/or family network and support	79	Very	84.8%	Yes
Presence/nature of physical disabilities	79	Very	84.8%	Yes
Current smoking status	79	Very	84.8%	Yes
Advanced diabetes mellitus	79	Very	83.5%	Yes
Muscle mass (risk of sarcopenia)	78	Very	83.3%	Yes
Life span expectations	79	Very	82.3%	Yes
Patient's level of physical mobility	79	Very	81.0%	Yes
Bone health	79	Very	73.4%	Yes
Financial means (e.g., ability to afford vitamins)	79	Very	59.5%	No
Thyroid disease	78	Not very	53.8%	No

* This list was added in response to an open-ended question asking voters to list factors they considered important in the decision to perform and how to perform surgical or endoscopic bariatric interventions. Order of factors is from highest to lowest percentage perceiving a factor as important.

Table A-7: Module 3 - Psychological issues (N = 94 voters in round 1; 79 in round 2)

Statements (N = 14)	N*	Rounds required	Most common selection	Percentage consensus	Consensus achieved
Patients undergoing bariatric surgery virtually always develop problematic alcohol use post-operatively.	91	1	Disagree	95.6%	Yes
Patients with severe psychiatric conditions, like schizophrenia or bipolar disorder, should not undergo bariatric surgery, unless the psychiatric condition is well controlled.	91	1	Agree	95.6%	Yes
A comprehensive psychological evaluation should be completed before bariatric surgery	94	1	Agree	93.6%	Yes
Candidates for MBS with predominantly cognitive depressive symptoms (e.g., difficulty concentrating, memory loss) usually do not exhibit any improvement in their depressive symptoms after surgery.	78	2	Disagree	89.7%	Yes
Most patients with depression experience worsening of their depressive symptoms after bariatric surgery.	88	1	Disagree	87.5%	Yes
Candidates for bariatric surgery who predominantly have somatic depressive symptoms — like asthenia, fatigue, and psychomotor retardation — tend to be less depressed after bariatric surgery.	79	2	Agree	84.6%	Yes
The best psychotherapeutic strategy for patients with obesity and a high risk of binge eating behavior is...	86	1	CBT	83.7%	Yes
Candidates for bariatric surgery with emotional eating are more prone to having other psychiatric conditions, like depression or an anxiety disorder.	88	1	Agree	83.0%	Yes
Patients with severe psychiatric conditions, like schizophrenia or bipolar disorder, should not undergo bariatric surgery, irrespective of whether the psychiatric condition is well controlled or not.	91	1	Disagree	79.1%	Yes
Patients with depression and obesity who experience significant weight loss after bariatric surgery usually also experience improvement in their depressive symptoms.	84	1	Agree	75.0%	Yes
Candidates for bariatric surgery with food addiction are more prone to having other psychiatric conditions, like depression or an anxiety disorder.	88	1	Agree	73.9%	Yes
Overall, patients who have undergone bariatric surgery have an increased risk of suicide.	79	2	Agree	70.9%	Yes
Bariatric surgery increases the suicide rate among candidates for bariatric surgery who already have clinical depression.	79	2	Agree	68.4%	No
Patients undergoing gastric bypass are more susceptible to developing problematic alcohol use post-operatively.	79	2	Agree	57.0%	No

N* = number of voters in the final/definitive round of voting on the statement
MBS = metabolic and bariatric surgery

Table A-8: Module 4 - Patient preparation for metabolic and bariatric surgery (N = 94 voters in round 1; 79 in round 2)

