HAUTE AUTORITÉ DE SANTÉ

TECHNOLOGICAL ASSESSMENT REPORT

Surgical treatment of severe and massive obesity by one anastomosis gastric bypass

September 2019

This technological assessment report, prepared with a view to mandatory National Health Insurance cover, can be downloaded from
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Abbreviations and acronyms

ATIH..... Technical Agency for Information on Hospital Care - *Agence technique de l'information sur l'hospitalisation*

CCAM ..... Joint classification of medical procedures - *Classification commune des actes médicaux*

OAGB..... One anastomosis gastric bypass

OLGB..... Omega loop gastric bypass

RYGB..... Roux-en-Y gastric bypass

CNAM ..... French National Health Insurance Fund - *Caisse nationale de l'assurance maladie*

CNP ..... French National Council for Healthcare Professionals - *Conseil national professionnel*

IFSO..... International Federation for the Surgery of Obesity and Metabolic Disorders

IGAS ..... Social Affairs General Inspectorate - *Inspection générale des affaires sociales*

BMI..... Body Mass Index

PPI ..... Proton Pump Inhibitor

NCT..... Trial number on the website *clinicaltrials.gov*

EBL ..... Excess BMI Loss

EWL ..... Excess Weight Loss

PHRC..... Hospital Clinical Research Programme - *programme hospitalier de recherche clinique*

SH ..... Stakeholder

SOFFCO.MM..... French and French-speaking Society for Obesity and Metabolic Diseases - *Société française et francophone de chirurgie de l'obésité et des maladies métaboliques*

Abstract

The HAS assessed the **one anastomosis gastric bypass** (OAGB) in the treatment of severe and massive obesity.

Another, older bypass technique is available to treat obesity, called the **Roux-en-Y gastric bypass** (RYGB). The RYGB has already been assessed and integrated in the 2009 HAS recommendations. It is reimbursed by the French National Health Insurance Fund since March 2005.

RYGB involves a surgical procedure comprising **two anastomoses** compared to **just one** for **OAGB**. OAGB has become more widespread over the last few years in France, without prior assessment and without any specific monitoring of this technique being possible. Use of this technique is debated among bariatric surgeons. OAGB is also known as mini-gastric bypass or omega loop gastric bypass.

The primary endpoint of the assessment is to determine whether the OAGB technique can replace the **RYGB** in all or part of its indications. The efficacy and safety of OAGB were therefore assessed in adult patients with massive obesity (BMI ≥ 40 kg/m^2) or severe obesity (BMI ≥ 35 kg/m^2) associated with comorbidity, compared to the RYGB.

The secondary objective is to assess the relevance of inclusion of OAGB on the joint classification of medical procedures (Classification commune des actes médicaux - CCAM), **for its reimbursement by the French national health insurance scheme in the claimed indication**.

The assessment covers the efficacy and safety of OAGB, identification of complications specific to this technique and the specific aspects of post-operative follow-up.

This work follows a standard assessment method based on:

- critical analysis of data from the literature identified after a systematic literature search and selected on the basis of explicit criteria ;
- consultation of a multidisciplinary work group of healthcare professionals (private and public sector) and patient representatives.

In light of all of these elements, and in particular preoccupying safety signals, the HAS considers that **one anastomosis gastric bypass (OAGB) carried out with a 200 cm (or longer) biliopancreatic limb is not a validated technique in the surgical treatment of massive and severe obesity (with comorbidity). It is therefore not an alternative to the Roux-en-Y gastric bypass (RYGB).**

Concerning OAGB performed with a 150 cm BP limb, too few data are currently available - in particular, no comparative data to RYGB and only expert opinions - to be able to conclude on its efficacy and safety. **The OAGB with a 150 cm BP limb falls under clinical research today and should benefit from multicentric randomised controlled trials for assessing its efficacy and safety**. The efficacy assessment should be based on a composite criterion including, in addition to long-term weight loss (five years), the resolution of comorbidities and quality-of-life measured by validated scores. The safety assessment should include an endoscopic examination after five years, in light of the risk of lower oesophageal cancer. The drop out rate should be reduced.

Concerning patients already having received OAGB surgery (around 5,000 patients in 2017 according to the estimations of the SOFFCO.MM), they must have, regardless of BP limb length, the same follow-up as patients having received RYGB surgery (lifelong follow-up

in accordance with the 2009 HAS recommendations “Obesity: surgical management in adults”) with close monitoring for the detection of nutritional complications (protein-energy malnutrition, micronutrient deficiency) and lower oesophageal cancer with an endoscopic examination five years after surgery. Patients having received surgery, their regular doctor (GPs) and their go-to professionals should be informed and trained respectively with a clear programme specifying the follow-up examinations to be carried out, their frequencies and warning signs of OAGB complications, and the criteria for referral to a specialist centre.

1. Introduction

1.1 Origins of the self-referral

The HAS undertook to assess the **one anastomosis gastric bypass (OAGB)** in the treatment of severe and massive obesity. At the same time, the Caisse nationale de l'assurance maladie (CNAM), in conjunction with the French and French-speaking Society for Obesity and Metabolic Diseases (Société française et francophone de chirurgie de l'obésité et des maladies métaboliques - SOFFCO.MM), asked the HAS to carry out the same assessment.

1.2 Objectives

The primary endpoint of the assessment is to determine whether the OAGB technique can replace the **Roux-en-Y gastric bypass (RYGB)** in all or part of its indications. The efficacy and safety of the OAGB were therefore assessed in the treatment of massive obesity (BMI ≥ 40 kg/m^2) or severe obesity (BMI ≥ 35 kg/m^2) associated with a comorbidity, compared to the RYGB in adults.

The secondary objective is to assess the relevance of inclusion of OAGB on the joint classification of medical procedures (Classification commune des actes médicaux - CCAM), for its reimbursement by the French national health insurance scheme in the claimed **indication**.

1.3 Reasons behind the self-referral

There are other older techniques for massive obesity. One of them, RYGB, involves a surgical procedure comprising two anastomoses compared to just anastomosis for OAGB. RYGB was already assessed in 2003 (1) by the National Health Accreditation and Assessment Agency (ANAES) (Agence nationale d'accréditation et d'évaluation en santé - ANAES)[1], and included in the 2009 HAS recommendations (2), and is reimbursed by the French health insurance scheme since March 2005.

As confirmed by the joint referral of the French health insurance scheme and the SOFFCO.MM, OAGB has become more widespread over the last few years in France, **without prior assessment and without any specific monitoring of this technique being possible.** In effect, there was no specific CCAM procedure name for this technique.

Use of this technique is debated among healthcare professionals. A French study comparing RYGB and OAGB[2], financed by a Hospital Clinical Research Programme (PHRC) for 2013[3], was recently published in March 2019. The preliminary results presented in a congress suggest that OAGB could be related to more common complications, the impact of which is discussed in this assessment.

[1] The ANAES was replaced by the HAS according to the provisions of the law of 13 August 2004.

[2] NCT02139813: https://clinicaltrials.gov/ct2/show/NCT02139813, viewed on 14/11/2018.

[3] PHRC-N, project no.: 13-0267, acronym: YOMEGA; https://solidarites-sante.gouv.fr/systeme-de-sante-et-medico-social/recherche-et-innovation/l-innovation-et-la-recherche-clinique/appels-a-projets/article/les-appels-a-projets-de-la-dgos-les-projets-retenus#PHRC, viewed on 14/11/2018.

2. Context

2.1 Information source

This context section was written based on a non-systematic literature review including general reviews, course or training materials, scientific articles and data from the databases of the Technical Agency for Information on Hospital Care (Agence technique de l'information sur l'hospitalisation - ATIH).

2.2 The pathology discussed is severe and massive obesity

Obesity is defined by the World Health Organisation (WHO) (3) “abnormal or excessive fat accumulation that presents a risk to health”.

It is a major risk factor for the appearance of other diseases, and also increases the risk of premature death and disability in adulthood (4, 5).

The body mass index (BMI) determines weight with respect to height, and is commonly used to estimate excess weight and obesity in adults. It is the weight divided by the height in metres squared, given as kg/m^2 (6).

The WHO defines obesity by a BMI equal to or higher than 30 kg/m^2, and describes several types of obesity (7) (*see* Table 1).

The risks related to obesity depend on the amount of adipose tissue, but also its distribution. Waist circumference is also measured in addition to the BMI calculation. It is the simplest anthropometric measurement for determining the extent of abdominal adipose deposits associated with metabolic and vascular complications. A waist circumference of over 90 cm in women and 100 cm in men characterises abdominal obesity (6).

Table 1. Classification of obesity according to BMI and the WHO, 2003 (7).

Classification	BMI (kg/m^2)
Class I obesity (moderate)	30-34.9
Class II obesity (severe)	35-39.9
Class III obesity (morbid/massive)	≥ 40

2.3 Prevalence of obesity in France

According to the data from the health study on the environment, biosurveillance, physical activity and nutrition (ESTEBAN) by Santé publique France, the prevalence of obesity among the 18-74-year-olds was 17.2% [15.2-19.3] in 2015 (8). Prevalence distribution by BMI class is given in Table 2.

Table 2. Prevalence of obesity (moderate, severe and massive) in the general population according to the ESTEBAN study, and according to Santé publique France, 2017 (8).

Classification	Prevalence in the 18-74 years population	Proportion of people with BMI > 30 kg/m^2 among the population
Class I obesity (moderate)	12.5%	73.5%
Class II obesity (severe)	3%	17.7%
Class III obesity (morbid/massive)	from 1 to 2%	8.8%
All classes of obesity	17.2%	100%

2.4 Information on surgical treatment of obesity

The 2009 HAS recommendations state that “bariatric surgery is a second-intention procedure after failure of well-conducted medical, nutritional, dietetic, and psychological treatment for 6-12 months” (2).

Bariatric surgery can be envisaged “for patients with BMI ≥ 40 kg/m^2, or whose BMI is ≥ 35 kg/m^2 and associated with at least one comorbidity likely to be improved after the surgery in particular(2):

- arterial hypertension ;
- obstructive sleep apnoea-hypopnoea syndrome (SAHOS) and other severe respiratory disorders ;
- severe metabolic disorders, especially type 2 diabetes ;
- debilitating osteoarticular diseases ;
- non-alcoholic hepatic steatosis”.

The surgical techniques recommended by the HAS are currently to the number of four (2): adjustable gastric banding, sleeve gastrectomy, Roux-en-Y gastric bypass (RYGB) and biliopancreatic bypass.

It should be noted that the 2009 recommendations state that the benefit/risk ratio of these four techniques[4] cannot be used to confirm the superiority of one technique over the other. These recommendations consider that expected weight loss, and also the complexity of the technique, the risk of postoperative complications, nutritional repercussions and mortality, all increase with the following types of surgery (2): banding, the sleeve, RYGB and biliopancreatic bypass.

In 2014, in a *Cochrane* systematic review by Colquitt *et al.*, the authors state that surgical management (sleeve or RYGB) is more effective on weight loss and on the resolution of comorbidities. However, the results did not make it possible to clearly rank the techniques (9).

In 2018, retrospective comparisons between banding, the sleeve and RYGB in particular (10), seven-year follow-up of patients operated by banding or RYGB (11), and an analysis of the French health insurance scheme databases were published (12). **The authors of these works conclude that RYGB is the technique that is the most effective in the long-term on weight loss and resolution of comorbidities. However, the RYGB is believed to present with the most major complications after 30 days** (10). The complications known with this technique are described in detail in chapter 2.6.

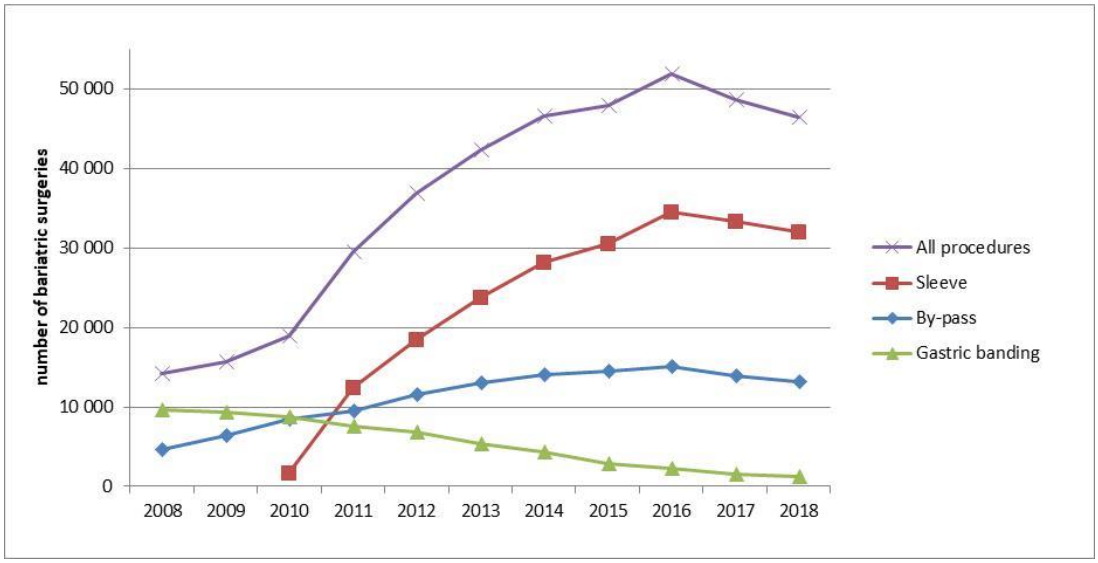
[4] OAGB was not included in the 2009 recommendations as the technique was not yet widespread in France.

2.5 Bariatric surgery in France - figures

According to the Technical Agency for Information on Hospital Care (Agence technique de l'information sur l'hospitalisation - ATIH), the number of bariatric surgeries, on the constant rise since 2008, currently represents around 50,000 procedures per year in France. The *sleeve* and the *bypass* are those performed the most often with more than 32,000 (69%) and 13,000 (28%) procedures per year respectively in 2018. For the bypass, the number of operations was collected without differentiating between the type of surgical procedure, with one anastomosis (OAGB) or two anastomoses (RYGB). In effect, at the time of data collection, there was no CCAM term to discriminate the data between the two bypass techniques (*see* Figure 1).

It must be noted that women underwent surgery in most of the cases, representing around 80% of operations, and were age around 40 on average (standard deviation +-12 years) (13).

Figure 1. Bariatric surgery in France - figures[5].



2.6 OAGB known complications

The overall rate of complications after OAGB in the short-term (up to 30 days) and the long-term (after 30 days) is estimated at between 5 and 10% (14).

The complications and their estimated frequencies from OAGB include in particular (2, 14, 15):

- anastomotic fistula (0.4 to 5.2%);
- haemorrhage (2 to 3%);
- intestinal obstruction (1 to 9.7%);
- Intestinal obstruction by internal hernia (4 to 5%);
- Dumping-syndrome (5 to 10%)[6] and hypoglycaemia (0.5%);

[5] Source: the graph was produced by the HAS based on data from the ATIH https://www.scansante.fr/applications/statistiques-activite-MCO-par-diagnostique-et-actes; the data presented represent the total number of procedures carried out in France per year for each technique and both approaches (laparoscopy and laparotomy). Name of the technique and CCAM laparotomy and laparoscopy code (bypass; HFCA001, HFCC003; sleeve; HFFA011, HFFC018; banding = adjustable gastric banding; HFMA009, HFMC007). As there were fewer than 140 biliopancreatic bypass procedures in France in 2017, this number is not shown on the figure.

[6] Dumping syndrome is a set of broad ranging symptoms of feeling unwell after a meal. It results from the sudden passage of food into the small bowel.

- nutritional and vitamin-related complications (16%);
- anastomotic ulcer (< 2%) and gastrojejunal anastomotic stenosis;
- fistula of stomach and duodenum (0.3 to 2.2%);
- cholelithiasis (> 25% in the absence of prophylactic treatment);
- mortality (0.5%).

2.7 Technique to be assessed: one anastomosis gastric bypass (OAGB)

2.7.1 OAGB description

The OAGB technique can take different names, such as the mini-bypass, single anastomosis gastric bypass, omega loop gastric bypass (16).

The OAGB described in 2001 by Rutledge was created especially to compensate for the technical complexity of the RYGB (17, 18).

