KCE REPORT 316Cs

Federaal Kenniscentrum voor de Gezondheidszorg
Centre Fédéral d'Expertise des Soins de Santé
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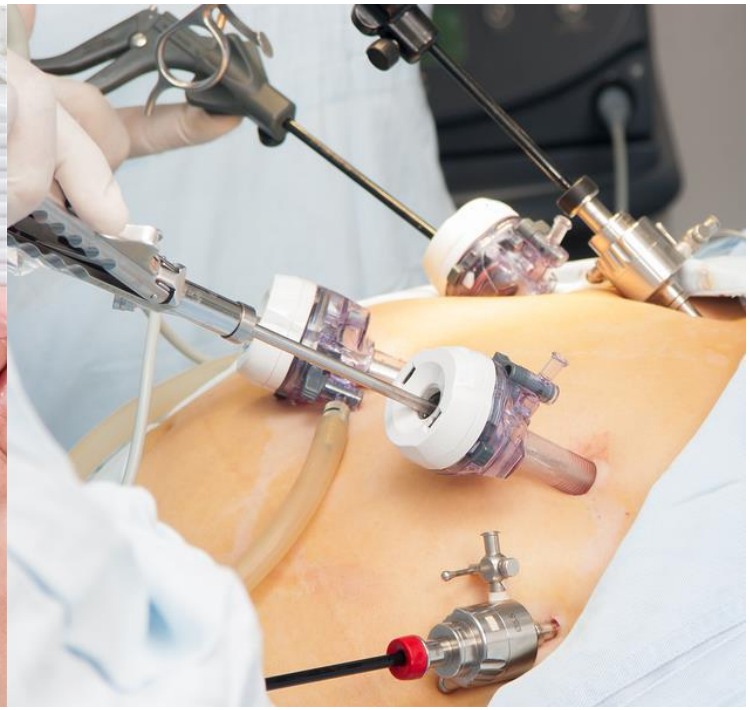
SYNTHESIS

OBESITY SURGERY: IS IT EFFECTIVE, SAFE AND COST-EFFECTIVE?



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HEALTH SERVICES RESEARCH

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OBESITY SURGERY: IS IT EFFECTIVE, SAFE AND COST-EFFECTIVE?

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PREFACE

Overweight or obesity is increasing worldwide, and threatens to develop into a true pandemic. According to the World Health Organisation (WHO), the number of people with obesity tripled worldwide between 1975 and 2016, and today one in seven adults in Belgium is overweight.

Obesity is a complex disorder. There are not only medical, but also important psychological and social, aspects. In fact, obesity increases the risk of all sorts of illnesses such as diabetes, heart and vascular diseases, some forms of cancer, and premature death. But it is also associated with stigmatisation and a great deal of psychological suffering, and occurs considerably more often in more vulnerable socioeconomic classes.

Adjustment of lifestyle to healthier dietary habits and more exercise is and remains the cornerstone of the conservative treatment. But unfortunately this does not always lead to the desired lasting result. And medication too has not played a large role in the approach to this problem so far. For someone who has already tried everything and is desperate, surgery therefore seems to be a “simple solution”…

Surgical procedures for obesity, also called “metabolic and bariatric surgery”, have been reimbursed by health insurance in Belgium under strict conditions since 2007. But the question arose of whether the procedure should be made accessible to two additional target groups, and the KCE received the assignment to evaluate this.

So we examined this treatment method and assessed the efficacy, risks and complications, and cost-effectiveness of this procedure. We also specifically reviewed the target groups for which an extension of reimbursement is being considered. In addition, we studied the available Belgian data. This took place in collaboration with the IMA, for which we sincerely thank them.

As is often the case, the answer to the question posed is nuanced, as you will read in the report. But one thing emerges clearly in any event: a surgical procedure for obesity has an impact on the rest of your life... Anyone considering the procedure must realise that a lasting adjustment in lifestyle and medical follow-up after the procedure will constitute an ongoing challenge.

Therefore the results of the present report will be taken over to a subsequent study in which a care trajectory for bariatric surgery will be outlined.

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General Director a.i.

CORE MESSAGES

- Obesity is a common condition that can lead to significant health problems. It is more and more often considered a chronic (often complex) disorder.
- A change in lifestyle (nutrition and physical activity) remains the basic treatment due to its relatively low cost and non-invasive nature, and thus also the limited risks.
- Metabolic and bariatric surgery[a] (MBS) is now reimbursed in Belgium for the indication of morbid obesity (BMI ≥40) or severe obesity (BMI ≥35) in combination with the following obesity-related disorders: severe, difficult-to-treat hypertension, type 2 diabetes or obstructive sleep apnoea syndrome (OSAS). Reimbursement is reserved for adults (≥18 years of age), after multidisciplinary consultation, if a diet for at least one year has had no lasting success.
- The most common MBS procedures are the RYGB (Roux-en-Y Gastric Bypass) also called a “Bypass”, and the SG (Sleeve Gastrectomy) also called “gastric reduction”. The “gastric band” (LAGB – Laparoscopic Adjustable Gastric Banding) is seldom used due to less weight loss and longer-term complications.
- On the basis of randomised studies, it appears that MBS leads to a significant and sustainable weight loss in the majority of those operated on. The physical components of the quality of life also improve. In patients with diabetes there is a higher rate of diabetes remission in comparison with non-surgical treatment, although the disorder occurs again in some patients after several years. Observational data indicate a drop in premature deaths due to disorders caused by obesity.
- The decision to have MBS cannot be made lightly, because it does not solve all problems (e.g. psychological problems), and side effects such as vitamin and micronutrient deficiencies can occur. A large number of repeat procedures is also observed.
- Although the list of possible side effects is long, the overall benefit-risk balance at the population level is favourable. But candidates for MBS should be adequately informed of these risks, and of the necessity of a lifelong adjustment in lifestyle.
- The economic evaluations of MBS for the currently reimbursed indications indicate a relatively low ICER (incremental cost-effectiveness ratio) or even cost savings. The current indications can thus be maintained.

- For two ‘new’ indications we establish the following:
  - For persons with type 2 diabetes and obesity with a BMI of 30 - <35, the efficacy for diabetes remission and the safety appear comparable to that for persons with a higher BMI. The underlying evidence is of poor quality (based on smaller studies). A number of RCTs on this are in progress and should be monitored.
  - For adolescents (< 18 years of age) mainly observational studies suggest that weight loss and safety in the short term are comparable to those of adults. But an extension of the indication to adolescents is not straightforward, because the scientific evidence in adolescents is much more limited and is primarily based on procedures conducted in specialised centres for a very high BMI (ca. 39-59 kg/m2 on average). Moreover, the data on long-term effects (efficacy and mainly safety) are less extensive than for adults. The decision to carry out the procedure should primarily be guided by the severity of the medical situation, rather than solely age. MBS in adolescents should therefore remain a very great exception.
- The economic evaluations of MBS in adolescents and diabetes patients with a BMI 30 - <35 also result in relatively low ICERs. These calculations are however mainly based on non-randomised studies and many assumptions. They therefore point to rather a potential cost-effectiveness and the importance of a further guided introduction (according to the IDEAL principle) of MBS in these populations.
- A restrictive reimbursement for the two aforementioned new indications can be envisaged. This will be further developed in an HSR (Health Services Research) report in progress, as will the pre- and post-trajectory for MBS, with attention to long-term follow-up.

[a] Although the term ‘metabolic surgery’ was initially used only for bariatric surgery in obese persons with type 2 diabetes, the term ‘metabolic and bariatric surgery’ (of MBS) is used more and more often as a synonym for bariatric surgery in general, as bariatric surgery also gives rise to metabolic changes and improvements in obese persons without diabetes.

OVERVIEW

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LIST OF ABBREVIATIONS

ABBREVIATION	DEFINITION
AUD	Alcohol Use Disorder
BMI	Body Mass Index
CPAP	Continuous Positive Airway Pressure
CRD	Centre for Reviews and Dissemination
EUnetHTA	European Network for Health Technology Assessment
GOR	Gastroesophageal reflux
GRADE	Grading of Recommendations Assessment, Development and Evaluation
HSR	Health Services Research
HTA	Health Technology Assessment
ICER	Incremental cost-effectiveness ratio
IDEAL	Idea, Development, Exploration, Assessment and Long-term study
IH	Internal hernia
IMA	Intermutualistic Agency
INAHTA	International Network of Agencies for Health Technology Assessment
LAGB	Laparoscopic Adjustable Gastric Banding
MBS	Metabolic and Bariatric Surgery
MZG	Minimum Hospital Data (Minimale Ziekenhuis Gegevens)
NICE	National Institute for Health and Care Excellence
OAGB	One Anastomosis Gastric Bypass
OECD	Organisation for Economic Co-operation and Development
OSAS	Obstructive sleep apnoea syndrome
PK	Pharmacokinetics
QALY	Quality-adjusted life year

RCT	Randomized Controlled Trial
RYGB	Roux-en-Y Gastric Bypass
SD	Standard deviation
SG	Sleeve gastrectomie
VT	Increased reimbursement (verhoogde tegemoetkoming)
WHO	World Health Organization

1. BACKGROUND

1.1. Objective of the study

Today one in seven adults in Belgium is overweight or obese. An attempt is first made to remedy this through an adjustment in lifestyle, or possibly by the use of medications. If this does not have the desired effect, an operation for overweight, called 'metabolic and bariatric surgery', can be considered. Although the term metabolic surgery was initially only used for bariatric surgery in obese persons with type 2 diabetes, it is now also used more and more often as a synonym for bariatric surgery in general, as bariatric surgery also gives rise to metabolic changes and improvements in obese persons without diabetes. Both terms can be used almost interchangeably. In this report we will use the acronym MBS (Metabolic and Bariatric Surgery) for ease in reading.

The RIZIV/INAMI now provides reimbursement for MBS for adults with a Body Mass Index (BMI, see text box 2) of at least 40, or a BMI of at least 35, the latter in combination with comorbidities such as diabetes (see Chapter 5). In the meantime, the conditions for compensation for this surgery are however more than 10 years old. Since then, new scientific evidence has become available, so that there may be a need for revision of this arrangement.