Statements (N = 23)	N*	Rounds required	Most common selection	Percentage consensus	Consensus achieved
General health (N = 10)					
A comprehensive medical and nutritional evaluation should be completed before bariatric surgery.	93	1	Agree	100.0%	Yes
Nutrient deficiencies should be evaluated and corrected in all candidates for bariatric surgery.	93	1	Agree	98.9%	Yes
Among smokers, smoking cessation is recommended before bariatric surgery.	93	1	Agree	96.8%	Yes
Sleep apnoea screening is recommended, with testing only necessary in patients in whom there is a high suspicion of sleep apnoea.	92	1	Agree	89.1%	Yes
Weight reduction decreases a person's future risk of developing cholangiocarcinoma.	79	2	Not yet known	86.1%	Yes
Computed tomography or magnetic resonance imaging should be used routinely to screen for hepatocellular carcinoma in patients with metabolic-associated fatty liver disease.	76	2	Disagree	81.6%	Yes
All antidiabetic drugs have an impact in reducing the risk of hepatocellular carcinoma in patients with metabolic-associated fatty liver disease.	81	1	Disagree	80.2%	Yes
Pre-operative endoscopy should be performed in every patient undergoing bariatric surgery.	88	1	Agree	76.5%	Yes
Screening for hepatocellular carcinoma should be performed in all patients with metabolic-associated fatty liver disease.	76	2	Agree	71.1%	Yes
There are differences between the different modes of weight reduction (calorie restriction, exercise, drugs, endoscopic and bariatric surgery) in terms of reducing the risk of hepatocellular carcinoma.	77	2	Agree	66.2%	No
COVID-19 (N = 13)					
Due to the increased risk of severe symptoms from COVID in patients with obesity, until the spread of COVID-19 is well controlled, bariatric surgery procedures should be reduced to a minimum to reduce the risk of viral exposure.	79	2	Disagree	94.9%	Yes
Considering that patients with obesity are at higher risk of a severe COVID-19 course, more restrictive measures should generally be undertaken during hospitalisation for bariatric procedures or related pre-operative evaluations.	78	2	Agree	93.6%	Yes
Especially during the pandemic, metabolically sicker patients with obesity should be prioritized for bariatric surgery, since they are at greater risk from the pandemic and treatment decreases their risk.	79	2	Agree	91.1%	Yes
Unvaccinated, metabolically-sicker patients with obesity should be prioritized for vaccination against COVID-19.	89	1	Agree	87.6%	Yes
Unvaccinated or incompletely vaccinated patients scheduled for bariatric surgery who test negative for COVID-19 at admission can be placed in double rooms with other patients who have tested negative.	79	2	Agree	83.5%	Yes

Since diabetes mellitus places patients at increased risk of a severe COVID-19 course, patients with diabetes or who are otherwise metabolically-compromised warrant special protective measures during their care.	78	2	Agree	83.3%	Yes
Outpatients undergoing pre-operative evaluations should have an antigenic COVID swab test on the day of the planned procedure or investigation.	79	2	Agree	82.3%	Yes
Before gaining any kind of access to the hospital, all patients with obesity should be contacted by telephone and asked to report any recent potential COVID exposure or symptoms, as well as any situations or behaviours that might have placed them at particular risk of becoming infected.	92	1	Agree	81.5%	Yes
Since *vitamin D* is thought to be a protective factor, measurement of and/or treatment with vitamin D should be considered prior to treating patients with obesity.	90	1	Agree	80.0%	Yes
Since elevated interleukin-6 is considered a risk factor for a more severe COVID-19 course and is disproportionately elevated in patients with obesity, the level of IL-6 should be measured in all patients being treated for obesity, either before or at the beginning of their treatment.	85	1	Disagree	76.5%	Yes
More stringent anticoagulation after surgery/endoscopy should be considered for patients undergoing MBS because of the increased risk of thrombosis due to obesity *per se* and COVID.	76	2	Agree	76.3%	Yes
Patients scheduled for bariatric surgery who require hospitalization should have a PCR swab 24 hours before hospital admission and, if their hospitalization is longer than 48 hours, should have a second PSR swab at the time of hospital discharge.	79	2	Agree	74.7%	Yes
Due to the increased risk of a severe COVID-19 course in patients with obesity, during the COVID-19 pandemic, patients undergoing bariatric surgery should be provided a single room, both pre- and post-operatively, throughout their hospitalization for surgery.	78	2	Agree	70.5%	Yes

N* = number of voters in the final/definitive round of voting on the statement
MBS = metabolic and bariatric surgery; COVID = coronavirus disease; PCR = polymerase chain reaction test

Table A-9: Module 5 - Bariatric endoscopy (surgeons and endoscopists only; N = 58 voters in round 1; 54 in round 2)

