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Sleeve gastrectomy as a single stage bariatric procedure

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Australian Safety and Efficacy Register of New Interventional Procedures - Surgical

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Executive Summary

Various strategies exist for the treatment of obesity: dietary changes, behavioural therapy and pharmacological interventions are widely utilised by clinicians and even patient's themselves as a means of controlling obesity. The basic principle of weight loss is relatively straightforward, reduce food consumption and increase physical activity. However, medical studies have shown that attaining weight loss and maintaining it is no simple feat. Only ~25% of patients have successfully maintained long-term weight loss after undergoing caloric-restriction programs (Martin and Hunter 1995). Extreme forms of obesity (≥40 BMI) have been shown to respond poorly to dietary, behavioural and pharmacological treatment, with relapse rates of 90% (Council of Scientific Affairs 1988, Segal et al. 1994). At the time of writing, bariatric surgery is the only proven technique capable of inducing long-term sustained weight loss in morbidly obese patients.

Recently, there has been substantial interest in a relatively new bariatric procedure, sleeve gastrectomy (SG). SG is essentially partial gastrectomy, where a majority of the stomach is resected to reduce stomach size. This should presumably result in reduced appetite and therefore decrease caloric intake. Previously, SG has been utilised as the first-stage procedure prior to biliopancreatic diversion or gastric bypass (Frezza 2007). This was mainly due to the perception that SG is not able to induce sufficient weight loss by itself. However, evidence has surfaced that SG may be capable of achieving substantial weight loss, therefore garnering considerable interest as a potential single-stage bariatric procedure.

Randomised clinical trials and comparative studies retrieved for discussion in this report have demonstrated that SG is capable of inducing substantial weight loss. Both of the included randomised trials revealed that SG results in significantly greater %EWL compared to lap-band surgery (Himpens et al. 2006, Langer et al. 2005). However, the results of comparative studies were mixed. Two studies highlighted that Roux-en-Y gastric bypass (RYGBP) and duodenal switch achieved significantly higher %EWL compared to SG (Lee et al. 2007, Hamoui et al. 2006). Meanwhile, Vidal et al. (2007) stated that weight loss attained by SG and RYGBP patients were similar. Despite these discrepancies, it is clear that SG is capable of achieving commendable weight loss (although significantly lower compared to RYGBP and duodenal switch) and there is strong evidence that SG is more effective than lap-band surgery.

Investigators have postulated that SG is not merely a restrictive procedure, but may have hormonal effects as well. This is due to the fact that during SG, the gastric fundus and the greater curvature (both key sites of ghrelin production) are completely resected, resulting in significantly decreased plasma ghrelin levels (Langer et al. 2006). This significant reduction in ghrelin could have contributed to the weight loss achieved by reducing the appetite of the patient, and may

explain the relatively superior outcomes of SG patients compared to lap-band patients (Himpens et al. 2006, Langer et al. 2005). The observed reduction of the feeling of hunger by Himpens et al. (2006) in 75% of SG patients may be attributable to decreases in plasma ghrelin levels.

Randomised trials demonstrated that SG has comparable and perhaps lower complication rates relative to lap-band (Himpens et al. 2006, Langer et al. 2005). However, it is important to note that one study reported more severe complications after SG despite attaining lower overall complication rates (Himpens et al. 2006). Relative to RYGBP and intragastric balloon implantation, SG appears to be significantly safer (Lee et al. 2006, Milone et al. 2005).

Despite the encouraging results from the retrieved studies, the long-term safety and effectiveness of this procedure has not been investigated thoroughly. The significantly higher %EWL achieved compared to lap-band should be viewed in context of the fact that SG is substantially more invasive and is not reversible. Nevertheless, SG appears to have substantial potential as a single-stage bariatric procedure. Further studies with larger patient cohorts and long-term data are required before the efficacy of SG relative to established bariatric procedure can be determined.

HealthPACT Advisory

When jurisdictional health authorities have made appropriate policy decisions on access and availability of services for the management of morbid obesity and for the subset of patients requiring surgical treatment; clinicians will have a range of surgical options to consider including sleeve gastrectomy.

At present gastric band has become the most common bariatric surgical procedure in Australia and it is the standard by which other procedures will be judged.

Sleeve gastrectomy is an appropriate surgical option for the treatment of morbid obesity, noting that further long-term data are needed. Post operative follow up may be simpler as repeated band adjustments are avoided; this may influence the cost impact of supporting bariatric surgery in the Public Sector.

Health Services will need to carefully address governance issues (credentialing, scope of practice and audit) if embracing any form of bariatric surgery.

Introduction

The Australian Safety and Efficacy Register of New Interventional Procedures – Surgical (ASERNIP-S), on behalf of the Medical Services Advisory Committee (MSAC), has undertaken a Horizon Scanning Report to provide advice to the Health Policy Advisory Committee on Technology (Health PACT) on the state of play of the introduction and use of SG for the treatment of obesity.