As also indicated in Text Box 1, in this report we evaluated the clinical efficacy, safety and cost-effectiveness of the most often used and best documented techniques for metabolic and bariatric surgery today: the **Roux-en-Y Gastric Bypass (RYGB)**, pronounced '*roo-en-wai*', and the **Sleeve Gastrectomy (SG)**. **Laparoscopic Adjustable Gastric Banding (LAGB)** was still often performed until recently, but its use is sharply declining.

We also devoted attention to two groups that do not fall under the general reimbursement at present: 1) adolescents and 2) adults with type 2 diabetes and a BMI between 30 and 35.

There is no consensus in the international guidelines on MBS for adolescents <18 years old or for adults with type 2 diabetes and a BMI between 30 and 35.

On the other hand, a number of leading professional diabetes associations propose MBS as a treatment option for adults with type 2 diabetes and a BMI between 30 and 35 who do not achieve lasting weight loss and improvement in comorbidities without surgery.

It is therefore useful to examine whether extension of the RIZIV/INAMI coverage for MBS is indicated for these two target groups.

In addition, we reviewed Belgian practice relating to MBS.

1.2. What we did not study

Older techniques, such as the **predecessors of the RYGB,** and on the other hand more recent and newer procedures such as the **One Anastomosis Gastric Bypass** (OAGB, or the so-called 'mini-gastric bypass'), the **gastric balloon**, the **endobarrier** and the **transoral endoscopic gastroplication** were thus not included in our study. There is still only limited scientific evidence on these techniques. Therefore they are best studied longer and more thoroughly first in clinical studies, before definitive conclusions can be drawn on their clinical results in the medium and long term.

The present study was conducted on request of the Flemish Knowledge Centre for Eating and Weight Disorders (*Vlaams Kenniscentrum voor Eet-en Gewichtsproblemen* – *www.eetexpert.be*). Both this centre and the Observatory for Chronic Diseases (*Observatorium voor de chronische ziekten*) have stressed the need for a **holistic approach** to obesity with **pre- and postoperative multidisciplinary guidance**. These aspects will be treated in a later KCE report.

Text Box 1 – Objective of the present report

- Evaluation of the clinical effectiveness of the most commonly performed procedures in adults, the Roux-en-Y Gastric Bypass (RYGB), the Sleeve Gastrectomy (SG) and the LAGB (Laparoscopic Adjustable Gastric Banding), often performed until recently (Chapter 3)
- Evaluation of the safety of RYGB and SG alone, and not of LAGB, because this is performed less and less often (Chapter 4)
- Evaluation of the clinical effectiveness and safety of MBS in adolescents (BMI ≥40), and in adults with type 2 diabetes with a BMI of 30-35 (sections 3.3 and 3.4)
- Description of Belgian practice (Chapter 5)
- Evaluation of the cost-effectiveness of MBS (Chapter 6)

The aspects of pre- and postoperative follow-up are treated in a separate KCE report.

2. WHAT IS OBESITY AND HOW SHOULD IT BE TREATED?

2.1. Obesity is a chronic disorder

Obesity is a disorder in which fat accumulates in the body to a point at which it can damage health. The causes are often an interplay between a certain genetic predisposition and environmental factors (e.g. lifestyle).

In rare cases obesity is caused by a specific disorder, such as hormonal abnormalities (e.g. reduced thyroid function) or a genetic disorder.

Text Box 2 – What is obesity?

When is someone obese?

The Body Mass Index (BMI) is a method that is often used to examine whether a person is overweight or obese. In this, the weight in kilograms is divided by the height in metres squared (m^2). The BMI is expressed in kg per m^2. For ease in reading we omit the unit 'kg/m^2' in this document.

BMI= weight (kg)/(height (m) x height (m))

In **adults,** the World Health Organisation (WHO) considers a BMI of 25 to 29.9 as overweight, and a BMI of ≥30 as obesity. Obesity is in turn subdivided into 3 classes: class I (BMI 30 to <35, or moderate obesity), class II (BMI 35 to <40, or severe obesity) and class III (BMI ≥40, or morbid obesity). In the literature the term super obesity (BMI ≥50) is also applied.[1]

Because children are still growing, the BMI criteria for adults cannot simply be applied to them. **Children and adolescents** between 5-19 years of age suffer from obesity according to the WHO if they have a BMI that is more than two standard deviations (SD) above the WHO Growth Reference median.[1]

The BMI is a surrogate measure for evaluation of obesity, as it does not take account of the body composition and gives no insight into the type of obesity and the underlying fat distribution (e.g. a high degree of abdominal fat usually entails a higher health risk).

2.2. A worldwide problem

In the western world (or the OECD member states) 54% of the population is overweight (BMI≥25) and 19% is obese (BMI ≥30; 20% of women on average and 19% of men).[2] Obesity is still increasing worldwide, even in countries that had a low incidence in the past.[1-3]

In Belgium 45% of the population (age group 3-64 years) is too heavy: 29% is overweight (BMI 25-<30:) and 16% is obese (BMI ≥30).[4] These figures are comparable to the figures of the European Social Survey (2014) for Belgium: 33% of the population is overweight and almost 14% is obese.[5] In children and adolescents (3-17 years of age), 11-15% is overweight and 3-5% is obese.[4]

2.3. Increased risk of health problems and premature death

A person with obesity runs a greater risk of, e.g., type 2 diabetes, heart and vascular diseases (such as stroke), obstructive sleep apnoea, osteoarthritis, some kinds of cancers and depression.[1, 6] The risk is further increased if the person, in addition to an elevated BMI, also has disorders such as (pre-)diabetes, high blood pressure, high cholesterol, a large abdominal circumference, and non-alcoholic fatty liver. And this is often the case with obesity. Approximately 85% of persons with type 2 diabetes are overweight or obese.[7] The higher the BMI, the more the risk of these disorders increases.

Obesity also reduces life expectancy.[8, 9] In comparison with someone with a normal weight, someone who is overweight loses one disease-free year, someone with moderate obesity 3 to 4 years, and someone with severe obesity 7 to 8 years.[10]

In addition, obesity causes a high economic burden for those concerned themselves, their families and society. Not only are there high care costs, but obesity also causes loss of productivity. In addition to a possible impact on employment, the primary impact is on absenteeism (see Chapter 6).

2.4. The approach to obesity

The health risks of obesity usually decrease as a person loses weight. The primary way to achieve this weight loss is a modification in lifestyle. If this does not achieve the desired effect, the use of medications can be considered. For very severe cases, MBS is an option.

In any event, even after the desired weight loss, a long-term, or sometimes even lifelong modification of lifestyle is required. Therefore obesity is more and more often considered a chronic (complex) disorder.

2.4.1. Modification of lifestyle

Overweight and obesity can in general be prevented and treated by healthy eating and/or eating less and by physical activity. These measures form the basis of every treatment; they are relatively inexpensive and the risk of adverse effects is small.

Usually in a treatment under guidance of a (general practitioner) physician and/or a dietician, a weight loss of 7 to 10% is the aim. To achieve this, many people with obesity also need intensive (psychological) behavioural therapy lasting at least 6 months. This individual or group therapy offers techniques to help in following the dietary and exercise recommendations.

An evaluation of the effectiveness of lifestyle modification and the impact of measures in the context of prevention and health promotion (e.g. prohibition of the sale of soft drinks in schools) are not a part of the present study.

2.4.2. Drugs

Drugs can be used for treatment of obesity as a supplement to modifications in lifestyle, e.g. in the event of no or inadequate weight loss.

The only two drugs that have been approved for weight loss and marketed in Belgium are Xenical®/Orlistat® (ingredient name orlistat) and Saxenda® (ingredient name liraglutide). These drugs are not reimbursed and have only played a limited role in our country to date. An evaluation of these drugs also falls outside the present study.

2.4.3. Metabolic and bariatric surgery

If lifestyle modification (possibly supplemented by drugs) does not deliver the desired results, an operation for weight loss or metabolic and bariatric surgery (MBS) can be considered. This is usually only recommended to persons with morbid (class III, BMI ≥40) or severe obesity (class II, BMI ≥35 in combination with certain other disorders). In any event a modification of lifestyle will also remain necessary after this procedure.

MBS has already existed for several decades and is performed more and more often. The procedure can be subdivided into three categories: **restrictive** (the stomach is reduced so the person can eat less), **malabsorptive** (the intake of calories and nutrients by the body is limited by 'bypassing' a section of the small intestine) and **mixed** procedures.

In addition, MBS causes a change in certain intestinal hormones, with favourable effects on the metabolism (including sugar metabolism) and an influence on feelings of hunger and satiety.

The primary bariatric procedures today are (see Figure 1):