Statements (N = 39)	N*	Rounds required	Most common selection	Percentage consensus	Consensus achieved
GENERAL STATEMENTS (N = 5)					
Endoscopic bariatric and metabolic therapies include a diverse set of minimally-invasive procedures that play unique and important roles in the treatment of obesity and related metabolic diseases and should be included as part of a multidisciplinary approach to managing these patients.	58	1	Agree	98.3%	Yes
A prerequisite for any bariatric endoscopist should be endoscopic bariatric training, a curriculum still undefined, but which should include learning about the various surgical procedures, the physiology of obesity, and endoscopic skills.	58	1	Agree	98.3%	Yes
Bariatric surgical centres should communicate a comprehensive care plan, both to patients and their primary care providers, including details about the surgical procedure, blood tests, required long-term vitamin supplements, and when patients need to be referred back.	56	1	Agree	98.2%	Yes
There is currently inadequate empirical evidence to support the use of ANY bariatric endoscopic procedure as an option in multidisciplinary weight loss programs**	54	1	Disagree	55.6%	No
No bariatric endoscopic procedure is justified in patients with obesity whose only reason for weight loss is to look better.**	54	1	Neither	50.0%	No
ASPIRATION THERAPY (N = 8)					
Aspiration therapy <u>should be/should not be</u> considered for patients with Class I obesity and obesity-related comorbidity.	54	2	Should not be	90.7%	Yes
With aspiration therapy, replacements of the A-Tube and continued use will be necessary to achieve adequate long-term weight loss.	53	2	Agree	86.8%	Yes
As an available option in multidisciplinary weight loss programs, there is currently enough empirical evidence to support the use of aspiration therapy.	54	2	Disagree	85.2%	Yes
Aspiration therapy <u>should be/should not be</u> considered for patients with Class 2 or 3 obesity.	54	2	Should not be	85.2%	Yes
In patients with obesity whose only real reason for weight loss is to look better, it is reasonable to carefully consider aspiration therapy.	58	1	Disagree	84.5%	Yes
The ability to induce meaningful weight loss and an acceptable risk profile are characteristics of aspiration therapy.	54	2	Disagree	79.6%	Yes
Generating enough weight loss to induce improvement in obesity-related comorbidities is achievable with aspiration therapy.	54	2	Disagree	75.9%	Yes
Aspiration therapy <u>should be/should not be</u> considered bridge therapy for patients with Class 2 or 3 obesity in need of weight loss to improve outcomes for a specific surgery or medical treatment/ procedure (e.g., orthopedic surgery, organ transplant, fertility therapy, bariatric surgery).	54	2	Should not be	74.1%	Yes
DUODENAL PROCEDURES (N = 2)					
As an available option in multidisciplinary weight loss programs, there is currently enough empirical evidence to support the use of duodenal mucosal resurfacing.	58	1	Disagree	82.8%	Yes
As an available option in multidisciplinary weight loss programs, there is currently enough empirical evidence to support the use of a duodenal-jejunal bypass liner.	58	1	Disagree	81.0%	Yes

ENDOSCOPIC GASTRIC BYPASS REVISION (N = 5)					
Endoscopic gastric bypass revision with an endoscopic suturing device or plication device should be/should not be considered for patients with class 2 or 3 obesity and >20% weight regain from a weight nadir after Roux-en-Y Gastric Bypass (RYGB).	53	2	Should be	79.2%	Yes
Endoscopic gastric bypass revision with an endoscopic suturing device or plication device should be/should not be considered for patients with >20% weight regain from a weight nadir after Roux-en-Y Gastric Bypass (RYGB), regardless of their class of obesity at the time of weight regain.	54	2	Should be	75.9%	Yes
In patients with obesity whose only real reason for weight loss is to look better, it is reasonable to carefully consider endoscopic gastric bypass revision with an endoscopic suturing or plication device	58	1	Disagree	72.4%	Yes
The ability to induce meaningful weight loss and an acceptable risk profile are characteristics of endoscopic gastric bypass revision with an endoscopic suturing or plication device.	54	2	Disagree	70.4%	Yes
Generating enough weight loss to induce improvement in obesity-related comorbidities is achievable with endoscopic gastric bypass revision with an endoscopic suturing device or plication device.	54	2	Disagree	68.5%	No
ENDOSCOPIC GASTRIC PLICATION (N = 7)					
Endoscopic gastric plication procedures should be/should not be considered in patients with Class 3 obesity when they are not good surgical candidates or have declined surgery.	54	2	Should be	87.0%	Yes
With endoscopic gastric plication procedures, adjunctive weight loss medications or repeat plication procedures may be necessary to achieve adequate long-term weight loss in some patients.	58	1	Agree	86.2%	Yes
Endoscopic gastric plication procedures should be/should not be considered for patients who are in the overweight category and have obesity-related comorbidities.	53	2	Should be	83.0%	Yes
In patients with obesity whose only real reason for weight loss is to look better, it is reasonable to carefully consider endoscopic gastric plication procedures, like POSE.	53	2	Disagree	81.1%	Yes
The ability to induce meaningful weight loss and an acceptable risk profile are characteristics of endoscopic gastric plication procedures, like POSE.	53	2	Agree	62.3%	No
As an available option in multidisciplinary weight loss programs, there is currently enough empirical evidence to support the use of endoscopic gastric plication procedures, like POSE.	53	2	Agree	56.6%	No
Generating enough weight loss to induce improvement in obesity-related comorbidities is achievable with endoscopic gastric plication procedures, like POSE .	53	2	Agree	56.6%	No
ENDOSCOPIC GASTRIC SUTURING (N = 4)					
With endoscopic gastric suturing procedures, adjunctive weight loss medications or repeat procedures may be necessary to achieve adequate long-term weight loss in some patients.	54	1	Agree	88.9%	Yes
Endoscopic gastric suturing procedures should be/should not be considered for patients who are in the overweight category and have obesity-related comorbidities.	54	2	Should be	85.2%	Yes
Endoscopic gastric suturing procedures should be/should not be considered in patients with Class 3 obesity when they are not good surgical candidates or have declined surgery.	55	1	Should be	72.7%	Yes
In patients with unsatisfactory weight loss after an endoscopic sleeve gastroplasty (ESG) procedure, endoscopic treatment can be repeated at most once, more than once, or not at all (in lieu of surgical revision)	53	2	Not at all	57.4%	No