The OAGB differs from the RYGB technique mainly in the creation of a long, narrow gastric pouch, formation of a biliopancreatic limb (excluded part) 200 cm long (from Treitz's angle to the anastomosis), and in the creation of a single anastomosis, the gastrojejunal anastomosis (17-20). It is widely performed by laparoscopy.

The RYGB has two anastomoses, gastrojejunal and jejunojejunal, the biliopancreatic limb being 100 cm (*see* Figure 2).

► Biliopancreatic limb length

The experts from the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) report, in their 2018 expert consensus based on a systematic review, that different limb lengths are found in the literature (16).

The 200 cm length for the biliopancreatic limb is the most commonly reported (16). It is also the length mainly described in the French YOMEGA study, financed by a PHRC[2,3], and in a French cohort of 1,000 consecutive patients (21).

The "ideal" limb length remains however debated. From 2008, authors suggested a "personalised" length according to the patient's BMI (22). However, this strategy does not appear to be optimal and is believed to carry the risk of nutritional and hepatic complications (20).

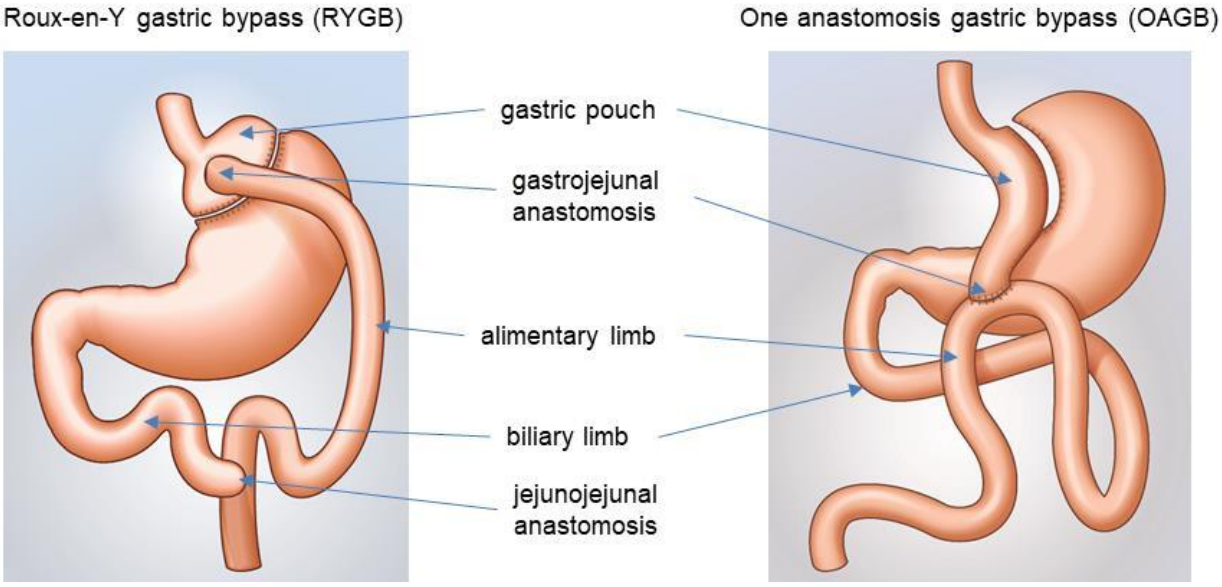
Other exploratory research published in 2018 comparing different limb lengths is believed to suggest that a "150 cm length" would prevent nutritional complications (23). **However, the level of evidence for these results remains highly limited**. The different groups were not in fact comparable. In effect, it was not a randomised trial as the patients were allocated to a limb length group (150, 180 or 250 cm) according to their characteristics. For example, patients with unstable type 2 diabetes or hypertension were included in a "long" limb group. Young patients, patients of childbearing age and vegetarians were included in a "short" limb group. The characteristics of each of the groups were not provided in the article (baseline BMI, age, comorbidities etc.). Numbers were small (n=101 in total) and follow-up short, at one year.

The ideal OAGB biliopancreatic limb length does not therefore seem to be determined to date.

► Gastric tube

In 2019, Rutledge *et al.* (18), to compensate for the "confusion among surgeons as to surgical technique", recalled the fundamental points and description of the OAGB technique. They state that, to avoid complications and bile reflux-related oesophagitis in particular, "the gastric tube must be as wide as the oesophagus and must not be narrow or create a restriction as in the sleeve; and in the same way, the gastrojejunal anastomosis must be wide (> 4.5 cm) and non-obstructive".

Figure 2. Illustration of the two gastric bypass techniques: Roux-en-Y and one anastomosis.



2.7.2 Potential indications, target population and role in treatment

The potential indications, mentioned in the joint referral of the SOFFCO.MM and the CNAM for OAGB, are those of the RYGB, and for all bariatric surgical procedures, in accordance with the 2009 HAS recommendations (2). This therefore refers to **treatment of massive obesity (BMI ≥ 40 kg/m²) or severe obesity (BMI ≥ 35 kg/m²), associated with one or more comorbidities likely to be improved by surgery**. Surgery is positioned in second-intention, after failure of well-conducted medical, nutritional, dietetic and psychological treatment for 6-12 months (2).

2.7.3 Main potential benefits compared to the RYGB

Patients are expected to experience similar or superior efficacy to that of the RYGB on weight loss and on improvement in comorbidities (17, 24).

A reduction in complications is also expected, due to the simplicity of the procedure compared to the RYGB. The presence of a single digestive anastomosis is believed to reduce the number of fistula. Due to the absence of mesenteric division, it is also expected that no more internal hernia be observed (15, 17, 21).

Also, the technique is believed to take less time and be more straightforward, and possibly require a shorter learning curve (17, 21, 25).

It should be noted that OAGB was suggested by certain authors as an alternative to RYGB in patients with "massive abdominal obesity", making the RYGB technically-complex to perform (due to a thick and short meso), without however the characteristics of these patients being precisely defined (19, 26, 27).

2.7.4 Main complications expected for OAGB

There are two types of complications specific to OAGB:

- **anastomotic ulcers**: which may become chronic have been reported, requiring revision surgery to adjust the procedure and change to either a RYGB or restore the normal anatomy (15, 26, 28);
- **bile reflux**: the technique remains controversial among bariatric surgeons due to the risk of bile reflux into the gastric pouch (29) (assessment application). Bile reflux may carry the risk of dysplasia and cancer of the gastric and oesophageal mucosa in the long-term. Bile reflux is believed to be symptomatic in fewer than 10% of cases. In the event of debilitating bile reflux, RYGB revision surgery is performed (15, 19);
- **nutritional complications**: the controversy also relates to the malabsorptive nature of this technique which is believed to be increased compared to the Roux-en-Y bypass, especially due to the length of the biliopancreatic limb which is believed to increase malabsorption (29). OAGB is believed to be responsible for more severe complications, especially anaemia, diarrhoea, fat-soluble vitamin deficiency and severe malnutrition(15, 19, 30);
- **hepatic involvement**: “negative” impact on liver enzymes (31), likely to lead to the decision to “reverse” the operation (restore the normal anatomy).

2.8 General context of bariatric surgery in France

According to the 2018 report by the Social Affairs General Inspectorate (Inspection générale des affaires sociales - IGAS) on bariatric surgery in France, “a portion of indications for this surgery is excessive or inappropriate in a general context in which there is an unclear framework for such practices”. The report addresses pre- and post-operative follow-up and mentions “significant shortcomings in the preparation of patients (tests, patient and primary care physician information, staff meeting organisation etc.) a significant percentage of whom do not have the appropriate post-operative follow-up, or any follow-up at all” (32, 33).

Also, OAGB has become more widespread over the last few years in France, without prior assessment and without any specific monitoring of this technique being possible. In effect, there was no specific CCAM procedure name for this technique.

2.9 Current conditions of reimbursement by the French health insurance scheme

In March 2005, further to assessment of the RYGB by the ANAES, two terms describing the RYGB (by laparotomy and laparoscopy) were entered on the CCAM (*see* Table 3).

The two terms cover however the description of the OAGB, which at the time (2005) was not widespread practice in France. This is why the OAGB could have been coded by the two terms.

To clarify matters and identify these interventions in order to report on and follow-up the patients involved, a descriptive CCAM code for the PMSI differentiating the two techniques is in force temporarily and under conditions (possible only in certain centres and on authorisation request) since 1st March 2019, pending the results of this assessment report.

Table 3. Extract from the CCAM and new descriptions as of 1st March 2019.

CCAM code	Descriptions	Changes as of 01/03/2019
HFCA001	Gastric bypass for morbid obesity, by laparotomy	HFCA001-**01*** - gastric bypass with **Y limb***, for morbid obesity, by laparotomy
		HFCA001-**02*** - gastric bypass with **omega loop***, for morbid obesity, by laparotomy
HFCC003	Gastric bypass for morbid obesity, by laparoscopy	HFCC003-**01*** - gastric bypass with **Y limb***, for morbid obesity, by laparoscopy
		HFCC003-**02*** - gastric bypass with **omega loop***, for morbid obesity, by laparoscopy

**: added on 1st March 2019, compared to the previous CCAM version.*

3. Assessment protocol

The assessment method was defined and described in a framework document on the HAS website (34).

3.1 Objective of the assessment

The primary objective of the assessment is to determine whether the OAGB technique can replace the RYGB in all or part of its indications. The efficacy and safety of OAGB were therefore assessed in adult patients with massive obesity (BMI ≥ 40 kg/m^2) or severe obesity (BMI ≥ 35 kg/m^2) associated with a comorbidity, compared to the RYGB. Also, this work aims to identify the practice requirements and specificities of post-operative follow-up.

The secondary objective is to assess the relevance of inclusion of OAGB on the joint classification of medical procedures (Classification commune des actes médicaux - CCAM), for its reimbursement by the French national health insurance scheme in the claimed indication.

3.2 Assessment method

This assessment method (35) is based on:

- critical analysis of data from the literature identified by a systematic search and selected on the basis of explicit criteria, conducted by the HAS;
- consultation of a multidisciplinary working group of professionals (private and public sector) from different disciplines brought to treat obese patients, and patients' representatives. The objective is to gather their expertise on the literature, the parts of the assessment for which no literature was identified, and also certain elements on the follow-up of the operated patients, and to identify the information necessary for patients;
- stakeholders' point of view (professional body and patient's association representatives) on the clarity and legibility of the provisional report, and their appropriation of this work and the physical and organisational consequences they may wish to express.

3.2.1 Literature search strategy

The OAGB was described in 2001 for the first time by Rutledge (17). The technique was disseminated worldwide, especially in France, from 2010.

A search of randomised controlled trials was therefore performed for the period from 2001 to February 2019, followed by watch through to May 2019. The search consisted of consulting databases and specialist sites in order to identify the randomised controlled trials or systematic literature reviews including this type of study. Searches were also performed to identify the technical consensuses describing and/or assessing the practice and learning requirements for this technique. In addition, recommendations addressing patient post-surgical follow-up were searched.

The following literature sources were queried:

- automated bibliographic databases;
- websites of learned societies with expertise in the field studied.

The search strategies and the list of queried sources are described in detail in Annexe 1.

3.2.2 Assessment questions and document selection criteria

The assessment is based on four assessment questions.

They seek to assess the success of the technique, to identify OAGB-related complications, its practice requirements and post-operative follow-up conditions. The document selection criteria applied are described in detail below and summarised in the PICOTS diagrams in chapter 3.2.4.

- Question 1: OAGB efficacy assessment.
- Question 2: OAGB safety assessment.
- Question 3: identification of optimal conditions in which to carry out OAGB.
- Question 4: identification of the specific features of OAGB post-op follow-up.

► Population

The target population is that eligible for bariatric surgery, according to the 2009 HAS recommendations for the surgical treatment of obesity, for which RYGB is envisaged (2).

It includes adult patients with BMI ≥ 40 kg/m^2, or whose BMI is ≥ 35 kg/m^2, associated with at least one comorbidity likely to be improved after surgery (arterial hypertension, sleep apnoea, type 2 diabetes etc.) in second-intention after failure of initial treatment (medical, nutritional, dietetic etc.) (2).

It must be noted that there is a sub-population of patients eligible for bariatric surgery which could benefit from OAGB in particular. These are patients presenting with massive abdominal obesity or very high BMI (> 50 kg/m^2)[7], potentially making RYGB complicated to perform (due to a thick and short meso) (19, 26, 27). A sub-group analysis, for persons with BMI > 50 kg/m^2 is planned on the data to be analysed for the assessment.

► Comparator

The Roux-en-Y gastric bypass (RYGP) is the standard of care. It is widely used and considered to be effective in the long-term, especially on comorbidities and mortality related to massive or severe obesity (2, 10, 11, 37, 38). The OAGB described in 2001 by Rutledge was created especially to compensate for the technical complexity of the RYGB (17, 18).

► Endpoints

It was decided to assess the efficacy and safety on the technique, which is carried out in order to reduce morbidity-mortality related to massive obesity, using endpoints to assess the said efficacy and safety of OAGB. Impact on quality-of-life is also assessed. The various endpoints are described in detail below.

Technique efficacy

- **Weight loss**, in particular objectified by calculation of *Excess Weight Loss* (EWL%)) percentages or *Excess BMI Loss* (EBL%)) percentages.
- **The impact of surgery on each of the comorbidities likely to be improved** is assessed. The comorbidities are those included in the HAS recommendations (2): arterial hypertension, obstructive sleep apnoea-hypopnoea syndrome and other severe respiratory disorders, severe metabolic disorders, in particular type 2 diabetes, debilitating osteoarticular diseases, non-alcoholic hepatic steatosis.

[7] The terms “super-obese” for a BMI of > 50 kg/m^2 (36) and “super-super obese” for a BMI of > 60 kg/m^2 are found in the literature (27). However, there does not seem to be a generally accepted description of the characteristics and BMI threshold to define patients with very high BMI.

- **The impact on quality-of-life**, where it is objectified by a validated questionnaire. The search criteria are those on which there is a consensus and appearing in the conclusions of the BARIACT (*BARIAtric and metabolic surgery Clinical Trials*) project, namely self-esteem, the patient's ability to move or carry loads, to work etc. (39).

Technique safety

- **Rate of early and late complications** per- and post-operatively described in detail in chapter 2.6.
- **Rate of revision surgery after revision of the procedure (by RYGB** or restoration of normal anatomy).

The rate of complications “presumed” to be more common or more severe after OAGB in particular is also assessed (*see* chapter 2.7.4):

- nutritional complications (malnutrition, vitamin deficiencies) ;
- bile reflux ;
- chronification of anastomotic ulcers.

Identification of potential complications specific to OAGB is an essential prerequisite to defining the specific characteristics of short and long-term post-operative follow-up. In effect, they are aspects that are necessary for organising OAGB patients to prevent onset of the expected complications mentioned in chapter 2.7.4. The specific features of follow-up will be described through assessment question 4.

Practice requirements

The practice requirements are assessed in terms of:

- length of surgery and hospital stay ;
- surgeon training (learning curve) ;
- average length of stay.

The epidemiological and clinical profiles of patients from selected studies and biliopancreatic limb length, gastric tube and gastrojejunal anastomosis diameters are reported in the literature analysis.

► Observation periods

The various endpoints are assessed up to at least two years and longer after the surgery, for an unlimited period. In effect, weight loss stabilises 24 months after surgery, before gradually continuing again (10, 11). Quality-of-life is improved the first year, then seems stable between two and six years (40).

► Study design

As these are studies covering a new bariatric surgery technique, patient selection could be influenced by their condition. Randomisation in this type of study assessing a new technique, is essential for guarding against the influence of selection bias. Therefore, as part of this assessment report, only the randomised controlled studies[8] are selected to assess the efficacy and safety of the technique.

Concerning the practice requirements, the search is extended to professional technical consensuses.

Concerning follow-up, the study design is the same as for technique efficacy and the search is extended to good practice recommendations.

[8] Along with the systematic reviews with or without randomised controlled trial meta-analysis.

3.2.3 Registers provided to the HAS

Concerning identification of OAGB-related complications, it is based on the literature selected to assess the efficacy of the technique (question 1). The search on OAGB-related complications is extended to French registers/databases in the HAS's possession, which compile both complications related to RYGB and OAGB: SOFFCO.MM bariatric surgery follow-up register and databases on adverse events reported to the HAS.