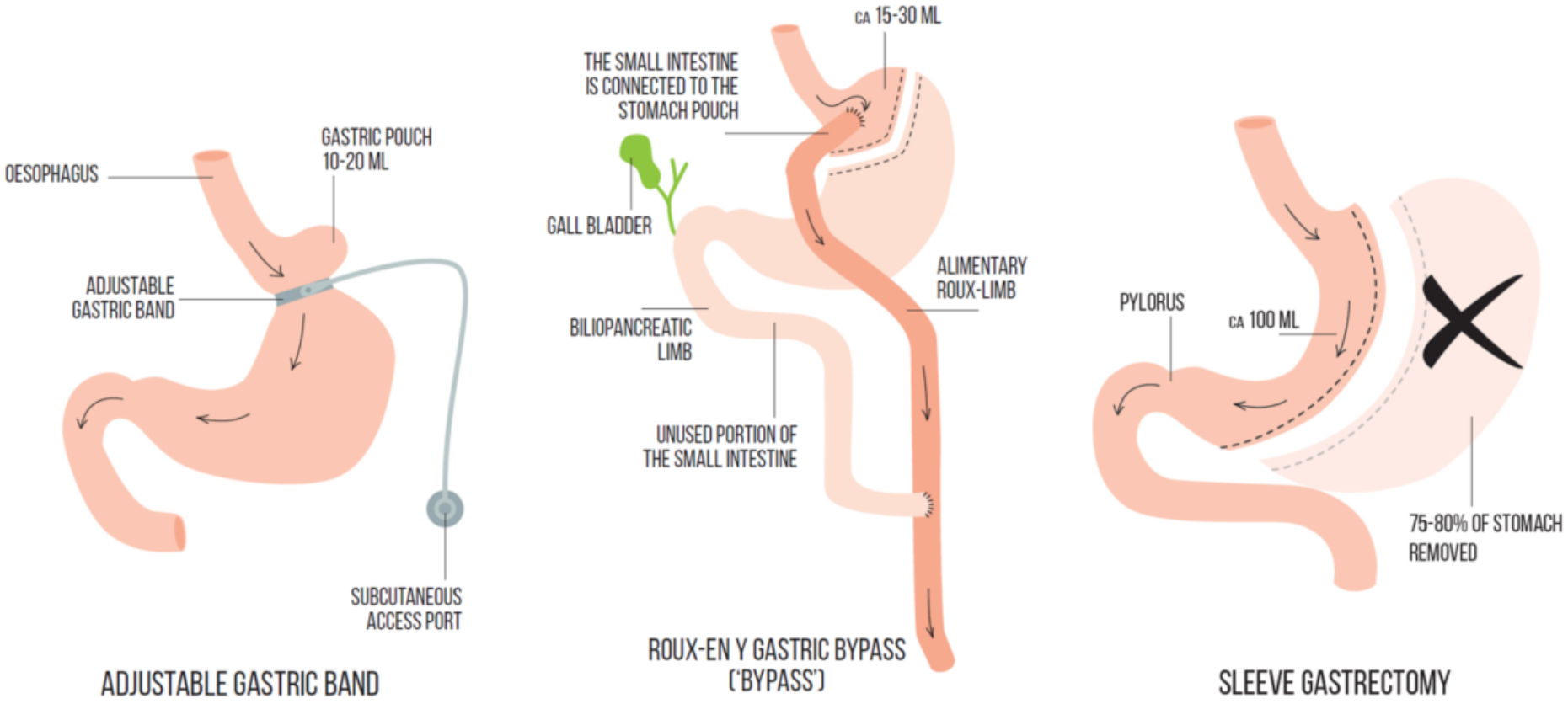
- The **Roux-en-Y gastric bypass (RYGB)**. This is a mixed procedure in which intake of food is restricted by forming a small gastric pouch and connecting this directly to the small intestine. Due to the reduction of the stomach much less can be eaten, and because a portion of the small intestine is bypassed, fewer nutrients and calories are also absorbed. This procedure is in theory reversible, but in practice this is much more difficult than for a LAGB (see below).
- The **sleeve gastrectomy (SG)** is being performed more and more often, in some countries sometimes even more often than a RYGB. It is a restrictive procedure in which the stomach is reduced by approximately 70%. There is only enough stomach left for a tube- or sleeve-shaped connection (sleeve) between the oesophagus and the small intestine, so that the person can eat less. It also leads to a decline in the hormone ghrelin , which reduces appetite. The procedure has no direct influence on the absorption of calories and nutrients in the body. It is not reversible per se, but it can still be converted into a different type of procedure.
- The **laparoscopic adjustable gastric band (LAGB)** is a purely restrictive procedure. Here, an inflatable band is applied around the uppermost part of the stomach. This creates a gastric pouch, so that the person can only eat smaller quantities. Here too there is no restriction in the intake of calories and nutrients by the body.

  The LAGB was very often performed until approximately 5-10 years ago. It is a relatively minimally invasive and reversible surgical procedure with a low risk of complications during or shortly after the operation. It has proven however to result in less weight loss than a RYGB or SG. Moreover, it has proven to cause many intolerance problems and/or complications (such as a shift of the band, or 'band erosion') in the medium and long term. This procedure is no longer often used in Belgium (see Chapter 5)

Today the **RYGB** and the **SG** are primarily performed via laparoscopy (keyhole surgery). This provides a significant reduction in the hospital stay and the number of complications during and shortly after the operation. Therefore use of the terms RYGB and SG in this report implies use of laparoscopy unless explicitly stated otherwise.

The ultimate choice of a certain type of procedure depends on various factors such as the eating behaviour and preference of the patient, the preference and experience of the surgical team, the comorbidities, the willingness of the patient to take nutritional supplements, etc.[11] MBS is considered successful when the patient loses at least 50% of his/her overweight, or when the final BMI is below 35.[12]

Figure 1 – The LAGB, RYGB and SG



3. IS BARIATRIC SURGERY EFFECTIVE ?

3.1. How did we proceed?

We evaluated the clinical efficacy of the most frequently performed procedures in adults, the Roux-en-Y Gastric Bypass (RYGB), the Sleeve Gastrectomy (SG) and the LAGB (Laparoscopic Adjustable Gastric Banding), often performed until recently.

To do so, we reviewed the international medical literature on MBS. In addition we conducted a systematic literature review in the databases of the Cochrane Library, Medline and Embase, where we searched for systematic reviews and meta-analyses of randomised controlled trials (RCTs). Ultimately we selected RCTs that compared MBS with a standard treatment (drugs, dietician, etc.). A number of these RCTs also include follow-up reports, which we also examined.

Because there is little scientific evidence from RCTs on the long-term mortality of MBS and MBS in adolescents, we also analysed a number of observational studies and meta-analyses that are largely based on observational data (see Text Box 3). As these observational data have weaker evidential value than RCTs, the results of these studies must be interpreted with the necessary qualification.

For the most important outcomes for the patient (survival and quality of life) the quality of the supporting evidence was assessed with the aid of the GRADE methodology (Grading of Recommendations Assessment, Development and Evaluation). You can find more details on the methodology used in section 4.1.5 of the scientific report.

Text Box 3 – definition of a randomised controlled trial and an observational study

What is a randomised controlled trial (RCT)?

In a randomised trial with a control group (Randomised Controlled Trial, abbreviated RCT) a certain procedure (e.g. surgery or drugs) is carried out in a specific group of patients, and the results are compared with those of a control group. A control group is a comparable group of patients with the same complaint or problem, but they are treated by a different means (e.g. the standard treatment or placebo).

Allocation of the patients to the various groups takes place at random, thus arbitrarily. An RCT often also takes place ‘double blind’; neither the researchers nor the patients know who receives which treatment. In this way the possibility that the result is (unconsciously) influenced by certain expectations can be ruled out. In surgery a double-blind study is of course not always possible.

Due to the controlled setup, RCTs have a high degree of evidential value. They form the cornerstone of evidence-based medicine (EBM). In assessing an RCT it is important to recognise distortion or bias, because this can have an influence on the causal relation between the procedure and the effect found. This distortion can for example occur if only a limited number or a selected group (e.g. men only) is included in the study, according to whether or not researchers and/or patients are blinded, or due to dropout of patients during the trial.

Sometimes however certain research questions cannot be answered with RCTs. Thus in some cases it is ethically irresponsible to deny patients a certain procedure in the framework of an RCT. In that case observational study can be an option.

What is an observational study?

In observational research patient data are collected, but the researcher himself performs no procedure that influences the possible outcomes. He only observes the current practice.

In principle, observational studies have less evidential value than RCTs, because there is no comparative group with which to compare the results, and because many external factors (e.g. smoking, weight, age, social situation - 'confounders') usually have an influence on the results. Connections/associations can be established via observational research, but no causal connection can be demonstrated. However, by collecting a great deal of information on external factors the influence of the external factors on a result can be assessed via statistical methods in certain cases.

3.2. Clinical efficacy in adults

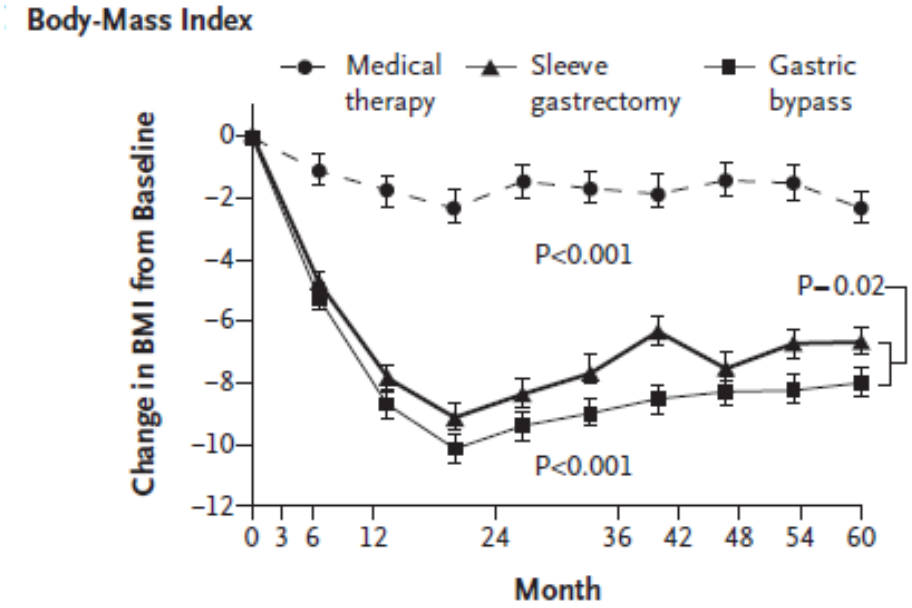
3.2.1. Significant weight loss

RCTs show that MBS leads to significant weight loss in obese persons, much more than the standard treatment with lifestyle modification and possibly drugs. The patient loses the most weight in the first two years after the procedure: almost 18 kg on average (after one year) and 28 kg (after two years) more than after standard treatment. The weight loss was dependent on the weight before the procedure: ca. 15 kg in persons with a BMI between 30 and 35 and ca. 26 kg in the group with a BMI ≥35.[13]

A number of RCTs observe a greater weight loss after RYGB than after SG, but in the largest RCTs the weight loss after SG is comparable to that after RYGB. The experience with SG is admittedly still less extensive and long-term than with RYGB. The weight loss after an LAGB is less than after the other two procedures.

Observational studies show that the weight loss is usually sustainable, despite a limited weight gain after two years (see Figure 2). After at least 10 years a significant weight decrease is often still maintained.