INTRAGASTRIC BALLOONS (N = 8)					
With intragastric balloons, adjunctive weight loss medications or repeat balloon placements may be necessary to achieve adequate long-term weight loss in many patients.	58	1	Agree	87.9%	Yes
The ability to induce meaningful weight loss and an acceptable risk profile are characteristics of intragastric balloons.	54	2	Agree	85.2%	Yes
Intragastric balloons should be/should not be considered for patients with Class 1 or 2 obesity.	58	1	Should be	82.8%	Yes
As an available option in multidisciplinary weight loss programs, there is currently enough empirical evidence to support the use of intragastric balloons.	58	1	Agree	81.0%	Yes
Intragastric balloons should be/should not be considered bridge therapies for patients with Class 2 or 3 obesity in need of weight loss to improve outcomes for a specific surgery or medical treatment/procedure (e.g., orthopedic surgery, organ transplant, fertility, bariatric surgery).	58	1	Should be	81.0%	Yes
Intragastric balloons should be/should not be considered for patients who are in the overweight category and have obesity-related comorbidities.	57	1	Should be	80.7%	Yes
In patients with obesity whose only real reason for weight loss is to look better, it is reasonable to carefully consider intragastric balloons.	54	2	Agree	72.2%	Yes
Generating enough weight loss to induce improvement in obesity-related comorbidities is achievable with intragastric balloons.	53	2	Agree	62.3%	No

N* = number of voters in the final/definitive round of voting on the statement; ** new statement added in Round 2 to clarify Round 1 responses
ESG = endoscopic sleeve gastroplasty; POSE = primary obesity surgery using an endoluminal approach

Table A-10: Module 6 - Outcomes and follow-up (N = 94 voters in round 1; 79 in round 2)