The SOFFCO.MM bariatric surgery follow-up register is set to ultimately contain all cases of bariatric surgery performed in France from 1st January 2018, by surgeons members of the learned society. The different types of bariatric surgery, and the main post-surgical complications are entered in the register.

Two databases compiling adverse events reported to the HAS were searched. The database of treatment-related serious adverse events (TRSAEs) reported by the regional health agencies (agences régionales de santé - ARS)[9]; and the database on feedback compiling treatment-related adverse events (TRAEs) as part of the doctor and medical team accreditation programme[10].

3.2.4 PICOTS diagrams and document selection criteria

► Question 1: OAGB efficacy assessment

Patients	Patients eligible for bariatric surgery: massive or severe obesity associated with comorbidities (as described in the 2009 HAS recommendations (2))
Surgery	One anastomosis gastric bypass
Comparator	Roux-en-Y gastric bypass
Outcome measures	Endpoints: • weight loss; • reduction in comorbidities likely to be improved; • impact on quality-of-life.
Observation period	The various endpoints are assessed up to at least two years and longer after the surgery
Publications (study design)	Documents published since January 2001: randomised controlled trials with collection and analysis of blinded endpoints and systematic reviews with or without randomised controlled trial meta-analysis

[9] Haute Autorité de santé. Feedback on treatment-related serious adverse events (TRSAEs). 2017 activity report. Saint-Denis La Plaine: HAS; 2018. https://www.has-sante.fr/portail/jcms/c_2882289/fr/retour-d-experience-sur-les-evenements-indesirables-graves-associes-a-des-soins-eigs

[10] Haute Autorité de santé. Mieux connaître l'accréditation. Saint-Denis La Plaine: HAS; 2018. https://www.has-sante.fr/portail/jcms/c_428381/fr/mieux-connaitre-l-accreditation

► Question 2: OAGB safety assessment

Patients	Patients eligible for bariatric surgery: massive or severe obesity associated with comorbidities (as described in the 2009 HAS recommendations (2))
Surgery	One anastomosis gastric bypass
Comparator	Roux-en-Y gastric bypass
Outcome measures	• Rate of early and late complications per- and post-operatively. • Rate of revision surgery (by RYGB or restoration of normal anatomy). • Identification of OAGB-related complications, among those known for RYGB, and identification of any OAGB-specific complications.
Observation period	Unlimited
Publications	Documents selected for question 1 and the SOFFCO.MM register, and the two HAS adverse events databases

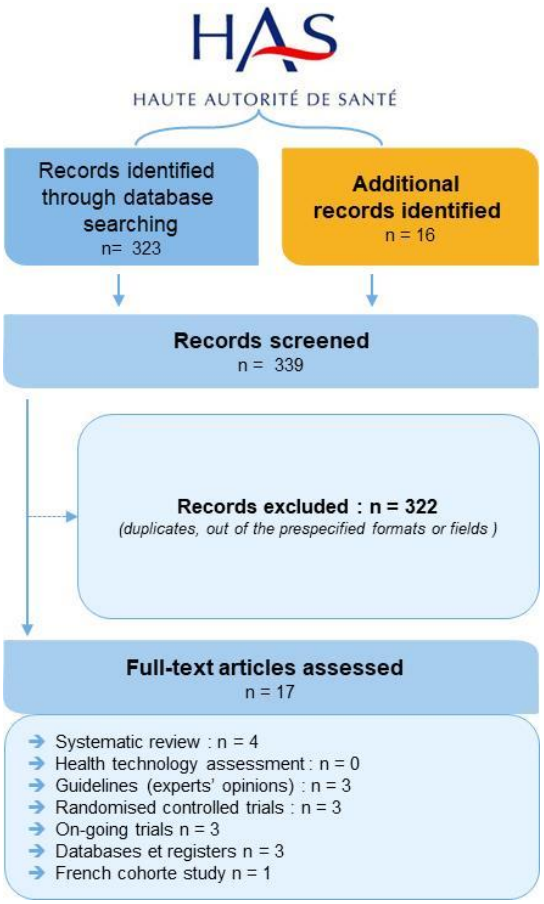
► Question 3: identification of optimal conditions in which to carry out OAGB

Patients	Patients eligible for bariatric surgery: massive or severe obesity associated with comorbidities (as described in the 2009 HAS recommendations (2))
Surgery	One anastomosis gastric bypass
Comparator	Roux-en-Y gastric bypass
Outcome measures	Endpoints: • length of surgery; • average length of stay; • surgeon's qualification (learning curve). The epidemiological and clinical profiles of patients from selected studies and bili-opancreatic limb length, gastric tube and gastrojejunal anastomosis diameters will be recorded in the literature analysis.
Publications (study design)	Documents selected for question 1 and technical consensus

► Question 4: identification of the specific features of OAGB post-op follow-up

Patients	Patients eligible for bariatric surgery: massive or severe obesity associated with comorbidities (as described in the 2009 HAS recommendations (2))
Surgery	One anastomosis gastric bypass
Comparator	Roux-en-Y gastric bypass
Outcome measures	Specific features of post-operative follow-up: • type of monitoring procedures to be implemented (vitamin level testing, endoscop-ic monitoring etc.); • frequency of follow-up procedures; • follow-up period.
Observation period	Unlimited time (life-long follow-up in bariatric surgery)
Publications	Documents selected for questions1 and 3 and good practice recommendations published since 2008

3.2.5 Literature search results



3.2.6 Ongoing clinical trials

Three ongoing clinical trials were identified on the website *clinicaltrials.gov* (see Table 4).

Table 4. Ongoing clinical trials identified.

Title	Remarks	*Clinical Trial no.*
One-anastomosis Gastric Bypass/Mini-Gastric Bypass Versus Roux-en Y Gastric Bypass (MGB-*vs*-RYGB)	RCT comparing the complications of OAGB and RYGB with 24-months follow-up	NCT03045679
Laparoscopic Roux-en-Y Gastric Bypass Versus Laparoscopic Mini Gastric Bypass (MGB)	RCT comparing excess weight loss after one year as primary endpoint and after three years with compilations into secondary endpoints	NCT02601092
Laparoscopic Roux-en-Y Gastric Bypass Versus Laparoscopic Single Anastomosis Gastric Bypass (MGB-*vs*-LGBP)	Medical and economic trials on the cost of hospitalisation comparing OAGB and RYGB	NCT02779322

3.3 Working group

3.3.1 Members

The specialities called upon via their learned society, their national professional board or their patients' group in order to participate in this assessment, are listed in the Table 5.

Table 5. Specialities asked to participate in the working group.

Specialities / Status	Bodies and associations contacted
Visceral surgery	French and French-speaking Society for Obesity and Metabolic Diseases (SOFFCO.MM)
Dietetics	French Association of Dieticians and Nutritionists (Association française des diététiciens nutritionnistes - AFDN)
Gastroenterology	French National Council for Hepatogastroenterology Professionals (Conseil national professionnel d'hépato-gastroentérologie - CNP HGE)
General medicine	French College of General Medicine (Collège de la médecine générale - CMG)
Physical medicine and rehabilitation	French National Council for Physical Medicine and Rehabilitation Professionals (Conseil national professionnel de médecine physique et de réadaptation - CNP MPR)
Nutrition	French Association for Obesity Studies and Research (Association française d'étude et de recherche sur l'obésité - AFERO)
Psychology, psychiatry	French Federation of Psychologists and Psychology (Fédération française des psychologues et de psychologie - FFPP), French National Council for Psychiatry Professionals (Conseil national professionnel de psychiatrie - CNPP)
Patient's association representative	French Obese Patients Associations Group (Collectif national des associations d'obèses - CNAO)

At the same time as these requests, a call for applications was published on the HAS website and was released in centres specialising in obesity.

Public declarations of interest were analysed for all the applications, according to the HAS code of conduct charter.

3.3.2 Members

In the aim of having as many disciplines represented as possible, taking account of the expertise of each and of a wide range of sectors of practice, the following persons were selected:

- Doctor Judith Aron-Wisnewsky, endocrinology - nutrition, Pitié Salpêtrière hospital - Paris
- Professor Jean-Luc Bouillot, visceral and digestive surgery, Ambroise Paré hospital - Boulogne-Billancourt
- Mrs Claudine Canale, users' representative, French Obese Patients Associations Group - Puteaux
- Professor Philippe Cornet, general medicine, Pierre et Marie Curie University - Paris
- Doctor Marlène Galantier, nutrition, private practice - Paris
- Doctor Laurent Genser, visceral and digestive surgery, Avicenne hospital - Bobigny

- Mrs Anne-Sophie Joly, users' representative, French Obese Patients Associations Group - Puteaux
- Doctor Léa Lucas-Martini, nutrition - general medicine, Cognacq-Jay hospital - Paris
- Doctor Francesco Martini, visceral and digestive surgery, Clinique des Cèdres - Blagnac
- Doctor Yann Matussiere, nutrition - general medicine, Clinique de la Sauvegarde - Lyon
- Mrs Justine Poissonnier, psychology, Saint-Omer regional hospital - Helfaut
- Professor Didier Quilliot, gastroenterology - nutrition, Nancy teaching hospital - Vandœuvre-lès-Nancy
- Professor Fabian Reche, visceral and digestive surgery, Grenoble Alpes teaching hospital - Grenoble
- Mrs Marion Sillières, dietetics, Clinique des Cèdres - Blagnac
- Doctor Adriana Torcivia, visceral and digestive surgery, Pitié Salpêtrière hospital - Paris

3.3.3 Declaration of Interest

None of the members of the working group declared any major interests in relation to the subject of this assessment.

Public declarations of interest (PDI) by the working group members can be consulted on the web-site www.dpi.sante.gouv.fr.

3.3.4 Working group justified position

The working group met on 11 June 2019. A list of questions was sent to each expert 15 days before the meeting, with the framework document and a draft version of this assessment report. The questions addressed to the experts are recorded in the work meeting report in Annexe 8.

The report from this meeting was approved by all the working group members and can be found in full in Annexe 8.

A report summary was then written by the HAS and features below in chapter 4.5.

4. Assessment results

4.1 Question 1: OAGB *vs.* RYGB efficacy assessment

4.1.1 Systematic reviews

Four systematic reviews comparing OAGB and RYGB were identified and selected: Wang *et al.,* Magouliotis *et al.,* Georgiadou *et al.,* and Mahawar *et al.* (41-44).

A summary table of these systematic reviews can be found in Annexe 3.

They included all cohort studies or observational studies and a single randomised controlled trial, that of Lee *et al.* (25), presented and analysed hereinafter in chapter 4.1.2.

These systematic reviews, based on the literature with low level of evidence (non-randomised studies), were not selected. The analysis of the literature focused on the randomised controlled trials available.

4.1.2 Randomised controlled trials

Three trials were identified and selected: one from 2005, Lee *et al.* (25), and two from 2019, by Ruiz-Tovar *et al*. (45) and Robert *et al*. (46). A summary table of the data from these trials, along with other critical analysis elements feature in Annexe 6.

An analysis of the bias risk was performed for each of the trials. The questions enabling this analysis are detailed and taken from an adaptation of the *Cochrane* collaboration guide (47) in Annexe 4. The summary for the bias risk analysis features in Annexe 5. **The analysis showed that all carry a high risk of bias or have a limited level of evidence**.

► Lee *et al.* (25)

This trial is monocentric and has small numbers (n=80 in total). **Also, its level of evidence is highly limited for this assessment as the necessary number of subjects was calculated to demonstrate a difference in length of surgery between the two techniques** and not to compare their efficacy or their safety. The data from this trial on the efficacy and safety of OAGB are therefore exploratory (*see* Table 6).

An excess weight loss of around 60% is reported (given as excess weight loss %) along with resolution of 45 cases of metabolic syndrome.

Table 6. Main efficacy results from Lee *et al.* (25).

Endpoints: EFFICACY	Results
Weight loss after two years	Non-significant difference. Excess weight loss of around 60% in the two groups (given as excess weight loss %).
Reduction in comorbidities	Non-significant difference on the number of subjects presenting with a reduction in “metabolic syndrome”. There were no data provided per individual comorbidity (type 2 diabetes, hypertension, dyslipidaemia etc.). All metabolic syndromes were resolved after two years.
Impact on quality-of-life	Non-significant difference.

The trial by Lee *et al.* (25) cannot be used to assess the efficacy and safety of OAGB compared to RYGB due to the protocol. It does not provide any elements for or against OAGB on the endpoints measured: weight loss after two years, resolution of comorbidities and impact on the quality-of-life.

► Ruiz-Tovar *et al*. (45)

This is a monocentric trial with 400 patients (OAGB and RYGB groups). The study endpoint was to compare patients undergoing sleeve, RYGB or OAGB surgery. This trial does not provide any elements on calculation of the excess BMI loss percentage (EBL %), or on the target BMI value used to confirm the weight loss. The authors made multiple comparisons and do not provide any information on alpha risk inflation. Management of missing data is not discussed either. **This study therefore carries a high risk of bias. In light of the protocol and for this assessment, the level of evidence of this trial is limited**. The efficacy results are provided in the Table 7.

In the two groups, after two years, weight loss (given as EBL %) greater than 80%, resolution of type 2 diabetes of more than 90% and hypertension of more than 84% were recorded.

Table 7. Main efficacy results from Ruiz-Tovar *et al*. (45).

Endpoints: EFFICACY	Results
Weight loss after two years	Weight loss significantly superior for OAGB (104.3±7) *vs.* RYGB (87.2±6.7) given as EBL %.
Reduction in comorbidities	Non-significant difference on the “remission rate” for type 2 diabetes and arterial hypertension. With around 90% resolution of type 2 diabetes, 85% resolution of hypertension.
Impact on quality-of-life	Was not assessed.

The authors demonstrated weight loss after two years in favour of OAGB (+17%). However, they made multiple comparisons without managing inflation of the alpha risk inducing a high risk of bias and not making it possible to confirm the superiority of OAGB compared to RYGB on weight loss.

This trial does not demonstrate a difference in resolution of the comorbidities measured: type 2 diabetes and arterial hypertension. The impact on quality-of-life was not assessed.

This trial does not confirm, with certainty, the superiority of OAGB compared to RYGB on the efficacy endpoints.

► Robert *et al*. (46)

This trial is multicentric (nine French centres) and has a per-protocol population of 234 patients. The primary endpoint of the study was to demonstrate the non-inferiority of OAGB compared to RYGB on weight loss after two years. Weight loss after two years was seen in the excess BMI loss percentage. The protocol states two target BMIs at 22.5 and 25 kg/m^2. Only the results at BMI of 25 are provided. The limit of non-inferiority of OAGB compared to RYGB is set at 7%, therefore at around 5 kg according to the authors.

The missing data rate is 30%, limiting the level of evidence for this trial. Multiple exploratory comparisons were made. No difference in resolution of comorbidities or improvement in quality-of-life was demonstrated.

In the two groups, after two years, weight loss (given as EBL %) greater than 85%, resolution (total or partial) of type 2 diabetes of more than 50% were recorded.

Table 8. Main efficacy results from Robert *et al.* (46).

Endpoints: EFFICACY	Results and remarks
Weight loss after two years	Main result: non-inferiority is significant. It is the difference in the excess BMI loss percentage (EBL %): OAGB - RYGB with target BMI at 25 kg/m^2: -3.3% (90%CI-9.1; 2.6) below the 7% threshold provided for in the protocol. The EBL % is more than 85% in the two groups. The results at BMI of 22.5 are not provided[11].
Reduction in comorbidities	Non-significant difference on the “total or partial remission rate” for type 2 diabetes of around 50%, on dyslipidaemia and other obesity comorbidities.
Impact on quality-of-life	Non-significant difference.

On the primary endpoint, weight loss after two years, this trial could not confirm with certainty the non-inferiority of OAGB compared to RYGB, especially due to the number of missing data. No difference was identified on resolution of comorbidities and improvement in quality-of-life in exploratory terms. It must be noted that no data on “super-obese” patients (BMI > 50 kg/m^2) was identified.

4.1.3 OAGB *vs.* RYGB efficacy data summary

Effect size after two years on weight loss and resolution of obesity-related comorbidities:

- on weight loss, is heterogeneous and ranges from 60 to over 100% (three studies);
- on resolution of type 2 diabetes, from 50 to 90% (two studies);
- on resolution of metabolic syndrome 100% (one study).