Figure 2 – Variation in BMI up to 5 years after RYGB or SG and after a standard treatment



Mean Value at Visit						
Medical therapy	36.4	34.1	35.0	34.8	35.1	34.0
Gastric bypass	37.0	26.9	27.4	28.2	28.6	28.9
Sleeve gastrectomy	36.0	26.9	27.7	28.1	28.2	29.3

Source: Schauer et al., NEJM, 2017[7]

3.2.2. Risk of death due to obesity drops

On the basis of observational studies, the relative risk of premature death due to disorders caused by obesity drops after MBS by ca. 30% to 45%.[14-16]

3.2.3. Quality of life: physical improvement after 2-5 years

The data from RCTs on quality of life have a number of methodological limitations, such as a small number of patients in the studies and a significant number of patients without follow-up data, so that robust information on quality of life after MBS unfortunately has very limited availability. In the best documented RCT, the impact after 3 and after 5 years was examined.[7, 17] Three years after the procedure a significant improvement in quality of life was observed in 5 of the 8 areas measured (physical functioning, pain, general health, energy and emotional wellbeing), in comparison with the non-operated group. After 5 years an improvement was still observed only in the areas of pain and general health, and there was no difference in the area of mental health. There are no longer-term data (more than 5 years after the procedure).

3.2.4. Type 2 diabetes: half have a better blood sugar level again within 2 years.

In type 2 diabetes insulin is still produced, but in insufficient quantities, and the activity of the insulin present is reduced. When people with type 2 diabetes have normal blood sugar again for an extended time without taking medication, this is called **remission**. This remission is possible with long-term weight loss. Over time the blood sugar will rise again in some of the patients and medication can be needed again. Remission therefore does not mean a definitive cure for type 2 diabetes.

In over half (55%) of the patients with type 2 diabetes, remission took place in the first 2 years after MBS, versus 8% of the patients with the standard approach. In many patients however, this result is lost over time; half of the operated patients with remission had abnormal blood sugar again within 5 years. In other words, after 5 years approximately 25% of patients who have diabetes and underwent MBS are still in remission.

There is no significant difference between the RYGB and the SG in the area of remission.[18, 19]

Diabetes can also cause damage over time to the large and small blood vessels (micro- and macrovascular complications). Examples of this are heart and vascular diseases and kidney, eye and nerve damage. On the basis of the RCTs we could not assess whether MBS is more effective than a standard diabetes treatment in reducing complications due to diabetes.

3.2.5. Impact on high blood pressure

The results here are not unequivocal; in one RCT a reduction in blood pressure was observed in half of the patients after the operation. In other studies no clear effect was demonstrated, but less medication for high blood pressure was used.

3.2.6. Impact on cholesterol level

RCTs showed that after MBS, cholesterol improved more than with the standard approach to cholesterol (medication). However, the difference was no longer statistically significant after 3 years. Five years after MBS it does appear that significantly less medication was prescribed to lower blood cholesterol.

3.2.7. Effect on obstructive sleep apnoea syndrome (OSAS)

Observational studies and clinical practice gave rise to the belief that MBS significantly reduces or eliminates OSAS. However, this is not supported by RCTs. The two RCTs that we selected were however also subject to criticism; they contain only a limited number of patients and they involve only the LAGB (which results in less weight loss than the RYGB and SG). No good RCTs were found that compare the impact of RYGB or SG on OSAS to that of a non-surgical procedure. For the Belgian observational data, we refer to section 5.8.3.

3.3. Clinical efficacy in adolescents

Because lifestyle modification often does not result in the desired weight loss, MBS is also considered a treatment option for young people with very severe obesity. In this study we focussed primarily on the age group between 14/15 and 18 years old, but many of the findings can also be highly relevant for people between 18 and 24 years of age. This mostly involves young people with very severe obesity (often with super-obesity) who often already have obesity-related disorders such as hypertension, diabetes, or a greatly increased risk thereof.

MBS is not presently reimbursed for children and adolescents under the age of 18. From the only RCT[20] that was identified for this age group it appears that the efficacy (after two years of follow-up) of MBS in adolescents is comparable to that for adults. In this RCT, 50 young people between 14 and 18 years of age, with an average BMI of 42, were supervised in modifying their lifestyle, and a number of them also had bariatric surgery (LAGB). In the LAGB group a weight loss of 35 kg or a drop in the BMI of 12.7 was recorded, as well as a greater increase in two of the 11 scores for quality of life.[20] In the group with lifestyle modification alone there was a weight loss of only 3 kg, or a BMI drop by 1.3.

The following aspects should also be taken into account:

- Most studies have been conducted in almost fully grown adolescents. It is therefore not ruled out that MBS in younger people who are not yet fully grown could cause vitamin and micronutrient deficiency and stunted growth.[11 21]
- The data come from specialised centres and the results may not be applicable to less experienced teams.[10 22] Moreover they come primarily from observational studies in young people with very severe obesity (average BMI of 39 to 58.5).
- In addition, we do not know the effects in the very long term; there are almost no data available from adults who underwent MBS as a teenager.[23]
- Many extremely heavy children and adolescents also suffer from psychological problems such as anxiety, depression, hyperactivity and emotional and eating disorders.[24] This, together with their young age, is an extra important focus in the evaluation that must be considered carefully by the adolescent, his/her parents, and the multidisciplinary team that conducts the preoperative evaluation. In that way a well-informed and conscious decision is made, one that does however have an important impact on the rest of one's life. This applies to all obese persons who are candidates and who are eligible for MBS, but is extra important in adolescents.

In adolescents no RCTs were found for the impact on diabetes remission. Observational studies (of adolescents with an average BMI between 39 and 59) show promising results with regard to type 2 diabetes and cardiovascular risk factors such as high blood pressure. These results should however be interpreted cautiously.

3.4. Clinical efficacy in persons with a BMI between 30 and <35 with type 2 diabetes

MBS is now reimbursed by the RIZIV/INAMI for a BMI of 35 or more under a number of conditions, including certain comorbidities such as diabetes. We studied whether MBS is also effective in diabetics (type 2 diabetes) with a BMI between 30 and <35. We found few RCTs however that studied diabetes remission in these persons. From the limited number of RCTs it appears that after 6 months to two years the blood values are normal again (remission) in 50 to 65% of these persons, just as in people with a higher BMI (see above). This proportion declines after 3 to 5 years to approximately 30% for all operated patients.[25, 26]

Additional studies on the impact of MBS on these patients are currently underway. A multicentre study (DiaSurg2 trial) was started in 2013 to compare the impact of RYGB with a standard medical treatment in 400 non-severely obese patients over 8 years.[27] Another RCT was started in 2015 and compares SG with a standard medical treatment in patients with newly diagnosed type 2 diabetes and a BMI between 30 and 42. In addition, the results for patients with a BMI between 30 and <35 will be considered separately.[28] It is not clear when the results will be available.

4. IS BARIATRIC SURGERY SAFE?

Today MBS offers the most effective long-term treatment for severe obesity. But a decision to have MBS must be well-considered, and patients must be evaluated and informed properly before the procedure. The procedure is after all invasive (and often irreversible) and demands lifelong adjustment and follow-up. Moreover, as we shall see below, there are a number of related risks.

4.1. Risk of death during or shortly after the procedure

As for all laparoscopic surgical procedures (abdominal keyhole surgery), there is a small risk of perioperative mortality and complications, that is, death during and in the first 30 days after the procedure. With the noteworthy progress in the past (two) decades the early postoperative mortality for MBS has fallen to approximately 0.1-0.3%, or 1-3/1000, for the RYGB and the SG.

These non-negligible figures are comparable to the mortality rates for other commonly performed scheduled operations such as gallbladder removal and hysterectomy, and they are lower than those for knee or hip prosthesis surgery or surgery of the large intestine.

These findings result from RCTs and observational research.

4.2. Possible complications during or shortly after the procedure

Short-term complications occur within 30 days after the procedure and are directly or indirectly connected with the recent operation. The most common important early complications are infection, bleeding, leaks/perforation, obstruction, venous thromboembolism and heart attack.

The risk of such complications is influenced by the general condition of the patient, e.g. the number and severity of other disorders.

Currently, readmission within 30 days is needed to handle these complications for approximately 5% of patients. Half of these are readmitted within a week.

4.2.1. Risk of complications after SG and RYGB

On the basis of observational data there seems to be a lower risk of serious short-term complications for SG (ca. 4% for SG versus ca. 6% for RYGB) and a lower chance of a repeat procedure within 30 days (ca. 1.6%) than for RYGB (ca. 2.5%).

Nausea, vomiting, dehydration and electrolyte disorders were in general more often a reason for readmission after SG, as were venous thromboembolism and postoperative leaks. On average, performing an SG takes less time than an RYGB and may be accompanied by less blood loss. Postoperative pain, bleeding, intestinal obstructions, wound problems, infection and heart attack were more often reported on average as a reason for readmission after RYGB.

4.3. Longer-term risks

Our findings on long-term safety are predominantly based on observational studies, because almost no solid data from RCTs are available on this.

When patients already have certain disorders or nutritional deficiencies before the operation, this can affect the risk of problems after the procedure. A great deal of discipline is also demanded from patients after the operation; they must maintain a certain diet and lifestyle, take nutritional supplements and be monitored medically. The degree to which patients comply with this is influenced by many factors, over which they do not always have control, but the chance of undesirable effects increases with poor compliance.

Some long-term adverse effects or complications are more specific and occur more often for a certain type of MBS. It goes without saying that serious medical problems can also have a psychological repercussion and vice versa.

4.3.1. Undesirable physical effects

4.3.1.1. Undesirable effects on the gastrointestinal tract

- Gastroesophageal reflux

Gastroesophageal reflux (GOR or heartburn) occurs very often in obese persons. Weight loss after MBS can have a favourable effect on this. After SG there is however a chance that already existing GOR is exacerbated or that GOR develops. An RYGB on the other hand generally reduces (symptoms of) reflux. Therefore the presence of serious GOR symptoms preoperatively is often taken into consideration in the choice between SG and RYGB.

- Gallstones

Gallstones (often asymptomatic) occur more often in obesity. Furthermore, in the initial period after MBS when rapid significant weight loss takes place, the risk of gallstone formation increases.