Statements (N = 32)	N*	Rounds required	Most common selection	Percentage consensus	Consensus achieved
Some degree of weight regain is normal between 2 and 10 years after MBS.	90	1	Agree	100.0%	Yes
Significant weight regain, as well as the presence of obesity-related medical problems, may require further medical, endoscopic, or surgical treatment after MBS.	88	1	Agree	100.0%	Yes
After bariatric surgery, annual follow-up is recommended life-long.	90	1	Agree	100.0%	Yes
Bariatric surgical centres should work jointly with primary care providers to provide follow-up and access to appropriate healthcare professionals, as clinically indicated.	90	1	Agree	100.0%	Yes
After MBS, if a patient still has severe obesity with obesity-related medical problems two years after MBS, additional therapy may be indicated (medical, endoscopic, or surgical).	89	1	Agree	98.9%	Yes
Follow-up after endoscopic bariatric treatment must always include nutrition counselling.	90	1	Agree	98.9%	Yes
Bone health should be evaluated in the postoperative period, especially in individuals considered at high risk for osteoporosis.	89	1	Agree	98.9%	Yes
Substantial net health benefits may be anticipated, on a societal level, from the wider use of bariatric surgical procedures in patients with severe obesity.	88	1	Agree	98.9%	Yes
Since severe obesity shows strong socioeconomic patterning, bariatric surgery has the potential to reduce obesity-related inequalities in health, as long as there is equitable patient selection.	89	1	Agree	98.9%	Yes
Patients presenting with significant weight regain after MBS require an extensive evaluation, including anatomic studies (EGD, UGI) and evaluation by the multidisciplinary team.	89	1	Agree	97.8%	Yes
Weight regain after MBS is multi-factorial, potentially including nutritional non-compliance, physical inactivity, mental health issues, and anatomical issues encountered during surgery.	91	1	Agree	96.7%	Yes
Relative to medical therapy, in patients with obesity and type 2 diabetes, bariatric surgery is generally, in the long run... (more effective, less effective, about the same) in terms of improving diabetes	89	1	More effective	95.5%	Yes
Patients presenting with GERD symptoms, with or without weight regain after MBS, require an objective assessment for GERD, including pH studies with or without manometry.	87	1	Agree	95.4%	Yes
Substantial net economic benefits may be anticipated, on a societal level, from the wider use of bariatric surgical procedures in patients with severe obesity.	87	1	Agree	95.4%	Yes
In patients undergoing MBS who experience unsatisfactory post-op weight loss, supplementary medical treatment (e.g., glucagon-like peptide-1 agonist) should be added as combination therapy.	89	1	Agree	93.3%	Yes
There is no uniformly-recognized definition for what constitutes significant weight regain after MBS.	90	1	Agree	88.9%	Yes
Follow-up after endoscopic bariatric treatment must always involve a complete multidisciplinary team (e.g., dietitian or nutritionist, psychologist, exercise therapist)	89	1	Agree	88.8%	Yes
Different definitions of MBS success include achieving >50% EWL, a BMI <35 Kg/m2, and >10% TWL%.	89	1	Agree	86.5%	Yes
The cost benefit of bariatric surgery is greater in patients with obesity-related comorbidity, greater in patients with no obesity-related co-morbidity, or about the same on these two populations.	88	1	Greater with comorbidity	86.4%	Yes
Similar cost-effectiveness may be anticipated in diverse groups undergoing MBS, including men & women, patients across a wide range of ages, & patients with different levels of social deprivation.	78	2	Agree	85.9%	Yes
Increasing patient selection for bariatric surgery to include patients who are less obese will increase the overall societal health benefits of bariatric surgery.	78	2	Agree	85.9%	Yes

There is no uniformly-recognized definition for what constitutes surgical success after metabolic and bariatric surgery (MBS).	89	1	Agree	80.9%	Yes
Due to the increased risks of surgery in those who are more obese, in patients who are very obese, bariatric surgery is less cost effective than in those who are less obese.	88	1	Disagree	80.7%	Yes
The cost benefit of bariatric surgery is greater in younger than older patients, greater in older than younger patients, or about the same in youths and seniors.	79	2	Greater in younger patients	79.7%	Yes
The most commonly used definition for significant weight regain after MBS is achieving less than 50% EWL.	79	2	Agree	78.5%	Yes
All forms of bariatric surgery are effective, overall, at improving patients' quality of life.	90	1	Agree	77.8%	Yes
Patients with a BMI between 40 and 50 kg/m^2 experience the greatest cost benefit from bariatric surgery.	85	1	Agree	77.6%	Yes
Weight regain tends to be greater in patients with super obesity (BMI >50kg/m^2).	84	1	Agree	76.2%	Yes
Weight regain depends on the type of MBS performed.	88	1	Agree	72.7%	Yes
Weight regain after MBS, even when significant, should never be called failure.	89	1	Agree	71.9%	Yes
The cost effectiveness of bariatric surgery is lost if patients regain all the weight they lost post-operatively within the next 5-10 years.	78	2	Agree	67.9%	No
For the 1st year after endoscopic bariatric treatment, some member of a patient's obesity-management team should see them to evaluate their overall response to treatment & identify complications.	79	2	At least monthly	57.5%	No

N* = number of voters in the final/definitive round of voting on the statement
MBS = metabolic and bariatric surgery