The three randomised controlled trials analysed cannot confirm with certainty the superiority (25, 45) or the non-inferiority (46) of OAGB compared to RYGB on the efficacy endpoints selected: weight loss, resolution of comorbidities and improvement in quality-of-life.

No element to assess efficacy on weight, comorbidities and quality-of-life from OAGB in “super-obese” patients (BMI > 50 kg/m^2) was identified.

[11] The investigator, contacted by e-mail, did not provide the results at BMI of 22.5 despite reminders.

4.2 Question 2: OAGB safety assessment

The method selected within the scope involved analysis of: 1) documents selected in question 1 (randomised controlled trials and systematic reviews with or without randomised controlled trial meta-analysis); 2) French registers/databases in the HAS's possession, which compile both complications related to RYGB and OAGB: SOFFCO.MM bariatric surgery follow-up register and databases on adverse events reported to the HAS. The study analysis is provided in detail in Annexe 5 and Annexe 6. The databases are provided in chapter 3.2.3. The summary of the document and register analysis is provided below.

4.2.1 Randomised controlled trials

The three trials selected are those from question 1 (25, 45, 46).

► Lee *et al.* (25)

The trial numbers are small, making it difficult to demonstrate a difference in the rate of complications between the two groups. Eight and three early complications and four and three late complications were reported in the RYGB and OAGB groups respectively.

The authors report that the three late complications from the OAGB group are not specific to OAGB. It must be noted however that the **anaemia** observed in the OAGB arm is, according to the authors, possibly "related to nutritional deficiencies which are to be assessed in the long-term".

The authors did not report any cases of OAGB conversion to RYGB or restoration of normal anatomy.

► Ruiz-Tovar *et al*. (45)

The authors report ten (RYGB) and seven (OAGB) complications without grading their severity. Must be noted however, among these complications for the OAGB group, two cases of **"uncontrollable bile reflux"** and three cases of **hypoproteinaemia**.

The authors report **two OAGB to RYGB conversion procedures** to manage the two cases of bile reflux.

► Robert *et al*. (46)

The authors report almost twice as many serious adverse events (SAEs) in the OAGB group as in the RYGB group (n=42 compared to n=24).

Among the SAEs, nine **nutritional complications** were reported in the OAGB group compared to none in the RYGB group, six of which in patients presenting with excess BMI loss greater than 100%. Among the nine nutritional complications, one patient presented with **Wernicke encephalopathy**[12].

The authors report **four OAGB to RYGB conversions** due to anastomotic leak, Wernicke encephalopathy, and two cases of severe bile reflux.

It must be noted that among the SAEs reported, there are five cases of abdominal pain for the RYGB and none in the OAGB.

Exploratory upper gastrointestinal endoscopy was performed in 121 patients (n=58 OAGB and n=61 RYGB) two years after surgery (therefore a little more than 50% of the per-protocol population). The authors report 11 cases of gastritis and nine cases of bile reflux in the OAGB arm compared to none in the RYGB arm. Among the patients presenting with bile reflux, one presented with metaplastic cells on the stomach and oesophagus biopsies.

[12] Severe neurological disorder related to thiamine (vitamin B1) deficiency.

It must be noted that almost three times more cases of diarrhoea were reported in particular after three months and 24 months in the OAGB group compared to the RYGB group.

The data from the three randomised controlled trials cannot be used to classify with certainty one technique over the other in terms of safety.

However, preoccupying safety signals emerge concerning OAGB, with in particular the results of the multicentric trial by Robert *et al*. (46) which reports **a frequency, of serious adverse events in the OAGB group, almost twice as high as in the RYGB group**.

Among the safety signals reported in the OAGB groups (not identified in the RYGB groups):

- **serious nutritional complications** with one case of **Wernicke encephalopathy**;
- cases of more or less severe **bile reflux** requiring, for some, conversion to RYGB, with one case of reflux possibly related to the appearance of metaplastic cells, two years after surgery.

4.2.2 Databases and registers available

► SOFFCO.MM register

The SOFFCO.MM bariatric surgery follow-up register is set to ultimately contain all cases of bariatric surgery performed in France from 1st January 2018, by surgeons members of this learned society. The different types of bariatric surgery, and the main post-surgical complications are entered in the register.

For 2018, 7,856 surgical procedures were entered, including 1,718 RYGB and 446 OAGB, therefore almost 22% and 6% of procedures respectively. OAGBs represent therefore around 20% of the total of the two types of gastric bypass. The register, having been designed with a predetermined list of 12 complications (including revision) likely to occur, regardless of the type of bypass, cannot be used to report on vigilance signals for complications specific to OAGB.

The complications entered are entered one month after surgery. For OAGB, among the complications reported were 18 cases of vitamin deficiency, four cases of anaemia and no cases of malnutrition. 11 cases of revision surgery are reported without any details.

The severity of these complications is measured using the Clavien-Dindo classification (48) in Annexe 7. General severity is mentioned without any details per type of complication. Among the complications entered, two were graded IIIb (meaning treatment involved surgical revision under general anaesthesia) and one was graded V (death).

► HAS database

Two databases compiling **adverse events reported to the HAS** were searched. The database of treatment-related serious adverse events (TRSAEs) reported by healthcare professionals to regional health agencies (agences régionales de santé - ARS)[13]; and the database on feedback compiling treatment-related adverse events (TRAEs) as part of the doctor and medical team accreditation programme[14].

[13] Haute Autorité de santé. Feedback on treatment-related serious adverse events (TRSAEs). 2017 activity report. Saint-Denis La Plaine: HAS; 2018. https://www.has-sante.fr/portail/jcms/c_2882289/fr/retour-d-experience-sur-les-evenements-indesirables-graves-associes-a-des-soins-eigs

[14] Haute Autorité de santé. Mieux connaître l'accréditation. Saint-Denis La Plaine: HAS; 2018. https://www.has-sante.fr/portail/jcms/c_428381/fr/mieux-connaitre-l-accreditation

Database of treatment-related serious adverse events (TRSAEs)

This data base is not exhaustive in the facts and cannot be used to estimate the frequency of TRSAEs.

No event related to omega loop gastric bypass (OAGB) was found in this database on the date of 14 February 2019. It must be noted that only four TRSAEs associated with bariatric surgery feature in this database which compiles the TRSAEs since March 2017.

Feedback database

The cases reported in this non-exhaustive database are reported on a voluntary basis. It cannot be used to estimate the frequency of TRSAEs either.

The following must be noted in relation to OAGB:

- **six cases of conversion to RYGB** (related to more or less severe bile reflux);
- **one case of obstruction**;
- **one case of malnutrition**;
- **two cases of chronic diarrhoea.**

One death is also reported, the imputability of which to the OAGB technique cannot be confirmed. The case involved biliary peritonitis by gastric perforation further to “collapse of the biliary limb” which became worse, leading to the patient's death.

► Other French cohort available

A French monocentric cohort of 1,000 consecutive patients having undergone OAGB between 2006 and 2013 with excluded limb length at 200 cm (21) was identified. Mean follow-up was 31 months (12 to 82 months; standard deviation 26 months).

The follow-up data are available for 666, 264, and 126 patients at one, three and five years follow-up respectively, therefore 17%, 41% and 28% of missing data for each of the follow-up periods.

The authors report two deaths of patients over the age of 60, 35 and 45 days after surgery, related to myocardial infarction (male, no details on BMI (pre-surgery) and pulmonary embolism (woman, BMI 62 kg/m^2).

They report 55 complications in total, of which 35 early and 20 late. The severity of these complications is determined by using the Clavien-Dindo classification (see Annexe 7) (48).

Among the 25 complications requiring medical treatment (severity I to IIIa as per Clavien-Dindo classification, management of the non-surgical complication), 17 cases of anastomotic ulcer were reported.

Thirty out of the 55 complications were awarded grade IIIb, meaning the treatment involved surgical revision under general anaesthesia. **Seven of the 30 grade IIIb complications were cases of bile reflux,** reported 23 months after surgery on average, having required **conversion to RYGB**[15].

It must be noted that after **five years, two cases of malnutrition occurred in patients** with an excess BMI loss percentage of over 100%, having required **parenteral nutrition**. The severity of the complication is not described in detail; however, **“revision” OAGB surgery was planned** according to the authors, without any details on the type of revision (restoration of standard anatomy or conversion to RYGB).

[15] The authors do not report any grade IV complications.

The data from the register, the databases and the cohort cannot be used to classify with certainty one technique over another in terms of safety.
The safety signals reported on OAGB mainly include cases of:

- **bile reflux** which is resolved by conversion to RYGB;
- **nutritional complications** some of which required **parenteral nutrition** and revision surgery.

4.2.3 OAGB *vs.* RYGB safety data summary

The data from the three randomised controlled trials, the registers and databases and the cohort cannot be used to classify with certainty one technique over the other in terms of safety.

It must however be noted that preoccupying safety signals are reported for OAGB.

The French multicentric trial by Robert *et al*. (46), on 234 patients, reports **a frequency of serious adverse events in the OAGB group almost two times higher than in the RYGB group** (n=42 compared to n=24).

Some of these serious safety signals for OAGB (and not RYGB) are congruent between the different data sources:

- cases of **nutritional complications**, some of which required heavy treatment with parenteral nutrition, in which surgical revision was planned and one severe case of **Wernicke encephalopathy**;
- cases of more or less severe **bile reflux** requiring, for some, conversion to RYGB, with one case of reflux possibly related to the appearance of metaplastic cells, two years after surgery.

4.3 Question 3: Identification of optimal conditions in which to carry out OAGB

The method selected during determination of the framework involves analysis of the documents selected in question 1 (25, 45, 46) and technical consensuses identified.

The literature search identified two documents resembling a technical consensus. They were two expert opinions addressing the practice requirements:

- one expert opinion resulting from a vote by 101 experts (Delphi approach), Mahawar *et al*., 2018 (49);
- one expert opinion based on a systematic literature review by the International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO) in 2018 (16).

The elements entered on OAGB practice requirements in the five documents are provided in Table 9.

The authors of the IFSO opinion (16) state that the “ideal OAGB surgical technique is not yet determined to date”.

Table 9. Summary of elements available on OAGB practice requirements.

Authors, year and type of documents	Biliopancreatic limb length	Length of surgery	Average length of stay	Surgeon's qualification (learning curve)
Lee *et al*., 2005 (25) RCT	200 cm	148±47 min OAGB 205±61 min RYGB Significant difference	5.5±1 day OAGB 6.9±3 day RYBP Significant difference	Estimates the learning curve at 30 cases for OAGB
Ruiz-Tovar *et al*., 2019 (45) RCT	200 to 350 cm	np	np	np
Robert *et al*., 2019 (46) RCT	200 cm	85±35 min OAGB 111±42 min RYGB Significant difference	5±1 day in both groups	The nine centres perform more than 150 procedures per year without further details
Mahawar *et al*., 2018 (49) Expert opinion	Up to 200 cm is acceptable for 80% of experts. Disagreement from 82% of experts on standard 150 cm length.	np	np	np
IFSO, 2018 (16) Expert opinion	In 46 studies: 27: 200 cm 9: < 200 cm 5: > 200 cm 5: np	18 studies from 45 to 210 min	From less than one day to six days	np

RCT = randomised controlled trial, np = not provided, ns = non-significant difference.

The analysis showed that:

- "**the ideal OAGB surgical technique is not yet determined to date**" for the IFSO;
- **the most commonly used limb length is 200 cm**, and IFSO experts disagree on a 150 cm "standard" length;
- **surgery seems to be shorter** for OAGB (significant in two studies, -50 min and -26 min on average);
- no elements can confirm that the length of stay is shorter for OAGB;
- surgeons' qualifications are not always reported.

4.4 Question 4: Identification of the specific features of OAGB post-op follow-up

The documents selected are those from question 1 (25, 45, 46) and those from question 3 (16, 49), and the good practice recommendations identified from the *British Obesity and Metabolic Surgery Society*, 2014 (50).

In the trials by Lee *et al.* (25), and by Ruiz-Tovar *et al*. (45) no information about follow-up of patients having undergone OAGB is provided, and the other documents provide little information on such follow-up.

The elements collected on follow-up are compiled in Table 10.

Monitoring of the consequences of bile reflux is mentioned in two documents:

- it involves endoscopy two years after surgery in the trial by Robert *et al*. (46);
- The 2014 recommendations by the *British Obesity and Metabolic Surgery Society* suggest "surveillance of the oesophagus and gastric pouch" (50) without any other details.

In 2018, bile reflux was qualified by the IFSO as a "theoretical risk" and did "not seem to be a major problem"(16).

Prophylaxis for anastomotic ulcers by proton pump inhibitors (PPIs) is suggested in one of the documents (49).

Only the expert opinion document by Mahawar *et al.* (49) addresses micronutrient supplementation and provides a list. However, the proposals for micronutrient supplementation are not precise in terms of dosage. None of the documents address assessment of nutritional deficiencies. It must be noted that the recommendations and the expert opinions were published before the results of the French study by Robert *et al.* (46) which points to nutritional deficiencies in particular.

Table 10. Summary of elements available on follow-up of OAGB patients.

Documents	Document type	Monitoring procedures
Robert *et al*., 2019 (46)	RCT	Monitoring of the consequences of bile reflux by upper GI endoscopy after two years.
Mahawar *et al*., 2018 (49)	Expert opinion	Prophylactic treatment of anastomotic ulcers by PPI for at least six months. Lifelong daily vitamin supplementation with Zn and Cu. Routine Fe, vitamin D, Ca, and vitamin B12 supplementation. Lifelong annual follow-up without other details.
IFSO, 2018 (16)	Expert opinion	Concerning bile reflux, it is "under declared" but does not seem to be "major problem" and remains a "theoretical risk". The "patients are encouraged to remain in multidisciplinary long-term follow-up" (without any other details on visit frequency, duration and type of monitoring). It is recommended that surgeons participate in national and international registers, with no other details.
British Obesity and Metabolic Surgery Society, 2014 (50)	Expert opinion	"Monitoring of the oesophagus and of the gastric pouch must be envisaged" (without any other details on visit frequency, duration and type of monitoring).

The documents identified provide little information on the possible specific features of post-operative follow-up from OAGB compared to RYGB. It is not possible to define OAGB post-operative follow-up precisely.

The result is that, among the complications identified in question 2, only the consequences of bile reflux could benefit from special monitoring.

Special monitoring is performed by endoscopy (without any further details on the duration and frequency of the follow-up).

Concerning the nutritional complications, no follow-up elements or elements to prevent occurrence were identified.

4.5 Working group summary

4.5.1 Efficacy

On the efficacy of OAGB with a 200 cm biliopancreatic (BP) limb, the working group (WG) confirms that the only comparative data (with RYGB) published are those from three studies analysed in the report. **These data cannot be used to determine whether efficacy on weight loss after two years with OAGB is superior, inferior or non-inferior to that of RYGB.**

Also, OAGB does not seem to be an alternative in the event of surgical difficulties during RYGB (patients with massive abdominal obesity presenting with a short and thick meso) and is not more indicated for the population of super-obese patients with a BMI of > 50kg/m^2.

The members of the WG state that assessment of the efficacy of OAGB (and of other bariatric surgery techniques) should not only be limited to determination of short-term weight loss, but should take resolution of comorbidities, long-term maintenance of weight loss and quality-of-life by validated questionnaires (e.g.: GIQLI) into account, and diarrhoea and steatorrhoea in particular.

4.5.2 Safety

The working group revealed emerging safety signals for OAGB with 200 cm or longer limbs, from publications (RCTs and cohorts) and from the clinical practice of certain experts. According to the experts, few data published are available on the complications of OAGB and their frequency.

According to the working group, these complications are:

- serious nutritional complications which are believed to be more common for OAGB than for RYGB, especially severe malnutrition associated with vitamin deficiencies, especially fat-soluble vitamins A and E, and debilitating diarrhoea for patient quality-of-life. Management of malnutrition is heavy, requires hospitalisation and parenteral nutrition and, if it fails, surgical revision with conversion to RYGB or reversion (reversal to normal anatomy);
- bile reflux (specific to OAGB due to the “surgical assembly”) and/or acid reflux, with one case of metaplasia reported in the PHRC and a risk of lower oesophageal cancer in the long-term (over several decades);
- internal hernias which are not exclusive to RYGB but which remain however less common with OAGB;
- marginal ulcers which are believed to be more common and more difficult to treat due to the bile reflux with OAGB than with RYGB.