- Early dumping

Dumping is characterised by gastrointestinal complaints (abdominal pain, diarrhoea, bloating and nausea) and vasomotor symptoms (hot flashes, heart palpitations, sweating, dizziness, and sometimes fainting). It is caused by fast gastric emptying and exposure of the small intestine to nutrients, especially 'fast sugars'. Early dumping occurs within the first hour after a meal, and often within fifteen minutes. On average, 10-15% of patients report symptoms of early dumping, usually after RYGB, but also frequently after SG.

- Chronic (recurring) abdominal pain without clear explanation

After MBS approximately 10% of patients are likely to have unexplained chronic or recurring abdominal pain that can be difficult to treat.[29] The problem occurs more often after RYGB than after SG. The severity of the symptoms varies from discomfort to severe cramps, nausea and vomiting.[29] Mild abdominal pain is reported by up to 95% of RYGB patients at some point after the procedure.

- Acute internal hernia (IH)

Because the anatomy of the abdominal cavity changes, the small intestine can become caught in an internal opening created by the procedure. This can cause an acute intestinal obstruction that requires urgent medical treatment (usually surgical).

IH is the most commonly occurring longer-term acute serious complication after an RYGB, and the risk of IH persists for a lifetime. It is estimated that approximately 9 to 14% of patients are affected by this.[18, 19] An IH can also be the cause of chronic or recurring abdominal pain.

4.3.1.2. Metabolic and nutritional problems

- Postprandial hypoglycaemic reactive syndrome or ‘late dumping’

This occurs between one and three hours after a meal when food with a high fast carbohydrate content has been eaten. Symptoms are those of hypoglycaemia (or low blood sugar): sweating, heart palpitations, hunger, weakness, confusion, shaking and possibly fainting. The complication can also cause falls and accidents. It is reported more often after an RYGB than after SG, but it occurs less often than early dumping.[30]

- Vitamin and micronutrient deficiencies

One of the most commonly occurring problems after MBS is a deficiency in micronutrients (especially iron (Fe), vitamin B12 and folic acid, and more rarely copper, selenium and/or vitamin K). This problem occurs more often after RYGB than after SG on average, because in RYGB a part of the small intestine is bypassed.

These deficiencies can be insidious, may cause symptoms and can lead to other (sometimes serious) complications. An example of this is anaemia (due to Fe deficiency). When properly treated, the undesirable effects of this are essentially reversible. A vitamin D deficiency can have an impact on bone metabolism and the risk of osteoporosis.

Late (and rarely, early) neurological complications are usually also caused by such deficiencies. Depending on the type of deficiency, possible symptoms are e.g. confusion, memory disorders, tingling and numbness, unsteady gait, fatigue, mood swings, neuritis or damage to the foetus (spina

bifida). If the deficiencies are not properly recognised and treated, they can lead to irreversible consequences in rare situations.

- Fatigue

After MBS most patients will ultimately feel more energetic, but others have complaints of fatigue, especially during the initial period of rapid and substantial weight loss after the procedure, a period characterised by a 'catabolic' state.

Therefore patients must comply with the dietary instructions and get adequate exercise to limit excessive loss of muscle mass and muscle strength. It is also important to take the recommended vitamin/micronutrient supplements and to avoid fast sugars (chance of hypoglycaemia), as this can of course also cause fatigue.

- Malnutrition

Macronutrient (carbohydrates, fats and proteins) deficiencies can also occur, which can lead to malnutrition and loss of muscle mass and muscle strength. Some publications report that protein malnutrition in particular can occur in ca. 5% of patients after a standard RYGB.[31]

- Effects on the skeletal system

One of the possible and best-known long-term consequences of serious vitamin D deficiency is the effect on the bones (risk of osteopenia, osteoporosis). The risk of vitamin D hypovitaminosis and inadequate Ca absorption is higher after RYGB, but both problems also often occur after SG (especially hypovitaminosis D). The results in the literature on the effects on bone loss and the occurrence of possible bone fractures are variable, from no significant effect to increased bone loss (based on bone density measurements) and a possible increased risk of fractures. Therefore special clinical attention is indicated in patients with an elevated risk of osteoporosis.

- Other possible risks

In addition to the risks enumerated above, MBS can also increase the risk of e.g. kidney stones or a number of rarer complications (see scientific report).

4.3.1.3. Excessive alcohol and drug use

Research shows that a greater risk of alcohol abuse (Alcohol Use Disorder or AUD) exists especially as of the second year after RYGB, and not (or much less) after SG or LAGB.

The risk appears to be greater for patients with a history of addiction before the procedure, for men, younger patients, smokers, those with regular alcohol use, drug use, a limited social network, etc. MBS is furthermore not recommended for people with an active AUD. Therefore it is recommended that candidates for MBS be screened in advance for AUD or a history of AUD and informed of the possible increased risk.[32]

In addition the sensitivity to alcohol also increases, even more in women than in men. Alcohol is absorbed more quickly and broken down more slowly by the body. The symptoms of alcohol intoxication can also change after RYGB. This has implications for driving automobiles, alcohol tests, operation of machinery or performance of more complex tasks.

The risk of excessive drug use can also increase.

4.3.1.4. Risk of altered pharmacokinetics (PK) of medications

Pharmacokinetics (PK) comprises the way in which a substance (in this case medications) is processed by the human body (absorption, distribution, metabolism, possible temporary storage, and excretion). MBS can change the PK of medications, and especially the degree and the rate at which they are absorbed into the bloodstream. The impact of MBS on pharmacokinetics is however a complex field, and the effects of the procedure on the absorption of medications are not always easy to predict.

The scientific literature on this topic is relatively scarce. The risk appears to be higher on average after RYGB than after SG. A possible example is reduced absorption of oral contraceptives after RYGB or other malabsorptive procedures.

4.3.1.5. Aesthetic and dermatological undesirable effects

Dermatological undesired effects can cause medical and psychological problems after the operation. A frequently reported problem is the development of excess skin folds, with possible aesthetic consequences and an impact on the body image and feeling of self-worth.

Excess skin folds can also lead to maceration, irritation and skin infection. Plastic surgery can then be necessary or desirable.

4.3.2. Aspects of psychological nature and wellbeing

Often the connection between obesity and mental problems works in both directions. Significant mental problems can increase the risk of eating disorders or problematic eating. Conversely, some psychotropic medications such as antidepressants and anxiolytics increase body weight.

Psychiatric disorders and problems occur more often in people with obesity than in the general population. Obese people often suffer from low self-image or have low self-esteem. This holds even more for children and adolescents with severe obesity, where very often the psychosocial and psycho-familial context are also very important, than for adults.

All of this means that the permanent lifestyle modification and the need to be medically monitored after MBS constitute a continuing challenge for the patient.

- Increased chance of suicide and mental disorders

From observational studies it appears that many patients experience an improvement in quality of life during the first to second year after a 'successful' procedure ('honeymoon period'). Their weight loss often improves their wellbeing and reduces their possible depressive feelings. This favourable mental effect can however decrease later, especially in patients who already had mental problems beforehand. There can then be a (slightly) increased risk of suicide and self-harm.

The reasons for this have not yet been fully explained, and may be multifactorial.

A previous mental disorder or a disorder already present before the operation can have a negative influence. A disappointing weight loss (and/or unrealistic expectations) can in turn exacerbate the mental problems or cause them to recur.

Although the risk seems to be greater in people who already previously had mental problems, vigilance is necessary, as problems can also occur in people without a known history of mental problems. It is important that the physician examine the mental history of the patient beforehand and provide information on the results and possible risks of MBS, including a possible increased risk of suicide and self-harm. Consequently, after the operation special attention must be paid to the mental health of the patient.

- Development or recurrence of problematic eating behaviour or eating disorders after MBS

After MBS it is possible that the subject may (again) develop problematic eating behaviour or even eating disorders. Examples of this are 'grazing' (continuous snacking), eating calorie-rich food or binge eating. Conversely, avoidance of food has also been reported. The latter can develop if the patient experiences discomfort after a meal or is excessively concerned with the dietary recommendations.

4.3.3. Effects on pregnancy

Obese women are on average less fertile than women in general. Weight loss (after MBS) improves their metabolic and hormonal profile, and so their fertility often increases too.

A lower weight also reduces the chance of gestational diabetes, a heavy baby, high blood pressure and other problems during pregnancy or childbirth.

On the other hand, women who become pregnant after MBS run a somewhat higher risk of premature birth and a higher risk of too low a birthweight of the baby, especially for malabsorptive or mixed procedures (such as the RYGB). For normal development of the foetus it is therefore important that these women take nutritional supplements properly and that they are regularly screened for nutritional deficiencies. Experts therefore recommend not becoming pregnant in the first 12-18-(24) months after MBS, until weight loss has stabilised.

4.3.4. Complications in adolescents

In this study we focused primarily on the age group between 14/15 and 18 years of age, but many of the findings can also be highly relevant for people between 18 and 24 years of age.

Data on the long-term effects, such as complications in the area of nutrition and development, are very scarce and originate from specialised centres. From these limited data it appears that the risk of complications shortly after MBS in adolescents is probably comparable to that in adults.

Nevertheless, there should be particular vigilance for possible effects of such a procedure on growth and maturation, nutrient deficiencies and mental health. Mental and social problems often occur in severely obese children and young adolescents.[33] MBS has a lifelong impact on not only the physical but also the mental health of the subject, as we have seen. In addition, it requires lifelong lifestyle modification and close (multidisciplinary) medical follow-up.

The experts consulted therefore believed that MBS in this age group should remain an exceptional procedure, and that the decision can only be made after a thorough, full evaluation. These adolescents should be fully or nearly fully grown.[33] The potential candidates (and their parents) should have realistic expectations of the advantages to be expected and the possible risks in the short and medium term. In addition, they should be aware that almost no solid data now exist on the long-term effects.

4.4. The need for a new bariatric procedure

An increasing number of patients need revisional surgery (e.g. reversal of the MBS and/or a new ‘re-do’ procedure) after their first MBS.

As already stated, morbid obesity is a chronic illness that demands an ongoing approach and follow-up. Some patients with inadequate initial weight loss (rarely) or with a significant weight gain after an initially good weight loss can therefore benefit from a repeat procedure.

This repeat procedure usually consists of conversion of one type of procedure into another type (in one or two steps). On the basis of the literature and the feedback from clinical experts, it can be tentatively stated that conversion of a restrictive operation into an RYGB is now one of the most common scenarios.

The other type of revisional surgery is reversal of a bariatric operation. This usually occurs now due to complications or serious intolerance, especially with the gastric band (LAGB). This is also the reason why an LAGB is rarely performed today.

No accurate data exist on the percentage of patients who need revisional surgery after the most commonly performed procedures (RYGB and SG). A cautious rough estimate based on observational data is that approximately 5 to 20% of patients will need revisional surgery after an SG or RYGB.

The lack of success of the first procedure can have to do with a number of factors that are anatomical or technical in nature, or that involve the patient (inadequate lifestyle modification, poor compliance). These causes must be identified precisely in a multidisciplinary way, and the risks and advantages of a revisional operation must be assessed and discussed with the patient.

4.5. Which surgery for which patient?

At present no generally accepted guideline or algorithm exists to determine which type of MBS is best suited to a specific patient. As already reported, obese patients who want to have MBS performed often have a complex profile that demands a holistic evaluation and approach. In addition, each type of operation has its own characteristics with regard to efficacy for weight loss, improvement in comorbidities and possible risks and complications. For the choice of the type of operation, a thorough preliminary evaluation is therefore needed in which, among other things, the efficacy and risks of each type of procedure, the physical status, the degree of obesity, the metabolic and other comorbidities, the medical and surgical history, the history of alcohol and drug use, the mental and psychological status and history, and a possible desire for pregnancy are taken into account.

Naturally the concerns, needs and preferences of the patient must also be taken into account. To be able to make a good choice together with the treating physician, the patient must be adequately informed about the procedure and its potential drawbacks, and the necessity for lifestyle changes and lifelong medical follow-up. In this way he can give informed consent and become an important participant in the course of the procedure and thereafter.

The process before and after the bariatric procedure will be developed in more detail in a subsequent HSR report.

5. BARIATRIC SURGERY IN BELGIUM

5.1. How did we proceed?

For this part of our research we consulted the administrative invoice data of the Intermutualistic Agency (*Intermutualistisch Agentschap*, IMA) and the Minimum Hospital Data (*Minimale Ziekenhuis Gegevens*, MZG) with regard to all admissions and stays for MBS for the period 2009 to 2016.

5.2. When is MBS reimbursed?

MBS has been (partially) reimbursed in our country since 2007. The following conditions must be satisfied:

- Adults (≥18 years old) with a BMI ≥40 OR
- Adults (≥18 years old) with a BMI ≥35 with one of the following disorders:
  - Diabetes treated with medication
  - Therapy-resistant hypertension (that is, >140/90 mmHg despite treatment for at least 1 year, with concurrent use of at least 3 antihypertensives)
  - Obstructive sleep apnoea (OSAS)
  - Revisional operation after a complication or inadequate effect of the previous MBS.

In addition:

- the patient must have followed a documented diet for at least 1 year without sustained success;
- a multidisciplinary consultation must have been held with, in addition to the surgeon, at least one specialist physician in internal medicine and a clinical psychologist or psychiatrist. The report of this consultation, with a joint statement on the indication for an operation, must be signed by at least three of these specialists. This report goes into the patient's medical record together with the documented diet.

5.3. Increasing number of procedures

The frequency of MBS has systematically increased in our country (see Table 1 and Figure 3) in the past decade. In 2016 there were over 13 000 procedures in all, a rise of almost 80% compared to 7 years previously.

As of 2009, **gastric bypass surgery (the RYGB and its predecessors)** was gradually used more often, until the number stabilised several years later at about 8000 operations per year.

Gastric banding (LAGB) systematically lost more ground between 2009 and 2016. In 2016 only 332 procedures were still performed, while their number was over 1600 in 2009.

Gastric sleeve operations (SG) were performed less often than the LAGB in 2009. This pattern was later completely reversed. While LAGB has almost disappeared, the number of SG operations has increased enormously. In 2016 they were performed 4648 times.

Table 1 – Variation in MBS in Belgium (2009 - 2016): numbers per type of procedure

First bariatric procedure				
Year	**SG**	**LAGB**	**RYGB**	**Total**
2009	821	1649	5036	7506
2010	1183	1346	5901	8430
2011	1583	1072	7499	10154
2012	2046	873	8012	10931
2013	2616	563	8092	11271
2014	3327	469	8158	11954
2015	3751	366	8027	12144
2016	4648	332	8402	13382

Figure 3 – Variation in MBS in Belgium (2009 - 2016) per type of procedure

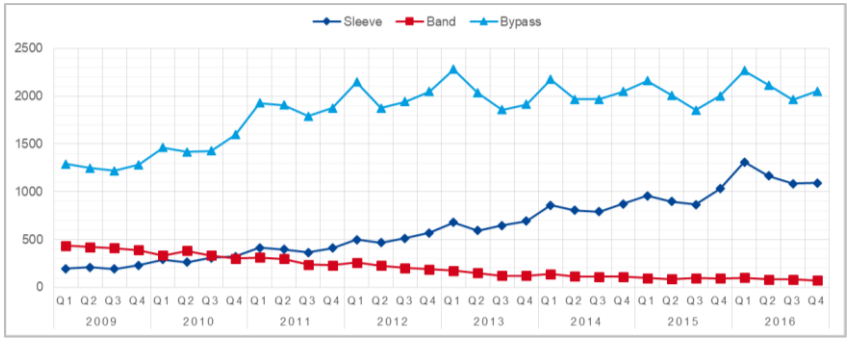
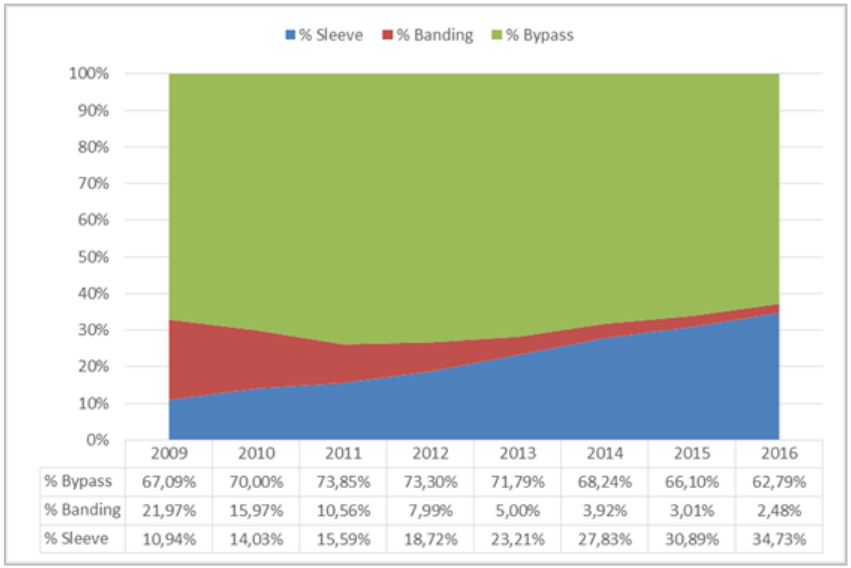


Figure 4 – Proportion of SG (sleeve), LAGB (banding) & Gastric bypass (RYGB) surgery per year



In 2016, the RYGB was the most commonly performed bariatric procedure in Belgium (almost 63% of cases - see Figure 4). SG operations also occur more and more frequently: from almost 11% (2009) to over 34% (2016). In 2009, LAGB still constituted 22% of the MBS procedures, while in 2016 this was only 2.5%.

5.4. Hospital stay

The average hospital stay for MBS between 2008 and 2014 shows a downward trend for the RYGB (from approximately 6 to approximately 3-4 hospitalisation days) and for the SG (from approximately 6 to approximately 4 hospitalisation days). The average hospital stay for LAGB remained relatively stable at approximately 2 hospitalisation days.

5.5. MBS costs

The cost price of a bariatric operation consists of:

- The costs reimbursed by RIZIV/INAMI (for LAGB ca. €3500, for SG ca. €4400, and for RYGB ca. €5000)
- + approximately €1000 to €1200 co-payment for the patient[34, 35]
- in a single-person room + approximately €1900 to €3700 extra in supplements (= fee supplements in particular)[35]

The reimbursed costs primarily cover the hospital stay, the fees and the materials costs for surgery. The costs for clinical biology, medications, and blood or plasma are limited.

5.6. RIZIV/INAMI expenditure for MBS

The costs of MBS for patients who fulfil the conditions are partially covered by the RIZIV/INAMI (see above). Due to the reduction in the hospital stay, the costs for SG and especially for RYGB have dropped somewhat over time. Yet the RYGB, with a reimbursed cost of around €5000, remains the most expensive procedure.

Due to the increase in MBS, the total government expenditures for costs directly related to hospital admission are rising, from approximately €40 million in 2009 to approximately €60 million in 2014 for SG, LAGB and RYGB together. In 2014 almost three quarters (72%) of these expenditures went to RYGB.

Due to the increasing number of bariatric operations and the rising proportion of patients with increased reimbursement (*verhoogde tegemoetkoming*, VT) (right to VT – see section 5.7.3), it can be expected that government expenditures for MBS will continue to increase.

5.7. Patient characteristics

5.7.1. Differences in areas of age, gender and medication use

We have determined that the patients who underwent an SG, gastric bypass (e.g. RYGB) or LAGB differed from each other in the areas of **age, gender** and **use of medication before the procedure**.

Patients in whom the reversible LAGB was performed had the lowest preoperative medication use (including diabetes and cardiovascular medication, antidepressants and cholesterol-lowering drugs) and were usually somewhat younger than patients who had an irreversible or less easily reversible MBS performed. The patients with an SG or RYGB differed less in the area of medication use, but did differ in the areas of age and gender. You will find more details on this in the scientific report.

5.7.2. Usually a BMI of 40 or more

The largest group of patients (approximately 3 out of 4) had class III obesity (BMI of 40 or more). A much smaller group had class II (BMI between 35-39), but also had other disorders, so that the procedure was eligible for reimbursement by the RIZIV/INAMI. Hypertension (in 1 out of 3 in both classes) and diabetes (3 out of 10 in class II) appear to occur most often among these comorbidities.