4.5.3 Practice requirements

The working group states that the practice requirements for OAGB are heterogeneous in France, in particular concerning BP limb length and patient information.

In terms of limb length, the experts say that BP limbs should no longer be used if they are 200 cm or longer due to the risk of nutritional complications.

Concerning OAGB with a 150 cm BP limb length, it is believed to be widely practised in order to minimise nutritional complications according to the WG. Some experts consider it to be the case and that efficacy is preserved. These are data from their experience, the WG specifying that there are no comparative data between OAGB with a 150 cm limb and a RYGB, from published, randomised controlled trials (RCTs). They are in favour of RCTs to assess the efficacy and safety of OAGB with 150 cm BP limb compared to RYGB. They recommend, in this future study, exhaustive five-year follow-up with endoscopy in light of the risk of lower oesophageal cancer.

Concerning information, the WG considers it must be impartial and complete, which implies presenting the various techniques, including OAGB and not only the sleeve and OAGB techniques. Information also involves communication about uncertainties in terms of efficacy and safety which

persist with OAGB: long-term (ten-year) efficacy, the risks of nutritional complications and its consequences on pregnancy and the risk of reflux-related lower oesophageal cancer.

The working group asks that the HAS report expressly mentions that the term “mini-*bypass”* is inappropriate to describe OAGB and to prefer the terms “omega loop bypass” or “one-anastomosis bypass”.

The working group considers that accreditation should apply to the bariatric surgery centre (and not to a surgeon) and to any bariatric activity (not only techniques). The working group considers that all bariatric surgery centres should offer RYGB (and not only the sleeve or OAGB).

Concerning the length of surgery, the working group says that it is shorter for OAGB than for RYGB (30 minutes on average) without any benefit for patients being confirmed.

Concerning the average length of stay, the working group says there are no elements in favour of reducing it, as it would probably be the same as for the RYGB.

4.5.4 Patient follow-up

The working group experts recommend very close lifelong follow-up for these patients in order to detect nutritional complications. However, in the more general context of bariatric surgery in France, a large portion of patients operated on is believed to not have appropriate post-op follow-up or even any follow-up at all.

They recommend lower oesophageal monitoring by endoscopy five years after OAGB, which should be carried out due to the risk of bile and acid reflux-related cancer.

They suggest communication for the patient, their regular doctor and primary care physicians which should include a clear programme specifying the follow-up examinations to be carried out, their frequency and the warning signs and methods of referral to a specialist.

4.5.5 Working group's additional comments

In light of the lack of data and uncertainty, some experts recommend not using OAGB:

- in young subjects (under the age of 50) due to the risk of lower oesophageal cancer;
- in patients with oesophagitis in whom RYGB would be more appropriate.

Most of the experts said it is necessary to inform women of childbearing age in particular of the lack of data on OAGB and on the potential risks in the case of pregnancy.

It appears, according to the experts, that reliable data is currently missing and that conclusive elements on OAGB to enable patients to make an informed choice cannot be provided.

One of the experts deplores the restricted arsenal of solutions for treating obesity, and that OAGB could represent one of the solutions, but the uncertainties as to this technique are to be removed by studies.

The WG states that some surgeons and bariatric surgery centres have specialised in OAGB and do not offer RYGB.

Finally, several experts relate their fears about the sleeve technique, with the risk of cancer from gastroesophageal reflux, in particular due to the lack of endoscopic surveillance, which should be carried out even in asymptomatic patients.

Conclusion and prospects

The one anastomosis gastric bypass (OAGB) was developed to make up for certain defects of the Roux-en-Y gastric bypass (RYGB), in particular the complexity and length of the procedure, internal hernias and anastomotic fistula. OAGB has been used in France for less than ten years, with no prior assessment. This technique is debated among bariatric surgeons and results suggest there are safety issues.

Faced with this situation, the HAS assessed this technique by firstly making a critical analysis of the literature identified by a systematic literature search, and selected on the basis of explicit criteria, and secondly by hearing the position of a group of experts from different professions, brought together in a working group (WG) which also included patients.

OAGB, as described initially in 2001 by Rutledge, involves one gastrojejunal anastomosis compared to two anastomoses in the RYGB (gastrojejunal and jejunojejunal) and a biliopancreatic (BP) limb - excluded limb - measuring 200 cm.

The term mini-bypass has often been used to describe this technique, which is however not appropriate as it leads us to believe it is less invasive than the RYGB, whereas the surgical procedure is similar (laparoscopy, trocar positions etc.). This term is no longer used in scientific journals and is rejected by the international obesity surgery learned society.

► 200 cm OAGB efficacy

Concerning short-term weight loss (24 months) after OAGB with a 200 cm limb, the three comparative studies conducted *versus* RYGB cannot be used to come to a definite conclusion as to its superiority, its inferiority, its non-inferiority or its “equivalence”. However, the results for groups treated with OAGB in these studies, and the opinion of the WG members, point to the fact that OAGB allows for substantial short-term weight loss.

However, the short-term weight loss criterion today no longer seems sufficient to assess the efficacy of a bariatric surgery technique. Other elements must in effect be included, such as long-term weight loss (five to ten years), resolution of comorbidities (e.g. type 2 diabetes, arterial hypertension etc.), impact on quality-of-life, especially intestinal quality-of-life. Yet, for these criteria, we do not have sufficient data, especially comparative, to come to a conclusion as to the usefulness of OAGB.

► 200 cm OAGB safety

On this point, preoccupying signals were identified during the assessment, the main signals being serious nutritional complications and bile reflux.

Serious nutritional complications is an umbrella term for severe malnutrition with protein and energy deficiencies and micronutrient deficiencies, especially fat-soluble vitamin and vitamin B1 deficiency. **These serious nutritional complications seem, according to the literature analysed and the WG experts questioned, to be more common with OAGB than with RYGB. The consequences for the patients can be serious, such as Wernicke encephalopathy (of which one case reported by the French YOMEGA study) likely to lead to permanent neurological damage.** Management of these cases of severe malnutrition is heavy and requires hospitalisation and even parenteral nutrition, and in the event of failure, can led to surgery with OAGB to RYGB conversion or reversal to normal anatomy.

Concerning bile reflux, it appears to be a complication specific to OAGB according to the studies and in the experts' opinion. It is believed to be related to acid reflux and is most often asymptomatic (according to the WG experts) making the diagnosis, prevention of the consequences on the lower oesophagus and management of the long-term cancer risk difficult.

Marginal ulcers appear to be more common and more difficult to treat due to the bile reflux with OAGB than with RYGB, according to certain WG experts.

Diarrhoea is believed to be more common with OAGB than with RYGB according to the YOMEGA study and according to the WG experts.

Internal hernias appear effectively less common with OAGB than with RYGB, but can still occur.

► OAGB-specific indications and non-indications

Authors had given as an advantage of OAGB, being able to perform OAGB in patients with massive abdominal obesity (the short and thick meso in these patients making it difficult to perform RYGB) and in super-obese patients (with BMI > 50 kg/m^2) in whom RYGB can be difficult to perform, depending on the case. No data was found in the literature however concerning the results of OAGB in these two populations and the WG was divided as to the specific usefulness of OAGB for these patients. On this basis, it cannot be confirmed that OAGB has specific indications in patients with BMI > 50 kg/m^2 or massive abdominal obesity.

Also, in light of the lack of data and uncertainty, some experts recommend not using OAGB:

- in young subjects (under the age of 50) due to the risk of lower oesophageal cancer;
- in patients with oesophagitis in whom RYGB would be more appropriate.

Finally, concerning the opinion of most of the WG experts, it is necessary to inform women of childbearing age in particular of the lack of data on OAGB and on the potential risks in the case of pregnancy.

► OAGB with 150 cm BP limb

Currently in France, according to the WG experts, different BP limb lengths are used. Some centres use 200 cm or longer limbs whereas other centres used 150 cm BP limbs, and the latter practice is tending to develop. Reducing limb length from 200 cm to 150 cm is believed to be in the aim of minimising nutritional complications from OAGB, since by shortening the BP limb, the OAGB is believed to be less “malabsorptive”.

However, there are no comparative data published for RYGB, nor on the efficacy or safety of OAGB with a 150 cm limb. We do not have published data with a sufficient level of evidence either pointing to a reduction in nutritional complications with such a limb, compared to a 200 cm limb. WG members confirmed however that it was the case, and that efficacy (short-term weight loss) was preserved.

On this basis, the efficacy and safety of OAGB with 150 cm BP limb are therefore today still uncertain.

► OAGB practice requirements

Concerning the length of surgery, it is shorter for OAGB than for RYGB (one anastomosis instead of two) without however any advantage related to shortening being identified for the patients (literature and WG position).

Concerning the average length of stay, there are no elements in favour of reducing it, and it would probably be the same for OAGB as for RYGB.

► OAGB patient follow-up

Few elements were found in literature on any specific details in the follow-up of OAGB patients. According to WG experts, very close lifelong follow-up is required for these patients, especially to detect nutritional complications. However, in the more general context of bariatric surgery, a large portion of OAGB patients is believed to not have appropriate post-op follow-up, or even any follow-up at all.

According to the WG, lower oesophageal monitoring by endoscopy five years after OAGB should be carried out due to the risk of bile and acid reflux-related cancer.

Patients and their regular doctors should receive information on a clear programme specifying the follow-up examinations to be carried out, their frequency and the warning signs and methods of referral to a specialist.

In light of all of these elements, and in particular preoccupying safety signals, the HAS considers that **one anastomosis gastric bypass (OAGB) carried out with a 200 cm (or longer) biliopancreatic limb is not a validated technique in the surgical treatment of massive and severe obesity (with comorbidity). It is therefore not an alternative to the Roux-en-Y gastric bypass (RYGB).**

Concerning OAGB performed with a 150 cm BP limb, too few data are currently available - in particular, no comparative data to OAGB and only expert opinions - to be able to conclude on its efficacy and safety. **The OAGB with a 150 cm BP limb falls under clinical research today and should benefit from multicentric randomised controlled trials for assessing its efficacy and safety**. The efficacy assessment should be based on a composite criterion including, in addition to long-term weight loss (five years), the resolution of comorbidities and quality-of-life measured by validated scores. The safety assessment should include an endoscopic examination after five years, in light of the risk of lower oesophageal cancer. The drop out rate should be reduced.

Concerning patients already having received OAGB surgery (around 5,000 patients in 2017 according to the estimations of the SOFFCO.MM), they must have, regardless of BP limb length, the same follow-up as patients having received RYGB surgery (lifelong follow-up in accordance with the 2009 HAS recommendations “Obesity: surgical management in adults”) with close monitoring for the detection of nutritional complications (protein-energy malnutrition, micronutrient deficiency) and lower oesophageal cancer with an endoscopic examination five years after surgery. Patients having received surgery, their regular doctor and their go-to professionals should be informed and trained respectively with a clear programme specifying the follow-up examinations to be carried out, their frequencies and warning signs of OAGB complications, and the criteria for referral to a specialist centre.

Annexe 1. Documentary search

Automated bibliographic databases

- Medline (National Library of Medicine, United States)
- Embase (Elsevier)
- The Cochrane Library (Wiley Interscience, United States)
- BDSP - Public health database
- Science Direct (Elsevier)
- HTA Database (International Network of Agencies for Health Technology Assessment)

Table 11. Documentary search strategy.

Study type/subject Terms used		Search period from
Recommendations on obesity (after selection by title)		
Stage 1	Obese or obesity or weight management or bariatric surgery or overweight [title] AND guideline* or recommendation* or consensus or guidance[title]	01/2009
Omega/Roux en Y bypass - Meta-analyses, systematic reviews		
Stage 2	Single anastomosis gastric bypass OR omega loop gastric bypass OR Mini-Gastric Bypass OR One Anastomosis Gastric Bypass OR OAGB OR single anastomosis duodenoileal bypass OR MGB/OAGB OR Mini/One Anastomosis Gastric Bypass Filters: Publication date from 2008/01/01; Field: Title/Abstract AND Anastomosis, Roux-en-Y"[Mesh] OR roux-en-y OR RYGB Filters: Publication date from 2008/01/01; Field: Title/Abstract	01/2001
AND		
Stage 3	"Meta-Analysis as Topic"[Mesh] OR "Meta-Analysis "[Publication Type] OR "Review Literature as Topic"[Mesh] OR “Meta Analysis” OR “systematic Review” OR “Literature review” Or "Quantitative Review" OR “pooled analysis” [title/abstract]	
Omega/Roux en Y bypass - Randomised controlled trials		
Stage 2		01/2001
AND		
Stage 4	"Random Allocation"[Mesh] OR "Randomized Controlled Trials as Topic"[Mesh] OR "Randomized Controlled Trial "[Publication Type]	
Omega bypass - Complications		
Stage 5	single anastomosis gastric bypass OR omega loop gastric bypass OR mini-gastric bypass OR one anastomosis gastric bypass OR oagb OR single anastomosis duodenoileal bypass OR mgb/oagb OR mini/one anastomosis gastric bypass Field: Title/Abstract AND "Postoperative Complications"[Mesh] Or "Malnutrition"[Mesh] or malnutrition Or complications or complication or complicated or adverse or side effects or Reflux Esophagitis or safety or nutritional deficiency or nutritional deficiencies Field: Title	01/2001

Literature watch was carried out on the topic until June 2019.

In addition, the contents of the following journals were analysed throughout the project: Annals of Internal Medicine, JAMA Internal Medicine, British Medical Journal, JAMA, JAMA surgery, The Lancet, New England Journal of Medicine, Presse médicale, revue Obésité, Obesity Surgery, International Journal of Obesity, Obesity Journal.

The international websites of the relevant societies cited below were searched in addition to systematically queried sources:

- Adelaide Health Technology Assessment
- Agencia de Evaluación de Tecnología e Investigación Médicas de Cataluña
- Agencia de Evaluación de Tecnologías Sanitarias de Galicia
- Agency for Healthcare Research and Quality
- Alberta Heritage Foundation for Medical Research
- Alberta Health Services
- American Association of Clinical Endocrinologists
- American Society for Metabolic and Bariatric Surgery
- American College of Physicians
- American Medical Association
- Association française d'étude et de recherche sur l'obésité
- Australian Government - Department of Health and Ageing
- Australian & New Zealand Obesity Surgery Society
- Blue Cross Blue Shield Association - Technology Evaluation Center
- Bibliothèque médicale Lemanissier
- British Obesity & Metabolic Surgery Society
- Canadian Agency for Drugs and Technologies in Health
- Canadian Association of Bariatric and Physicians and Surgeons
- Centers for Disease Control and Prevention
- California Technology Assessment Forum
- Centre fédéral d'expertise des soins de santé
- CISMeF
- CMAInfobase
- Quebec College of Physicians
- Cochrane Library Database
- Centre for Review and Dissemination databases
- Department of Health (UK)
- ECRI Institute
- Decision aid health technology assessment
- Euroscan
- GIN (Guidelines International Network)
- Haute Autorité de santé
- Horizon Scanning
- Institute for Clinical Systems Improvement
- Institut national d'excellence en santé et en services sociaux
- Institut national de veille sanitaire
- Instituto de Salud Carlos III / Agencia de Evaluación de Tecnologías Sanitarias
- International Federation for the Surgery of Obesity and Metabolic Disorders (IFSO)
- Iowa Healthcare collaborative
- National Coordinating Centre for Health Technology Assessment
- National Horizon Scanning Centre
- National Health and Medical Research Council
- National Health committee
- National Institute for Health and Clinical Excellence

- National Institutes of Health
- New Zealand Guidelines Group
- Servicio de Evaluación de Tecnologías Sanitarias OSTEBA
- Ontario Health Technology Advisory Committee
- Scottish Intercollegiate Guidelines Network
- Singapore Ministry of Health
- Société française et francophone de chirurgie de l'obésité et des maladies métaboliques
- Sociedad Española de Cirugia de la Obesibad
- Société française de chirurgie digestive
- West Midlands Health Technology Assessment Collaboration
- World Health Organization

Annexe 2. Tables and figures

Annexe 3. Systematic reviews identified with or without meta-analysis

Reference Publication type	Remarks and analysis
Wang *et al.,* 2018 (41) Systematic review with meta-analysis	This review includes ten non-randomised cohort studies and only one randomised controlled trial (RCT) Lee *et al.,* 2005 (25), analysed in Annexe 6. The authors say the results are based on small numbers and contain bias. **Document not selected, not meeting the selection criteria.**
Magouliotis *et al.,* 2018 (42) Systematic review with meta-analysis	This review includes six cohort studies (the same as those by Wang *et al.,* 2018 (41)), and only one RCT Lee *et al.,* 2005 (25). The authors say the results are based on only one randomised controlled trial and that they should be interpreted with caution. They add that other studies are necessary for "demonstrating difference between the techniques". **Document not selected, not meeting the selection criteria.**
Georgiadou *et al.,* 2014 (43) Systematic review	This review includes ten cohort studies with no RCT. **Document not selected, not meeting the selection criteria.**
Mahawar *et al.,* 2013 (44) Systematic review	This review includes 13 cohort studies (of which only one publication is the same as for Wang *et al.,* 2018 (41)), and only one RCT Lee *et al.,* 2005 (25). **Document not selected, not meeting the selection criteria.**

Annexe 4. Endpoints for the level of risk of bias related to each study

Q1: Were the treatments randomly allocated?	
Low risk of bias	• The treatments were randomly allocated (computer procedure; permutation box; random throw; envelope etc.).
High risk of bias	✶ The treatments were allocated according to arbitrary determinism (date of birth; consultation date; record number; patient's or clinician's choice; choice according to preliminary test results etc.).
Uncertain risk of bias	⌑ Study characteristics not provided or not clearly described.

Q2: Was treatment allocation unpredictable?	
Low risk of bias	• Investigators and participants alike could not predict the treatment to be received (centralised allocation; non-identifiable treatment consecutive numbering; opaque, sealed and consecutively numbered envelopes and so on).
High risk of bias	✶ The treatment to be received could be predictable (open list; non-”secure” envelopes; alternation; date; record number etc.).
Uncertain risk of bias	⌑ Study characteristics not provided or not clearly described.

Q3: Were the subjects and nursing staff blinded to the treatment received?	
Low risk of bias	• Blind absent or incomplete but it is considered that this situation could not influence the endpoints evaluated by inducing, during the study, changes in behaviour from knowing which treatment was used (for the subjects treated, knowing which treatment they are receiving can affect compliance (treatment administration, attendance at follow-up etc.) or subjective assessments; for the nursing team, knowing this can influence the treatment proposed (concomitant treatments and follow-up frequency not superimposable between groups due to the convictions related to knowing which treatment is used)). • Subjects and nursing staff blinded with low risk of blind removal during the trial.
High risk of bias	✶ Blind absent, incomplete or probably removed and having influenced the endpoints assessed by leading to changes in behaviour from the treatment used being known.
Uncertain risk of bias	⌑ Study characteristics not provided or not clearly described.

Q4: Were the study endpoints assessed blinded with respect to the treatment received?	
Low risk of bias	• Blind absent, incomplete or probably removed but it is considered that this situation could not have influenced the endpoints assessed (“objective” and so-called “hard” endpoints). • Endpoints assessed blinded with low risk of rupture.
High risk of bias	✶ Blind absent, incomplete or probably removed accompanying endpoints which can be perceived as having likely been influenced by this blind problem (“subjective” endpoints).
Uncertain risk of bias	⌑ Study characteristics not provided or not clearly described.

Q5: Were missing data taken into account?	
Low risk of bias	• No missing data. • Failings probably independent of the endpoint and occurring in equivalent proportions between groups for similar reasons. • For binary data, missing data in proportions not sufficient to change the clinical sense of the ratios compared. • For continuous data, possible effect size within missing data not likely to modify the clinical sense of the overall effect observed. • Missing data taken into account using imputation methods deemed appropriate.
High risk of bias	✶ Failings possibly non-independent of the endpoint and occurring in unequal proportions between groups or for different reasons. ✶ For binary data, missing data in proportions sufficient to change the clinical sense of the ratios compared. ✶ For continuous data, possible effect size within missing data likely to modify the clinical sense of the overall effect observed. ✶ Per-protocol analysis used despite significant changes in randomised treatments (uncompleted analysis limited to the results available taking treatment administered and not randomised treatment into account). ✶ Missing data taken into account using imputation methods deemed inappropriate.
Uncertain risk of bias	⌑ Study characteristics not fully described (randomised numbers not specified, reasons for exclusion not defined etc.).

Q6: Were the results analysed selectively?	
Low risk of bias	• The study protocol can be consulted and all the endpoints targeted by the assessment are reported according to the method stipulated in the protocol. • The study protocol cannot be consulted/is not recorded but it seems obvious that all the expected endpoints were reported in the final publication as provided for before the study (note: in practice, details published rarely sufficient).
High risk of bias	✶ Not all the primary endpoints provided for in the protocol are included in the final publication. ✶ One or several endpoints are analysed according to a non-previously specified method or subgroup. ✶ One or several primary endpoints reported were not mentioned before the analysis (except if clear reasons are provided, such as the occurrence of an unexpected serious adverse event). ✶ One or several endpoints in the meta-analysis are incomplete and cannot be taken into account. ✶ One patent primary endpoint is not reported.
Uncertain risk of bias	⌑ Study characteristics not fully described (note: in practice, most studies would be allocated to this category).

Q7: Are there other potential risks of bias?	
Low risk of bias	• The study does not seem to be subject to other risks of bias.
High risk of bias	✶ There is at least one other significant risk of bias (specific study design; significant initial imbalance between groups; early termination related to data; protocol violation etc.).
Uncertain risk of bias	⌑ There is a potential risk of bias but the details provided cannot be used to assess the extent of the bias, or the rationale is not sufficient or facts proving that the problem identified can introduce a bias.

Annexe 5. Table summarising the risks of bias associated with each study analysed

	Q1: randomised treatments	Q2: unpredictable randomisation	Q3: blinded subjects and carers	Q4: blind endpoint assessment	Q5: missing data	Q6: selective results	Q7: other risks of bias
Lee *et al.*, 2005 (25)	?	?	?	?	?	✗	✗
Ruiz-Tovar *et al.*, 2019 (45)	?	?	✗	✗	✗	✗	✗
Robert *et al.*, 2019 (46)	✓	?	✗	✗	✗	✓	?

Level of risk of bias

✓ *low* ? *uncertain* ✗ *high*

Annexe 6. Randomised controlled trials meeting the literature selection criteria

Publication: Lee *et al.*, 2005 (25)

Trial presentation
Randomised controlled trial, monocentric: Taiwan
Study population: patients 18-59 years BMI > 40 kg/m^2 or BMI > 35 kg/m^2 with a comorbidity.
Blind: no details on patient blinding from the people collecting/analysing the variables.
RYGB: 15 to 20 mL gastric pouch, 100 cm alimentary limb (Roux-limb) if BMI < 49 kg/m^2 o^r 150 cm if BMI > 50 kg/m^2, 50 cm biliary limb from Trietz's angle. Gastrojejunal anastomosis diameter not specified.
OAGB: gastric pouch, 1.5 to 2 cm in diameter (no volume specified), 200 cm biliopancreatic limb, gastrojejunal anastomosis diameter not specified.
Objective: to compare the safety and efficacy of the two techniques.
Endpoints: the endpoints are neither defined nor ranked. **Safety endpoint**: no details. **Efficacy endpoint**: no details.
Main patient selection criteria:
Inclusion: history of obesity > 5 years, BMI > 40 kg/m^2 or BMI > 35 kg/m^2 with one comorbidity (with no details on the related comorbidities), previous attempts to lose weight, “good reason for surgery”, 18 to 59 year age limit.
Exclusion: bariatric or gastric surgery, or history of large abdominal hernia; pregnancy, psychiatric condition or BMI > 60 kg/m^2.
Characteristics of patients included: 56% of patients present with metabolic syndrome defined by at least three of the following characteristics: waist circumference > 102 cm in men and > 88 cm in women, triglycerides ≥ 150 mg/dL, HDL-Cholesterol < 40 mg/dL in men and < 50 mg/dL in women, blood pressure > 130/85 mm Hg, blood sugar ≥ 110 mg/dL.
Mean follow-up: 24 months.
Conflicts of interest: none mentioned.

Remarks and critical analysis
No details on obesity-related comorbidities for the patients operated on and comorbidities likely to be improved by the surgery not mentioned.
Monocentric with small numbers.
The number of subjects is calculated to demonstrate a difference in length of surgery and not in the efficacy or safety of the technique.
Endpoints not defined or listed in order apparently.
No details on randomisation.
Bile reflux not monitored (no endoscopic follow-up).
Anaemia possibly related to nutritional complications (Fe, Vit B, folate and other deficiency).
Study at high risk of bias which was not designed to evaluate the efficacy and safety of OAGB

Efficacy results

	RYGB n=40	OAGB n=40
Weight loss after two years	59.2±15.1	64.4±8.8
	p=ns	
	Given as excess weight reduction with no details on the calculation	
Reduction in comorbidities	0	0
	Number of cases of metabolic syndrome after surgery. Initially 56% of patients (n=45 i.e. 23 OAGB and 22 RYGB) presented with metabolic syndrome, two years after surgery no patients had metabolic syndrome.	
Impact on quality-of-life	113.3±16.1	113.9±17.0
	GIQLI score (symptoms, physical, emotional social) after one year	

Safety results

	RYGB n=40	OAGB n=40
Early complications	8	3
	p<0.05	
	2 major complications (anastomotic leaks)	0
	6 minor complications: upper GI bleeding, intestinal obstruction, drain leak.	3 minor complications: wound infection, upper GI bleeding.
Late complications	1 case of purulent pleurisy, 1 case of bowel obstruction, 1 case of haemorrhagic ulcer. Haemoglobin (g/dL): 12.9±1.6.	2 haemorrhagic ulcers, 1 case of obstruction. Haemoglobin (g/dL) 12.0±1.9 (p<0.05). Anaemia possibly related to nutritional complications.
Revision surgery rate	1 case with alimentary limb too short and dilated	0

Practice requirements

	RYGB n=40	OAGB n=40
Length of surgery (min)	205.0±60.5	147.7±46.7
	p<0.05	
Average length of stay (days)	6.9±2.8	5.5±1.4
	(stay after surgery) p<0.05	
Surgeon's qualification	No details	

Follow-up specific features

Types of monitoring procedures	No details
Procedure frequency	No details
Follow-up period	No details

Publication: Ruiz-Tovar *et al.*, 2019 (45) NCT03467646

Trial presentation
Randomised controlled trial, monocentric: Spain **Blind**: open-label trial. **Study population**: patients > 18 years with no details on age limits, BMI > 40 kg/m2 or BMI > 35 kg/m^2 with a comorbidity. **RYGB**: gastric pouch calibrated with 36 Fr bougie i.e. 1.2 cm length 6 cm, 150 cm alimentary limb if BMI, 100 cm biliary limb. **OAGB**: 20 cm long gastric pouch calibrated with 36 Fr bougie i.e. around 1.2 cm diameter, 200 cm to 350 cm biliopancreatic limb. **Objective**: compare efficacy on weight loss in the short- and long-term and resolution of comorbidities of RYGB, OAGB and sleeve bypass. **Endpoints: Primary endpoint**: weight loss after one, two and five years; no other endpoints defined. **Main patient selection criteria:** *Inclusion*: adults BMI > 40 kg/m^2 or BMI > 35 kg/m^2 with a comorbidity (with no details on related comorbidities). *Exclusion*: other concomitant surgery, if the patient has further surgery, no BMI limit mentioned. **Characteristics of patients included**: no patients excluded, no patients allocated to a group other than randomisation. **Mean follow-up:**: five years **Conflicts of interest**: the authors declared to not have any conflicts of interest.

Remarks and critical analysis
No details on weight loss calculation. We do not know what the reference BMI chosen or ideal weight chosen are. The secondary endpoint is not defined even though it is mentioned in the objective. Open-label, monocentric study. **Missing data not managed.** **Management of increase in alpha risk not mentioned.** Drop-out rate 10%. Weight loss expressed in two different ways after two and five years without justification or explanation on the calculation. Values missing for EBMIL% after five years. Figures provided without confidence interval. Bile reflux not monitored (no endoscopic follow-up). **Study at high risk of bias, the results of which cannot be used to evaluate the efficacy and safety of the OAGB technique**

Efficacy results

	RYGB n=200	OAGB n=200
Weight loss after two years	87.2±6.7	104.3±7
	p<0.05	
	Given as excess BMI loss % reduction with no details on the calculation.	
Weight loss after five years	77.1±6.1	97.9±7
	p<0.05	
	Given as excess weight loss % with no details on the calculation.	
Type 2 diabetes remission rate (after two and five years)	91.5	95.7
	p=ns	
	86.4	95.7
	p=ns	
Arterial hypertension remission rate (after two and five years)	84.3	86
	p=ns	
	73.5	83.5
	p<0.05	
Impact on quality-of-life	Not determined	

Safety results

	RYGB n=200	OAGB n=200
Non-graded complications	10	7
	p not tested	
	4 internal hernias 3 cases of weight gain 3 anastomotic ulcers	2 cases of uncontrollable bile reflux 2 anastomotic ulcers 3 hypoproteinaemia
Number of cases of revision surgery	8	2
	4 hernias 3 cases of weight gain 1 ulcer	2 Roux-en-Y conversions due to bile reflux

Practice requirements

Length of surgery	No details
Average length of stay	No details
Surgeon's qualification	No details

Follow-up specific features

Types of monitoring procedures	No details
Procedure frequency	No details
Follow-up period	No details

Publication: Robert *et al.*, 2019 (46) NCT 02139813

Trial presentation
Multicentric, randomised controlled trial (nine centres): France
Study population: patients 18-65 years BMI > 40 kg/m^2 or BMI > 35 kg/m^2 with a comorbidity (type 2 diabetes, arterial hypertension, obstructive sleep apnoea syndrome, dyslipidaemia, arthritis). **Non-inferiority trial, per-protocol analysis.**
Blind: open-label trial.
RYGB: 30 cc gastric pouch, 150 cm alimentary limb, 50 cm biliary limb. Gastrojejunal anastomosis diameter not specified.
OAGB: long gastric pouch (no details) calibrated with 37 Fr bougie i.e. around 1.2 cm diameter, 200 cm biliopancreatic limb, gastrojejunal anastomosis diameter not specified.
Objective: demonstrate that OAGB efficacy is not inferior to RYGB on weight loss.
Endpoints: the endpoints are neither defined nor ranked.
- Primary endpoint: weight loss after two years confirmed by the EBL% with reference BMI at 22.5 or 25.
- Secondary endpoints: weight and BMI at 1, 3, 6, 12, 18 and 24 months, complications (early and late onset) and their severity after two years, mean length of stay, length of surgery, quality-of-life after two years, incidence of gastroesophageal reflux and diarrhoea (GIQLI questionnaire), steatorrhoea after six months (%g lipids in 24h stools), dumping syndrome, metabolic profile (fasting blood sugar, HbA_{1C}, TG, cholesterol HDL, LDL and total, diabetes drug consumption, antihypertensive and lipid-lowering agent use, histological changes in mucosa after two years (stomach and oesophagus), nutritional status (albumin, pre-albumin, haemoglobin, ferritin, transferrin saturation coefficient, parathyroid hormones, calcaemia and vitamins B1, B9, B12, D).
Main patient selection criteria:
Inclusion: BMI > 40 kg/m^2 or BMI > 35 kg/m^2 with a comorbidity (type 2 diabetes, arterial hypertension, obstructive sleep apnoea syndrome, dyslipidaemia, arthritis), previous attempts to lose weight, “good reason for surgery”, 18 to 65 year age limits.
Exclusion: oesophagitis, severe gastroesophageal reflux resistant to proton pump inhibitors, Barrett's oesophagus, history of bariatric surgery.
Characteristics of patients included: similar in the two groups, around 27% of diabetics, 31% with hypertension, 18% dyslipidaemia and 56% sleep apnoea syndrome.
Follow-up period: 24 months.
Conflicts of interest: reported in the article.