5.7.3. Growing proportion of patients entitled to increased reimbursement

We have also determined that the share of bariatric patients entitled to increased reimbursement (VT) is increasing, especially for SG; 27% of the patients with an SG were entitled to VT in 2016 (in 2009 this was 21%). For RYGB this was 21% in 2016 (17% in 2009). These are patients with a lower income and/or a special status (people with disabilities, the long-term unemployed, people with welfare benefits, etc.).

VT gives entitlement to increased financial coverage from the health insurance fund for e.g. physician consultations, hospitalisation or medication. Those concerned must pay a maximum of €450 annually in co-payments and are entitled to additional benefits such as the direct payment scheme for primary care.

5.8. Complications and impact of MBS

A direct comparison of efficacy among the different types of MBS is not possible, because the outcomes are based on non-equivalent patient groups before the operation (observational studies). Moreover, the Belgian databanks contain no data on the annual weight loss after the procedure.

5.8.1. Mortality after the operation

From the Belgian data it appeared that the mortality for all types of surgery shortly after the operation is low (30-day mortality: 1/1000).

After 2 to 5 years the mortality figures appear to be somewhat higher than for the general population, but it is difficult to ascertain whether these deaths were caused by overweight or by the MBS.

5.8.2. Medication use

Medication use was followed up to 5 years after the procedure for bariatric patients who regularly took diabetes or cardiovascular medication (e.g. blood pressure reducers, beta blockers and diuretics), cholesterol-lowering drugs or antidepressants before the operation.

For patients who regularly took **antidepressants** before the procedure (17-21% of the operated patients), there was a limited decrease in the first year after the procedure. The vast majority (ca. 70%) of the patients who took antidepressants before the procedure still took them 2-5 years after the operation, however. This result is comparable to that of a randomly chosen control group (without an operation) who use antidepressants.

For patients who regularly took **diabetes medication** before the procedure (3-9% of the operated patients), use dropped in the first two years after the procedure. Approximately 70% stopped regular consumption of antidiabetics. Thereafter (up to 5 years after the procedure), medication use stabilised, and there was no clear indication that medication use increased again. By way of comparison, there was also a drop in a randomly chosen control group of users of diabetes medication (without an operation), but it was, at approximately 30%, quite a bit less pronounced than in the operated patients.

Cardiovascular medication is the medication most commonly taken by bariatric patients (ca. 25-35% incidence, depending on the type of operation). As for diabetes medication, a drop was also observed in cardiovascular and hypertension medication in the first 2 years after the procedure, followed by a stabilisation phase after 3 to 5 years. Here too, the drop in medication use is somewhat greater in bariatric patients than in the control group (after 5 years, 57% of the RYGB patients and 62% of the SG patients still used cardiovascular medication, versus 85% of the control group).

5.8.3. OSAS & CPAP use

A CPAP (Continuous Positive Airway Pressure) breathing device is used during the night to treat OSAS (Obstructive Sleep Apnoea Syndrome). Only a very limited proportion (ca. 2-5%) of Belgian bariatric patients appear to use such a device in the 2 years before the operation, however. Up to 2 years after the procedure, a drop in CPAP use by 36% was recorded for these people. In a control group without MBS (controlled for gender, age and VT entitlement) this reduction was however also 18%. These observational data, which were obtained without an optimal control group, must therefore be interpreted with the necessary caution. Age does appear to make a difference: in the bariatric patients *under the age of 40* who did use a CPAP device 2 years before the operation, there appears to be no significant difference in CPAP use 2 years after the operation in comparison to a general (less obese) control group (without an operation). In bariatric patients *above the age of 40* the postoperative CPAP use was somewhat lower than in a control group of (less obese) patients (without an operation).

5.8.4. Repeat operation & surgical intervention side effects

In general, 5 years after the initial MBS there is a risk of 14 to 30% of rehospitalisation due to causes related to MBS. These involve the “undo” operations (undoing the operation), the “redo” operations (performing an MBS again, whether or not of the same type as the first procedure), laparoscopic keyhole operations and operations due to negative effects after MBS (such as obstructions or hernia).

Within a period of 5 years after the first procedures, fewer operations were recorded for SG than for RYGB and LAGB. For LAGB there were somewhat more repeat operations due to obstructions, laparoscopic keyhole operations and conversions to RYGB. Note that it is difficult to attribute these differences only to the type of operation, because each type of operation appeals to a different type of patient.

6. IS BARIATRIC SURGERY COST-EFFECTIVE?

From Chapter 3 it appears that MBS is effective. But is the procedure also cost-effective, in other words is it worth its added cost? Does it deliver sufficient benefits compared to the standard treatment of lifestyle modification under (para)medical guidance?

6.1. How did we proceed?

We have conducted a systematic search for economic literature on the cost-effectiveness of MBS. For this we consulted the HTA database of the CRD (Centre for Reviews and Dissemination) and the websites of HTA agencies (affiliated with the INAHTA - International Network of Agencies for Health Technology Assessment) and of NICE (National Institute for Health and Care Excellence). We also consulted the non-public POP database (planned and ongoing projects - May 2018) that is accessible to EUnetHTA partners (European Network for Health Technology Assessment, in which the KCE is a partner).

6.2. Unambiguous results on the basis of existing economic evaluations

Forty relevant economic evaluations were identified. In view of the large number of studies and the unambiguous results, it was decided not to develop a new economic model.

6.2.1. What is the cost-effectiveness of MBS under current reimbursement conditions?

From the economic analyses studied it appears that reimbursement of MBS leads to a **relatively low ICER (incremental cost-effectiveness ratio), and according to a number of studies is even better and cost-saving for the treatment of severe obesity with comorbidities and morbid obesity**.

Virtually all European studies calculate an ICER of less than €10 000 per QALY (quality-adjusted life year) for a time horizon longer than 10 years. The procedure does have its initial cost price (see Chapter 5), but primarily thanks to the drop in diabetes, a possible improvement in survival and quality of life of the patients (the latter mostly based on assumptions) a relatively low ICER is obtained, or it can even be concluded that the procedure can be cost-saving if a sufficiently long time horizon is modelled. In these economic models it is not in fact always clear whether and how complications and revisions have been recorded in the long term.

No explicit ICER threshold value exists in Belgium. In the UK it is £20 000-30 000 per QALY in general. If a similar willingness to pay existed in Belgium, the procedure could be considered cost-effective. These findings support the current reimbursement conditions of the RIZIV/INAMI.

6.2.2. The potential cost-effectiveness of MBS for extension of the reimbursement

At this time MBS is not reimbursed by the RIZIV/INAMI for patients under the age of 18 and for patients with type 2 diabetes and a BMI below 35.

The economic evaluations for **adolescents** are largely based on very small non-randomised studies (three studies with 11, 18 and 28 adolescents and a larger prospective cohort study with 228 patients). None of the economic evaluations for adolescents is based on the results of an RCT. The adolescents in these economic models have a very high initial BMI (e.g. >40 of >50).

From these studies it appears that MBS in adolescents with morbid obesity can also lead to relatively low ICERs in the longer term. The authors also stress however the need for further proof on a larger scale for the impact on quality of life and long-term complications.

The procedure also results in relatively low ICERs or may even be cost-saving in **diabetes patients with a BMI <35** and in **persons without diabetes with a BMI <40** according to the economic evaluations. The results should however be interpreted cautiously, as they are not adequately based on RCTs.

Moreover, in most studies it is assumed that MBS in this group of patients will have the same impact on the quality of life as in patients with a higher BMI. The results of these studies should thus be interpreted with the necessary caution. There is a clear need for more reliable data on the impact on quality of life and complications for this group of patients.

6.3. Impact of MBS on productivity

Most economic evaluations are conducted from the perspective of the healthcare payer. There are very few studies that investigate the impact of MBS on productivity.

We found two recent systematic literature reviews[36, 37] on the impact of MBS on productivity. Only a few publications indicate an improvement in labour participation. In most studies and a meta-analysis of five investigations, no significant changes in employment were found after the procedure. Further studies are therefore required to be able to reach definitive conclusions on this. On the basis of non-randomised studies, a significant decline in absence due to illness was noted. Inclusion of this effect can only improve the cost-effectiveness of MBS.

7. CONCLUSION

Bariatric and metabolic surgery (MBS) clearly offers **various benefits**. RCTs indicate a clear weight loss after the operation, in which the BMI declines by 7.2 to 12.7 kg/m^2. The greatest weight loss takes place in years 1 and 2 after the procedure, and is then usually followed by a relatively limited weight gain. In that same period, type 2 diabetes remission is also observed in 55% of the patients, versus 8% of patients without an operation. Half of this 55% admittedly relapses within 5 years after MBS. From RCTs it also appears that the physical aspects of quality of life improve in the 2-5 years after the procedure.

The most commonly applied techniques in Belgium are the RYGB (63%) and SG (35%), while LAGB (2.5%) has only limited use. In the area of initial weight loss, the RYGB and SG appear to have rather comparable efficacy according to the current state of affairs. The incidence of SG, a comparatively more recent procedure, has increased greatly worldwide in the meantime, but longer-term experience with it is still somewhat more limited than with the RYGB. The overall efficacy of LAGB is less pronounced than that of the SG or RYGB.

On the basis of observational data with follow-up of variable duration, MBS reduces the relative risk of premature death due to obesity-related disorders by ca. 30% to 45%. These figures should be applied with the necessary caution, given the nature of the underlying observational research data.

On the other hand, MBS does not solve all problems. For example, obese persons often have psychological problems. From observational studies it appears that MBS often has a favourable psychological effect up to two years after the procedure, but that this can decrease over time. Moreover, despite weight loss after surgery, depressive disorders can persist.

In addition, MBS can also cause physical problems. The procedure is associated with a (relatively low but not non-existent) perioperative mortality risk of 0.04% to 0.38%. Early complications can lead to readmissions for approximately 5% of patients within 30 days after the operation. There are also a number of possible side effects in the longer term. Because the findings are primarily based on observational research data, our analysis was mainly qualitative or at best semi-quantitative in nature.