Remarks and critical analysis
Significant uncertainty as to the result with almost 30% missing data and a non-inferiority threshold at 7%. **Almost 30% missing data on the primary endpoints**. Missing data managed. Two multiple imputation techniques and four sensitivity analysis scenarios.
Scenario: - in PP without imputation; - in ITT with the two multiple imputation techniques; - in PP with multiple imputations and penalisation of OAGB with 7% increase in EBL; - in PP imputation of the group mean. Amendment to the protocol for choice of reference BMI; 25 instead of 22.5 as initially expected. No data to determine whether non-inferiority is confirmed with the reference BMI at 22.5[16]. **Non-inferiority is confirmed for each of the scenarios.**
Envelope randomisation. Alpha risk on secondary endpoints not managed; the data are therefore exploratory.
Studies with high percentage of missing data, the results of which cannot be used to definitely confirm the non-inferiority of the OAGB technique.

[16] No response from the study investigator contacted by e-mail and to whom several reminders were sent.

Efficacy results

	RYGB n=117	OAGB n=117
Weight loss after two years	-85.8%±23.1	-87.9 %±23.6
	Non-inferiority p=0.0024 OAGB-RYGB difference -3.3%(90%CI-9.1; 2.6) Non-inferiority threshold at 7%	
	% excess BMI loss (EBL%)	
Total + partial remission of type 2 diabetes	12+2/20	6+1/16
	p=ns	
Dyslipidaemia	p=ns	
Impact on quality-of-life: BAROS and IWQOL scores	p=ns	

Length of surgery	85±35 min OAGB 111±42 min RYGB
Average length of stay	5±1 day in both groups
Surgeon's qualification	Centre performing more than 150 procedures per year

Types of monitoring procedures	No details
Procedure frequency	No details
Follow-up period	No details

Safety results

	RYGB n=94	OAGB n=96
Diarrhoea after 3 months	3	25
	p<0.05	
	RYGB n=71	OAGB n=71
Diarrhoea after 24 months	5	14
	p<0.05	
	RYGB n=92	OAGB n=95
Dumping syndrome after 3 months	22	8
	p<0.05	
	RYGB n=71	OAGB n=71
Dumping syndrome after 24 months	11	10
GOR	1	4
	upper GI endoscopy	
	RYGB n=63	OAGB n=58
Gastritis	2	11
Oesophagitis	4	6
Bile reflux	0	9
Metaplastic cells on gastric and oesophagus biopsy	0	1
Serious adverse event		
	RYGB n=117	OAGB n=117
Surgery-related serious adverse event	24	42
	p<0.05	
Nutritional complications	0	9
Anastomotic ulcer	3	5
Obstruction	3	0
Abdominal pain	5	0

Efficacy results	Safety results

Serious adverse event (continued)

	RYGB n=117	OAGB n=117
Diarrhoea/anal fissure	0	6
Gallstones	5	8
Kidney stones	0	2
Peritonitis	1	3
Roux-en-Y conversion	na	4 (anastomotic leak, Wernicke encephalopathy, 2 severe bile reflux)

Annexe 7. Clavien-Dindo Classification (48)

Grades	Definition
Grade I	Any undesirable post-operative event not requiring medical, surgical, endoscopic or radiological treatment. The only treatments authorised are antiemetics, antipyretics, analgesics, diuretics, electrolytes and physiotherapy.
Grade II	Complication requiring medical treatment not authorised in grade I (blood transfusion and parenteral nutrition).
Grade III	Complication requiring surgical, endoscopic or radiological treatment.
Grade III-a	Surgery without general anaesthesia.
Grade III-b	Surgery with general anaesthesia.
Grade IV	Life-threatening complication requiring intensive care treatment.
Grade IV-a	Organ failure.
Grade IV-b	Multiple organ failure.
Grade V	Death.
Suffix “de”	Complication ongoing at the time of discharge of the patient requiring subsequent monitoring (d=*discharge*).

Annexe 8. Working group report

Meeting type: Working group

Title: Assessment of the surgical treatment of severe and massive obesity by omega loop gastric bypass

Date: 11 June 2019

Participants:

- Doctor Judith Aron-Wisnewsky, endocrinology - nutrition, Pitié Salpêtrière hospital - Paris
- Professor Jean-Luc Bouillot, visceral and digestive surgery, Ambroise Paré hospital - Boulogne-Billancourt
- Mrs Claudine Canale, users' representative, French Obese Patients Associations Group - Puteaux
- Professor Philippe Cornet, general medicine, Pierre et Marie Curie University - Paris
- Doctor Marlène Galantier, nutrition, private practice - Paris
- Doctor Laurent Genser, visceral and digestive surgery, Avicenne hospital - Bobigny
- Mrs Anne-Sophie Joly, users' representative, French Obese Patients Associations Group - Puteaux
- Doctor Léa Lucas-Martini, nutrition - general medicine, Cognacq-Jay hospital - Paris
- Doctor Francesco Martini, visceral and digestive surgery, Clinique des Cèdres - Blagnac
- Doctor Yann Matussiere, nutrition - general medicine, Clinique de la Sauvegarde - Lyon
- Mrs Justine Poissonnier, psychology, Saint-Omer regional hospital - Helfaut
- Professor Didier Quilliot, gastroenterology - nutrition, Nancy teaching hospital - Vandœuvre-lès-Nancy
- Professor Fabian Reche, visceral and digestive surgery, Grenoble Alpes teaching hospital - Grenoble
- Mrs Marion Sillières, dietetics, Clinique des Cèdres - Blagnac
- Doctor Adriana Torcivia, visceral and digestive surgery, Pitié Salpêtrière hospital - Paris

Participants on behalf of the HAS:

- Doctor Cédric Carbonneil
- Doctor Denis-Jean David
- Doctor Jean-Charles Lafarge

1. Objective

Essentially express their position on the omega loop gastric bypass (OAGB), especially concerning its efficacy, safety, practice requirements and patient follow-up. Comment and complete, if necessary, the intermediate version of the assessment report issued by the HAS and sent to the members of the WG.

2. Working group discussion report

2.1. HAS preamble

In addition to a presentation from the HAS for the evaluation of health technologies, the experts were reminded that:

- the work objective is to assess the relevance of inclusion of OAGB on the joint classification of medical procedures (Classification commune des actes médicaux - CCAM) , for its reimbursement by the French national health insurance scheme in the claimed indication; it is not an authorisation or prohibition to perform the procedure;
- discussions should remain confidential until publication of the HAS assessment report;
- they are asked to participate in a private capacity, and not as representative of an association, learned society or other organisation;
- the working group's opinion is advisory;
- the public Declaration of Interests must be updated as and when necessary up to publication of the report.

The questions listed below were sent to the experts 2 weeks before the work meeting. The responses were provided by the group at the meeting.

2.2. Question 1: OAGB efficacy assessment

2.2.1. To your knowledge, are there randomised controlled trials (RCTs) comparing the omega loop gastric bypass (OAGB) and the Roux-en-Y gastric bypass (RYGB) other than the three (Lee *et al*. (25) Ruiz-Tovar *et al*. (45) and Robert *et al*. (46)) analysed in the assessment report?

According to the WG members, no other RCTs have been published to date. Expert members note that one RCT is ongoing and for which the protocol was published by Kraljevic *et al.* (51), with three years' follow-up. It is a non-inferiority trial. There were only 72 patients and the study is expected to end in December 2020.

2.2.2. The analysis shows that the three RCTs cannot be used to come to a definite conclusion on the superiority or even the non-inferiority of the OAGB to the RYGB based on the efficacy criteria (see chapter 4.1.2 p.22-24 and Appendices 4, 5 and 6 of the report).

► Do you have any comments on the study results?

The members note that assessment of the efficacy should not only be based on short-term weight loss but should also take account of the resolution of comorbidities, long-term maintenance of weight loss (after five or ten years or more) and quality-of-life, and especially diarrhoea and steatorrhoea.

According to them, the trials by Lee *et al.* (25) and by Ruiz-Tovar *et al*. (45) have a very limited level of evidence as their primary endpoint was length of surgery for the first and weight loss after one year for the second.

They then recall that the trial by Robert *et al*. (PHRC YOMEGA) (46) has many missing data, amounting to around 30%. This point is believed to reflect, according to them, the complexity and the difficulty of following-up on patients having had bariatric surgery in France. Due to these missing data, they state also that under-reporting of OAGB-related adverse events is likely.

The members of the WG deplore the absence of data published on quality-of-life for the two techniques. The GIQLI (*Gastrointestinal Quality of Life Index)* score evaluating intestinal comfort is cited as a relevant score. The PHRC measured quality-of-life with various scores, including BAROS and IWQOL, to compare OAGB and RYGB. The study does not report a significant difference between the two arms.

The WG members say that in these three RCTs, OAGB was performed with a 200 cm biliopancreatic limb (BP limb) and that to date, there are no RCTs on OAGB with 150 cm BP limb, practice which, according to them, seems to be developing in France to replace a 200 cm limb.

► **General comments on OAGB and bariatric surgery**

Some experts, regularly performing OAGB or following up on patients, consider however OAGB efficacy to be satisfactory with regard to their clinical or surgical experience. OAGB is believed to be more effective, in their experience, on weight loss and resolution of type 2 diabetes, than RYGB. However, patients having undergone OAGB and RYGB could be different, which prevents any comparison being made (selection bias). They confirm significant heterogeneity of practices between centres and surgeons in terms of limb length.

Some experts reiterate that the data for bariatric surgery are not sufficient to date to rank the techniques (2009 HAS recommendation (2), *Cochrane* 2014 review by Colquitt *et al*. (9)). Data from cohorts with non-exhaustive follow-up at three and seven years are available (Courcoulas *et al.,* 2013 and 2018), but cannot be used to rank the various techniques with certainty (adjustable banding, RYGB) (11, 52).

The experts say that there are no long-term comparative data for OAGB on the long-term maintenance of weight loss (ten years) whereas these data are available for RYGB compared to banding, with especially the articles by Courcoulas *et al*. (11, 52).

2.2.3. The literature review shows that OAGB was suggested by certain authors as an alternative to RYGB in patients with "massive abdominal obesity" (page 12), making the RYGB technically-complex to perform (due to a thick and short meso), without however the characteristics of these patients being precisely defined, or in super-obese patients.

► **Are you aware of any literature defining 'massive abdominal obesity' and 'super-obese patients' more specifically?**

According to the experts, the concept of massive abdominal obesity is not clearly defined. The term "super-obese" is better defined. Conventionally we would refer to patients as "super-obese" when they have a BMI of > 50 kg/m^2. However, the BMI is not sufficient for characterising the two types of patients. Waist circumference measurement must be added, without standard limits having been determined however as a criterion for recourse to OAGB.

► **No element validating this suggestion has been identified in the literature. Are you aware of any literature (RCT) which could be used to assess this proposal?**

According to the majority of experts, there are no elements validating this concept published in the literature. Faced with surgical difficulty preventing a RYGB, the sleeve is the backup technique.

► **Does a thick and short meso actually create specific technical difficulties for a RYGB? If so, is it possible to get around this difficulty by performing an OAGB?**

Two opinions were offered by the members of the WG on this point:

1) Some experts practising OAGB disagreed on this point as in OAGB, the gastric tube is long, which makes up for difficulties caused by a short meso.

2) According to most WG members, the alternative is a sleeve or transmesocolic bypass. However, the latter alternative is complicated in technical terms. OAGB does not make it possible to get around the short meso problem.

► **Is "super-obesity", i.e. BMI > 50 kg/m^2 a condition making RYGB technically difficult in particular? If so, is it possible to get around this difficulty by performing an OAGB?**

According to the experts, this difficulty cannot be get around by performing OAGB for super-obese patients, and the alternative can be a sleeve.

Some experts reiterate that surgical difficulties are unpredictable. It is stated that android obesity[17] can be more complex to operate on than gynoid obesity[18] without this always being the case each time.

2.3. Question 2: OAGB safety assessment

2.3.1. The data from the analysis of the literature and databases show that various safety signals (chapter 4.2 p.24-28), some of which confirm the complications expected for OAGB (chapter 2.7.4 p.12-13) were identified: nutritional complications and bile reflux.

► **In your experience, what are: - the complications specifically related to OAGB; the complications specifically related to RYGB, which do not occur after OAGB; and the complications arising from both OAGB and RYGB?**

Severe malnutrition and serious nutritional complications

Most WG experts say that the main complication of OAGB, with a 200 cm or longer BP limb, is severe malnutrition. They say that severe malnutrition and nutritional complications seem to be more common with OAGB than RYGB. They specify however that they work for centres and wards managing serious nutritional complications and say they are “probably subject to observation bias” in that they manage the most serious cases.

Some experts carrying out OAGB or following up on patients after surgery, say that severe malnutrition is not observed only with OLGBO but also with the other surgical techniques (sleeve, RYGB, biliopancreatic bypass).

The experts performing OAGB or following up on patients having undergone the procedure, say they do not have such complications with a 150 cm BP limb. They add however that nutritional complications occur after OAGB using a 200 cm (or longer) limb. The occurrence of serious complications is believed to have led to a change of OAGB practice requirements towards a shorter, 150 cm BP limb, believed to carry a lower risk of nutritional complications. The same members consider that these complications can be detected early on during standard patient follow-up. They say they ensure they inform patients of the “risks of deficiencies”, which according to them are higher with OAGB (including with a 150 cm limb), as the technique is more malabsorptive than RYGB, and, as a result, requires even closer monitoring than for RYGB.

The members of the WG say, for OAGB (and the other types of surgery), that the fact that these complications may occur in patients lost to follow-up cannot be ruled out and those patients may be treated in a different centre from the centre they patient initially had the surgery in.

The WG states that the frequency of these nutritional complications from OAGB is not definitely established. In the PHRC, the precise definition of these serious nutritional complications is not provided. It states that those reported in the literature are those requiring surgical revision (i.e. and not all nutritional complications, thus providing only a partial vision). The nutritional complication rates, according to one expert, are less than 0.5% to almost 4% in the YOMEGA study, and in a cohort of Iranian patients by Khalaj *et al*., 2019 (53). One of the experts says that in the worst case scenario, if a 4% rate is confirmed, there would be around 320 cases of serious nutritional complications (requiring readmission to hospital) per year in France, bearing in mind that half of bypasses performed in France are OAGBs, which seems to them to be very high.

Some experts say that the signs suggesting malnutrition are oedema, reduced albuminaemia, chronic diarrhoea and/or steatorrhoea having a significant impact on the patient's quality-of-life.

[17] Android obesity is characterised by excess fat mainly on the abdomen.

[18] Gynoid obesity is excess fat on the lower body, generally on the buttocks and thighs.

They consider that when severe malnutrition is suspected after bariatric surgery, including OAGB, the limit for referring the patient to a specialist centre is albuminaemia under 30 g/L.

Some WG members say that it is difficult to diagnose malnutrition in obese patients regardless of the technique. They observe diagnostic errors as there are currently no formal referral criteria for patients or general practitioners or other primary care physicians. Late management can lead to serious neurological complications and permanent damage. It is also stated that assessing malnutrition in an obese patient is counter-intuitive to the representation that society has of obese patients, representing “excess good health” and thus delaying treatment and accentuating the diagnostic error.

One expert recalls that some surgeons have stopped performing OAGBs due to the nutritional complications that they considered to be more common than with RYGB. However, he is sorry these cases were not reported or published.

Post-OAGB severe malnutrition management

The experts observe great heterogeneity in practices for the management and prevention of complications, including during preoperative preparation.

The WG members treating these complications specify that treatment involves hospitalisation and parenteral or enteral nutrition. If successful, oral food intake is reintroduced gradually thereafter. It involves significant food fractioning which has a considerable impact on quality-of-life; and which for some can be very difficult to combine with a work life.

According to certain experts, revision surgery for failed medical treatment of malnutrition is performed for 1% of OAGB patients, the revision surgery being RYGB conversion or assembly “reversal”.

Vitamin deficiencies

Deficiencies in fat-soluble vitamins A and E are believed to be more common with OAGB according to some experts, on the basis of data published from patient follow-up by Parmar *et al*. (27). The WG members also reiterate that dietary supplements with special compositions are marketed for OAGB, with higher vitamin A and E content in particular than in post-RYGB dietary supplementation. This point corroborates the existence of more severe nutritional complications for OAGB than for RYGB for certain experts.

Malnutrition and OAGB indications

In light of the risk of nutritional complications, some experts have reservations about offering OAGB to women of childbearing age.

Marginal ulcers

Some experts mentioned that marginal ulcers are believed to be more common and more difficult to treat due to the bile reflux with OAGB than with RYGB.

Internal hernia

The experts say that internal hernias may occur in OAGB whereas this technique was initially presented as not causing any. They are however less common than for RYGB for which they are a major complication.

Acid reflux and bile reflux

One of the experts says that bile reflux related to acid reflux occurs in OAGB. He specifies that this reflux can be asymptomatic and that it is difficult in OAGB to determine which symptoms are related to acid reflux and which are related to bile reflux.

All the experts say that bile reflux is specific to OAGB due to the anatomic assembly promoting bile reflux into the stomach and which may come into contact with the lower oesophagus.

Experts mention results of studies in rats having received an assembly similar to the OAGB, and it is believed to represent an animal model for lower oesophageal cancer. One of the experts recalls that these results in animals are heterogeneous on the appearance of lower oesophageal cancer due to the difference in the surgical procedures used (oesophagus assembled on the duodenum directly or maintenance of a gastric tube between the oesophagus and the duodenum, leaving out the stomach). It is recalled that a decision to take on a procedure or not cannot only be based on experimental data in animals.

The risk of lower oesophageal cancer by reflux from OAGB is theoretical for some experts and a fact for others. There is no consensus on this point. In particular, some experts specify that the YOMEGA study demonstrated one case of metaplasia, two years after OAGB surgery. All the experts say there is insufficient data to assess this risk. **All the experts say that doubt remains as to the occurrence of lower oesophageal cancer from OAGB, and on the time to occurrence, and estimate the time scales at 15 or 30 years.**

Reflux and OAGB indications

In light of the doubts as to the “actual or theoretical consequences” of bile reflux and the risk of lower oesophageal cancer, some experts would not recommend OAGB in a young population, which is to say before the age of 50.

“Concomitant” complications: reflux, marginal ulcers and malnutrition

Experts treating post-OAGB complications say that some patients have several concomitant complications with OAGB: reflux, marginal ulcers and malnutrition. This triad is, in their opinion, a vicious circle and is believed to be more common with OAGB using a 200 cm BP limb. There is no consensus on this point. Other experts report that this triad is not exclusive to OAGB and can occur after a sleeve for example. It should be noted that some experts say there is no bile reflux with the sleeve and that only acid reflux can occur.

Chronic steatorrhoea and diarrhoea

The clinical experience of certain experts suggests that there are more cases of chronic steatorrhoea and diarrhoea following OAGB. Some experts note six cases of diarrhoea in the OAGB arm of the YOMEGA study compared to none in the RYGB arm. Certain experts reiterate that this is a secondary endpoint and that the numbers are very small, and that it is therefore difficult to come to a conclusion based on this data alone.

Hypoglycaemia

Some experts mention that it is less common in OAGB in their clinical experience but they specify that no data has been published to this effect.

Other complications

Oxalic lithiasis is believed to be more common in OAGB. There is no consensus on this point. There are no publications on this point.

There is believed to be no difference in dumping syndrome. There are no publications on this point.

Some experts report that fistulas occurring in OAGB are more serious than in RYGB due to the presence of bile and sepsis, which in most cases requires surgical revision. There is no consensus on this point in the absence of comparative data with good level of evidence.

2.4. Question 3: identification of optimal conditions in which to carry out OAGB

One expert recalls that OAGB was introduced to replace RYGB based on the following arguments: shorter surgery, simplicity of the procedure and to overcome the abdominal pain which is common with RYGB.

2.4.1. Are you aware of any randomised controlled trials comparing OAGB with RYGB with a limb length other than 200 cm?

The WG members are not aware of any RCTs making this comparison. There are no RCTs with a 150 cm limb for OAGB either.

2.4.2. Do you have any further comments on limb length?

All the experts report great variability in practice requirements in France. Some surgeons are even believed to create BO limbs longer than 250 cm, or even 300 cm, which carries a greater risk of serious nutritional complications.

The members of the WG specified that the length is somewhat estimated, since on the one hand, different surgical tools can be used, and on the other hand, the surgeon can place the bowel more or less in tension during measurement. The experts specify that there is no tool for accurately estimating small bowel length preoperatively (e.g. by imaging), only individual size is believed to be correlated to length, without it being accurately estimated.

More generally, given the interindividual variability in bowel length (between 4 and more than 12 metres), ideally the remaining small bowel length could be estimated, and therefore measured, to ensure the common limb is long enough. This potential practice comes up against risks related to handling the remaining small bowel (risk of perforation), and to the time required to make the measurement. Another expert specifies that given the standard anatomy, with a 150 cm limb, a sufficient length should be left over to prevent nutritional complications.

The WG specifies that there has been a change in BP limb length in OAGB from 200 cm to 150 cm. Initially, the technique was described with 200 cm, then to get around complications, especially nutritional, a 150 cm limb was preferred. Some experts say that shortening the length could however increase bile reflux. Some experts have reservations on the results of the 2015 French cohort (21) which, “surprisingly”, only reports two nutritional complications, whereas the OAGB BP limb measured 200 cm. Also, after five years, the data published again report a large number of lost to follow-up (28%) (21). Also, some experts specify that the recommended limb length used by the authors of this paper has changed, and is currently 150 cm. They wonder what the reasons are for this change of practice.

Finally, the WG considers that it is not recommended to “create” BP limbs longer than 200 cm given the nutritional complications, that with a 200 cm limb the risk of such complications remains, and that 150 cm could be the length which minimises them. The WG specifies however that to date, efficacy and safety data are missing for OAGB performed with a 150 cm BP limb, and that, in particular, there are no RCTs comparing this OAGB with RYGB or OAGB with 200 cm limb. The members of the WG are therefore in favour of a comparative study to assess OAGB with 150 cm limb, of the same type as the YOMEGA PHRC, but with longer follow-up and routine endoscopy to have data on the risk of lower oesophageal cancer.

2.4.3. Do you have any additional comments about OAGB practice requirements? (other than limb length, e.g. surgeon's qualification, length of stay, length of surgery etc.)

► Activity threshold

On the activity threshold, the WG members recall the conclusions of the 2018 IGAS report (32, 33). They say that it is not a question of defining a minimum threshold per type of obesity surgery or by

surgeon, but an overall threshold (i.e. all types of bariatric surgery) per centre (i.e. all bariatric surgeons), as it is a well-trained staff team that is able to manage patients properly. They say that bariatric surgery centres must offer several bariatric surgery techniques and that RYGB must be feasible in all centres (and not only the sleeve and OAGB) in order to guarantee patients can make an informed choice and to have several alternatives in the event of surgical difficulties.

A maximum threshold per centre is also mentioned as some experts underline that with too many patients in one centre, it is difficult to organise optimal follow-up, let alone lifelong follow-up.

► Accreditation

The experts are in favour of centre accreditation for bariatric surgery on the whole, but not for a specific techniques as they should all offer several techniques, including RYGB.

► Length of surgery

The experts say that surgery is shorter by 30 minutes on average for OAGB compared to RYGB. However, they specify that no gain has been confirmed for patients in terms of reduction in the thromboembolic risks for example or reduction in the risk of rhabdomyolysis. Most WG experts consider that shorter length of surgery as it is, is not an argument in favour of OAGB.

► Average length of stay

The experts report that no reduction in length of stay has been confirmed either.

2.4.4. Is there any information specific to OAGB (compared to RYGB) which could be provided to patients when they decide on the surgical technique, and during the surgery? If so, can you provide details in particular concerning information on technique efficacy, safety and risks or other information required so patients can make an informed decision.

All experts reiterate that some centres and surgeons do not completely fulfil their role in providing impartial and full information to patients on techniques before the decision to operate, and along with their teams do not take every step to ensure appropriate follow-up.

Given the characteristics of OAGB, some experts consider that on informing patients, it is necessary to emphasise the major importance of regular follow-up, to warn them about the consequences of deficiencies and to inform them on the warning signs of complications, so patients can contact professionals trained in the management of these complications as soon as possible.

Some experts report a lack of or incorrect information. In certain cases, the patients do not know which type of surgery they had. Patients may only be informed during management of a complication with an imaging examination or endoscopic examination.

The information should also mention there are no data available on the consequences of OAGB on pregnancy, and that if a patient wishes to fall pregnant, she should inform the team following her from the start in order to provide for optimal management of the pregnancy.

The group reiterates that the term mini-bypass should not be used in any circumstances to infer a less invasive and therefore less morbid nature of the surgery compared to other types of surgery. On this subject, this point is ratified by scientific journals and the international obesity surgery learned society (IFSO) (16). They ask that this point feature explicitly in the HAS report to “deconstruct” the term “mini”.

2.5. Question 4: identification of the specific features of OAGB post-op follow-up

2.5.1. With regard to the complications identified in the report (chapter 4.2 p.24-28) and those cited in question 2, especially the nutritional complications and bile reflux, what, in your opinion, are the specific features of the post-operative follow-up for OAGB patients? Whether in terms of consultations (questioning and physical

examinations), technical examinations (imaging, blood tests etc.) (specifying if possible the frequency and duration of monitoring).

All members of the WG say that patients and primary care physicians (general practitioners especially) and obesity centre professionals (CSO) alike should have training in diagnosing malnutrition in obese patients.

Some experts recall the primary importance of monitoring OAGB patients, especially in terms of diet adjustment to prevent vomiting or other digestive discomfort related to bile reflux into the stomach.

Beyond OAGB, some experts insist on the complexity of management of obese patients having undergone surgery or not and presenting with another disease, caused by the changes in the pharmacokinetics of certain oral treatments.

The discussions between experts and patient representatives show that to improve follow-up, “coercive” measures or measures “obliging” patients to have follow-up could be envisaged.

More generally, it is recalled that “human beings are naturally non-compliant”, and that concerning obesity, the experts mention that life events, and social dispositions make compliance with follow-up complex for patients. It is said that the patient feels “cured” and in some cases only consults for a complication.

The experts note the lack of data on follow-up for OAGB patients, in particular endoscopic follow-up. They say that endoscopic follow-up is necessary to detect lesions caused by chronic reflux, in light of the risk of lower oesophageal cancer. Follow-up is not currently standard. It is reported that certain centres performing OAGB are currently calling back patients for an endoscopic examination five years after surgery. **The WG considers that endoscopy after five years for OAGB seems to be the most appropriate approach for preventing too many examinations and to have optimal follow-up in as many patients as possible, to prevent them being lost to follow-up.**

Concerning OAGB, and bariatric surgery in general, some experts request that a clear programme be sent to general practitioners to facilitate follow-up, on the discharge letter for example, stating the examinations to be carried out, their frequency and the warning signs and instructions for referral to specialists.

During follow-up of OAGB patients, apart from endoscopy for bile reflux, there are no specific examinations compared to OAGB. However, there should be close monitoring given the specific complications identified such as nutritional complications and steatorrhoea. In this latter case, fat-soluble vitamins “A, D, E and K should be monitored in particular”, with added supplementation compared to RYGB with plasma concentration monitoring.

3. Conclusion and prospects

The experts say that based on the available data and their experience, OAGB with 200 cm or longer BP limb probably lead to more nutritional complications than RYGB.

The experts say that it is essential to conduct a study to assess OAGB with a 150 cm BP limb. They suggest conducting a randomised controlled trial to ensure that OAGB with 150 cm limb does not carry a higher risk of nutritional complications than RYGB. All experts agree that weight loss is not a sufficient endpoint. The endpoint should be a composite endpoint and include quality-of-life and complications (especially malnutrition and the risk of lower oesophageal cancer after at least five years).

The experts state that one of the difficulties of the study is its numbers. In effect, if the primary endpoint is a complication, a high number of patients must be followed-up. They recommend long-term five-year follow-up, with endoscopy to “monitor” the lower oesophagus after five years.

The experts request that all data from the YOMEGA PHRC be published, especially on the nutritional status of all patients, to identify the types of vitamin and micronutrient deficiency in the nine patients presenting with serious nutritional complications.

The experts confirm that there are no population subgroups in whom this technique is specifically indicated. Conversely, in light of the lack of data and uncertainty, some experts recommend not performing it:

- in young subjects (under the age of 50) due to the risk of lower oesophageal cancer;
- in patients with oesophagitis in whom RYGB would be more appropriate.

Most of the experts said it is necessary to inform women of childbearing age in particular of the lack of data on OAGB and on the potential risks in the case of pregnancy.

It would appear that there are still no (2009 HAS recommendation (2), *Cochrane* (9)) formal criteria for ranking the techniques, and that reliable data for providing elements free from uncertainty on OAGB so patients can make an informed choice are currently missing.

One of the experts deplores the restricted arsenal of solutions for treating obesity, and that OAGB could be useful, but the uncertainties as to this technique are to be removed by studies.

Several experts relate their fears about the sleeve technique, due to the risk of cancer from gastroesophageal reflux, in particular with respect to the lack of endoscopic surveillance, which should be carried out even in asymptomatic patients.

Finally, the WG states that some surgeons and bariatric surgery centres have specialised in OAGB and do not offer RYGB.

Additional contributions from the experts after reading this report:

One of the experts specifies that malnutrition is believed to be the cause for OAGB to RYGB conversion in 25% of cases (54). He recalls the two cases of severe malnutrition in the French cohort (21). He indicates a risk of osteoporosis which is not specific to OAGB. He mentions the lack of data on deficiency, and considers that two thirds of patients would need vitamin B12, folate and iron supplementation (55).

Concerning marginal ulcers, one of the experts says the frequencies of these ulcers reported by series of cases are highly heterogeneous regardless of the surgical technique. It is therefore difficult, according to this expert, “to confirm that OAGB is related to a higher rate of marginal ulcers post-operatively, and that these ulcers are extremely difficult to treat”.

Concerning the characterisation of obese patients, one expert specifies that waist circumference indirectly reflects intra-abdominal obesity (including subcutaneous and visceral adipose tissue). Sagittal diameter could be a better marker of abdominal obesity (56, 57) but no studies have confirmed it to be useful in determining the surgical technique.

Concerning follow-up of OAGB patients, one of the experts adds pH-impedance measurement to endoscopy.

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Fact sheet

Title	Description
Work method	Health technology assessment
Date of on-line publication	September 2019
Date of issue	Only available in electronic format at www.has-sante.fr
Purpose(s)	*See* chapter 1.2
Professional(s) concerned	*See* chapter 3.3
Requested by	HAS self-referral and CNAM SOFFCOMM joint referral
Sponsor	French National Authority for Health (HAS), Diagnostic and therapeutic procedure assessment department (SEAP)
Project management	Coordination: Jean-Charles LAFARGE, project manager, SEAP (Head of Department: Cédric CARBONNEIL, Deputy Head of Department: Denis-Jean DAVID) Secretarial duties: Suzie DALOUR, assistant, SEAP
Participants	Independent expert appraisal: Doctor Judith ARON-WISNEWSKY, Professor Jean-Luc BOUILLOT, Mrs Claudine CANALE, Professor Philippe CORNET, Doctor Marlène GALANTIER, Doctor Laurent GENSER, Mrs Anne-Sophie JOLY, Doctor Léa LUCAS-MARTINI, Doctor Francesco MARTINI, Doctor Yann MATUSSIERE, Mrs Justine POISSONNIER, Professor Didier QUILLIOT, Professor Fabian RECHE, Mrs Marion SILLIERES, Doctor Adriana TORCIVIA *See* chapter 3.3.2
Documentary search	Documentary search strategy described in Annexe 1 Conducted by the archivist Emmanuelle BLONDET, assisted by the assistant archivist Sylvie LASCOLS, under the responsibility of Frédérique PAGES, Head of Documentation - Monitoring Department, and Christine DEVAUD, Assistant Head of Department
Authors of rationale	Jean-Charles LAFARGE, project manager, SEAP, under the responsibility of Denis-Jean DAVID, Deputy Head of Department, SEAP
Approval	Review by the National Committee for the Evaluation of Medical Devices and Health Technologies (CNEDiMTS): July 2019 HAS College: September 2019
Other formats	No formats other than the electronic format available at www.has-sante.fr
Accompanying documents	HAS decision and opinion (September 2019) available at www.has-sante.fr

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