On the basis of Belgian data, a large number of repeat procedures (14-30%) related to MBS is recorded within 5 years. After SG, there is on average a higher risk of exacerbated or newly occurring gastroesophageal reflux (heartburn, regurgitation). After RYGB, one of the most important long-term complications is the occurrence of an internal hernia (internal rupture) that can cause acute intestinal obstruction requiring urgent medical treatment. This problem can in principle occur over a lifetime. MBS can also cause metabolic disorders and nutritional deficiencies, which occur more often on average (but not exclusively) after RYGB than after SG or LAGB. This is a frequent problem with potentially important consequences. Therefore, proper intake of the prescribed supplements and lifelong medical follow-up are necessary after MBS. Furthermore, many patients also report general discomfort such as abdominal pain, bloating and nausea in the longer term. Observational data also appear to indicate an increased risk of problems with alcohol use, probably primarily after RYGB. MBS requires lifelong lifestyle modification to reduce a number of these side effects.

Although the list above is long, this does not in any way mean that the overall benefit-risk balance is unfavourable; on the contrary. MBS is now recognised as the most effective sustainable long-term treatment for morbid obesity (BMI ≥40) and for severe obesity (BMI ≥35) in combination with certain important obesity-related disorders. Yet a change in lifestyle (nutrition and exercise) remains the initial basic treatment for obesity, due to the low cost and non-invasive nature, and so also the limited risks. The role of prevention lay outside the scope of this study, but its importance should also not be overlooked.

Our overview of potential side effects demonstrates that the patient should be informed not only of the benefits to be expected, but also of the most important potential drawbacks or undesirable effects.

For **adolescents** the available data, mainly from observational studies, suggest that the effects of MBS on weight loss and the short-term safety appear to be fairly comparable to those for adults. Yet a straightforward extension of the indication for MBS to young adolescents is not simple and not always valid, due to a number of differences between these two populations. The scientific evidence in adolescents is much more limited and is primarily based on procedures in adolescents with a very high BMI (39-59 on average) that were performed in specialised centres. Furthermore, it is not clear as of what age a young adolescent can be considered mentally ready to make a therapeutic decision with a lifelong impact. In addition, many of these young people have psychological problems, which often makes the decision-making process even more difficult. The long-term effects on the efficacy and especially safety of MBS in young adolescents have also not been sufficiently documented to allow definite conclusions to be drawn.

The threshold for resorting to MBS in young adolescents should therefore lie higher than that for adults. The decision to perform the procedure should be primarily guided by the severity and urgency of the medical situation, rather than solely by age. Points for special clinical attention are, among others, growth and development, nutrient deficiencies, adherence to therapy and follow-up (compliance) and psychological health effects.

For **persons with a lower BMI of 30 - <35 and with type 2 diabetes**, RCTs demonstrate that the diabetes remission percentages are largely comparable to those in patients with a BMI ≥35. This evidence is however based on a limited number of RCTs with rather small patient groups. According to most international guidelines, MBS can be considered as a possible option for adults with type 2 diabetes and a BMI between 30 - <35 kg/m^2 who have not achieved sustainable weight loss and improvement in co-morbidities (including glycaemic control) with reasonable non-surgical methods.[38, 39] This is in line with the recommendations for adults with type 2 diabetes and a BMI between 35 - <40 kg/m^2. Currently two RCTs are underway that study the impact of MBS on type 2 diabetes patients with a BMI <35. As soon as they are finished, their results can be used to adjust the present conclusions and policy as necessary.

From a **health economics** viewpoint, the literature is unambiguous. In the short term MBS demands an investment from society, but the benefits it offers ensure a relatively low ICER or even a cost savings. The current reimbursement conditions are therefore not questioned. For an extension of the indications to adolescents and people with a BMI of 30 - <35 and with type 2 diabetes, the existing economic evaluations indicate a *possibly* relatively low ICER. The shortcomings of the supporting evidence (non-comparative research, small sets, little information on the impact on quality of life) are also applicable to the economic calculations that are based on it. Moreover, the results for these specific groups are based on results from specialised centres, and thus cannot simply be generalised. A guided further introduction, in which further information is collected on the impact on quality of life, short- and long-term complications, etc., and in which the results of studies in progress are also further followed up, is thus indicated. The IDEAL principle for medical devices (see KCE reports 249 and 297 and Text Box 4) can serve as a model for this.

The current HTA (Health Technology Assessment) study on MBS indicates clinical, safety and other points for attention. These can be relevant for the **second KCE report on MBS. In this HSR (Health Services Research) report** the organisational aspects of care for bariatric patients will be addressed. In this context it is appropriate to further develop the content of the pre- and post-MBS process, with a focus on long-term follow-up. In addition, adequate attention should be devoted to the way in which adolescents in particular (with adequate attention to, among other things, the psychological aspects) and type 2 diabetes patients with a BMI between 30 and 35 are selected and where they are treated. The conditions that hospitals must fulfil for this should be further developed in this HSR report.

Text Box 4 – The IDEAL framework: no surgical innovation without evaluation

The IDEAL model[40] (http://www.ideal-collaboration.net/) was designed by a group of surgeons and experts, among others, for the introduction of surgical procedures. IDEAL stands for Idea, Development, Exploration, Assessment and Long-term study. It describes the steps to be followed in developing and assessing new invasive techniques and procedures.

Idea: when a surgeon tries a procedure for the first time (Idea/proof of concept)

All new procedures must automatically be reported to the hospital and in an online register that is accessible to all surgeons. Undesirable effects and failures in particular must be published to prevent repetitions in the future.

Development: if the first reports give the impression that the procedure provides benefits, others can also try this procedure

The procedure is applied in a limited group of patients. In this phase experience is acquired and the technique is refined or modified. Precautionary measures are taken to prevent negative consequences for patients by, for example, working with mentors during the learning curve. All procedures must be collected in a register with clear reporting of the outcomes for all cases, without omissions.

Exploration: understanding the potential advantages and disadvantages

Once the procedure has been described and the most important technical aspects have been worked out, exploratory prospective clinical studies without a control group can be set up. This can take place in parallel with start-up of an RCT.

Assessment: Is this technique better than existing alternatives in the areas of clinical efficacy and cost-effectiveness?

This phase is intended to assess the efficacy/effectiveness versus the current alternatives. RCTs are best suited for this purpose, and the choice of the comparator is very important.

Long-term study

In this stage established procedures are assessed for rare and long-term outcomes. This is typically done by making use of a register. The value of the results depends on, among other things, the representativeness of the data. To encourage complete data entry it is recommended that only the most significant outcomes and relevant information be collected.

There is no exact point in time that indicates when an "innovation" moves from one phase to another. A formal scientific evaluation of a new procedure, in which it is compared with existing alternatives, making use of a suitable study design, is however recommended before this procedure is used on a large scale. Transparent reporting of research protocols and results is also necessary in each phase.

RECOMMENDATIONS[b]

This HTA (Health Technology Assessment) report on obesity surgery should be read in conjunction with a subsequent HSR (Health Services Research) study, in which the roles and responsibilities of the various partners in the care process will be further explored. Based on the current HTA report, we formulate the following recommendations:

To the caregivers

- **Give the patient adequate and clear information on the most important advantages and disadvantages of MBS, create proper expectations, and point out the importance of maintaining a modified lifestyle and of follow-up after the procedure.**
- **A change in lifestyle (nutrition and exercise) should be recommended as the first-line treatment for obesity in view of the low cost, non-invasive nature, and limited risks.**

To the federal Minister of Social Affairs and Public Health, the RIZIV/INAMI, the Federal Public Service Public Health and the caregivers:

- **On the basis of medical and health economics arguments, KCE recommends that the currently reimbursed indications for persons with a BMI ≥40, or BMI ≥35 in combination with certain comorbidities (diabetes treated with medication, therapy-resistant hypertension or obstructive sleep apnea (OSAS)), are maintained.**

<u>Extension of indications: adolescents</u>

- **For adolescents (young people up to 18 years of age) with a BMI ≥40, or a BMI ≥35 in combination with certain comorbidities, who do not achieve sustainable weight loss and improvement in the comorbidities with the accepted non-surgical methods, MBS should remain a rare exception that is only performed in the event of great medical need. Therefore, reimbursement of MBS should be linked to evaluation, determination of the indication and treatment by a multidisciplinary team in a specialised centre, pending further scientific evidence on the procedure in this group.**
- **As this involves an extension of existing surgical techniques to a new indication, it should take place in a guided way, by analogy with the IDEAL principle (see KCE reports 249 and 297). This means that, among other things, the number of centres is limited pending high-**

[b] The KCE bears full responsibility for the recommendations.

quality data, and that in these centres there is proper registration of the stipulated indications, procedures and relevant follow-up data. The data registered must allow scientific information to be collected to further support and/or adjust future policy, and more precise reimbursement criteria to be defined as necessary.

<u>Extension of indications: adult patients with type 2 diabetes and a BMI of 30 - <35</u>

- **MBS can be considered as a treatment option for adults with type 2 diabetes and a BMI of 30 - <35 who do not achieve sustainable weight loss and improvement in the co-morbidities (including glycaemic control) with accepted non-surgical methods. KCE recommends to provide reimbursement under strict conditions. Reimbursement for performing this procedure should be linked to a precise determination of the indication and follow-up in a specialised centre by a multidisciplinary team. Pending the results of the RCTs in progress, the number of centres should be limited and there should be proper registration of the stipulated indications, procedures and relevant follow-up data. Future policy should be further supported and adjusted on the basis of these data.**

To the Minister of Social Affairs and Public Health, the RIZIV/INAMI, the Federal Public Service Public Health, Healthdata.be, the caregivers and their scientific associations, and other scientifically relevant partners and institutions:

- **A research agenda should be drawn up so that all relevant information is collected in a consistent way with a view to quality monitoring and future policy decisions.**
- **More scientific data should be collected on, among other things:**
  - **The number of repeat procedures, with adequate attention to the longer term (including >5 years) and the underlying reasons for these repeat procedures.**
  - **The impact on the patient's quality of life in both the short term and longer term. The impact on the psychological aspect should also not be lost sight of in this.**
  - **The most important side effects (vitamin and mineral deficiency, metabolic disorders, etc.), with adequate attention to the longer term.**
- **New surgical techniques in this domain must also be introduced according to the IDEAL principle.**

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COLOPHON

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