Sleeve gastrectomy is a bariatric procedure that was initially utilised in combination with other procedures (e.g. duodenal switch) to treat morbidly obese patients. Recent studies have suggested that sleeve gastrectomy may be capable of achieving adequate weight loss in morbidly obese patients as a sole/single-stage procedure. Sleeve gastrectomy (SG) is currently in use within Australia; however, it is relatively uncommon compared to laparoscopic gastric banding/lap-band which is utilised as the bariatric procedure of choice in most cases.

This Horizon Scanning Report is intended for the use of health planners and policy makers. It provides an assessment of the current state of development of SG, its present use, the potential future application of the technology, and its likely impact on the Australian health care system.

This Horizon Scanning Report is a preliminary statement of the safety, effectiveness, cost-effectiveness and ethical considerations associated with sleeve gastrectomy.

Background

Morbid obesity[1] is a chronic lifelong, multifactorial, congenital disorder[2] which causes the patient to have excessive fat deposits and associated medical, psychological, social and economic problems. Clinical observations have demonstrated that obesity is associated with a variety of illnesses and can lead to substantial physiological burden to the affected individual with increased risk of mortality due to cardiovascular disease and cancer.

To date, various strategies have been utilised as a means of controlling obesity; these include dietary advice, behavioural changes and pharmacological intervention. It is clear that obesity has a strong link to caloric intake; therefore it is widely believed that reduction of caloric intake below expenditure will result in predictable weight loss related to the energy deficit. However, achieving and maintaining weight loss is not as straightforward as it seems. Although the implementation of a low-fat diet and an exercise program is often advocated as an effective means of weight loss, the success rates[3] of caloric restriction programs have been somewhat disappointing. Only 25% of patients are successful in maintaining weight loss after 4 years with the condition that the programs were run well enough to maintain high participation rates for at least one year (Martin and Hunter 1995). Further illustrating the difficulty of achieving sustained weight loss, Stunkard (1987) reported that the nadir of weight loss for a very low calorie diet is achieved within 4 months; following this, patients tended to increase in weight.

Pharmacological intervention typically involves the prescription of appetite suppressants and lipase inhibitors. The health technology assessment report by the Agency of Healthcare Research and Quality (AHRQ) concluded that sibutramine, orlistat, phentermine, diethylpropion (probably), bupropion, fluoxetine and topiramate are capable of promoting weight loss when utilised along with dietary changes (Shekelle et al. 2004). The authors stated that the amount of extra weight loss attributable to these drugs are somewhat modest (<5kg at one year) but may still be clinically significant. However, Shekelle et al. (2004) highlighted that the *relative* clinical effectiveness of these drugs cannot be conclusively answered due to the lack of head-to-head RCTs that compare different pharmacological agents.

[1] Classification of overweight and obesity according to the body mass index (BMI):

Classification	BMI
Underweight	< 18.5
Normal weight range	18.5 to 24.9
Overweight	25 to 29.9
Obese	≥ 30
Morbidly obese / Severely obese	≥ 40
Super-obese	≥ 50

(Australasian society for the study of obesity 2005)

[2] Although not strictly a congenital disorder, there appears to be a genetic component in a large proportion of affected individuals.

[3] Successful candidates are those who maintained initial weight loss after 4 years.

Furthermore, the lack of randomised trials to elucidate the effectiveness of combined pharmacological intervention with more aggressive behavioural therapies and dietary changes makes it difficult to determine if this combination of treatments results in synergistic benefits for weight loss (Shekelle et al. 2004).

Studies have demonstrated that extreme forms of obesity (≥40 BMI) are unlikely to respond to dietary, behavioural or pharmacological treatment. Relapse rates of up to 90% have been documented for non-surgical treatments of morbid obesity, irrespective of the choice of conservative treatment (Council of Scientific Affairs 1988, Segal et al. 1994). Considering these factors, bariatric surgery appears to be the most potentially effective treatment for sustained weight loss in morbidly obese patients at the time of writing (Lee and Wang 2005, Buchwald et al. 2004). The US National Institutes of Health and the Australian National Health and Medical Research Council (NHMRC) have stated that bariatric surgery is the most effective treatment for morbid obesity that is capable of inducing long-term weight reduction and is statistically associated with decreased comorbidity for the majority of patients (National Institutes of Health 1992, NHMRC 2003). There are three main types of bariatric surgery: restrictive, malabsorptive and combined restrictive/malabsorptive. Restrictive operations (adjustable gastric banding, vertical banded gastroplasty) limit food intake by creating a narrow passage from the upper part of the stomach to the lower part, therefore reducing the amount of food that the stomach can hold and slowing the passage of food through the stomach. Malabsorptive procedures do not limit food intake, but excludes most of the small intestine from the digestive tract as a means of reducing calorie and nutrient absorption. Purely malabsorptive operations are no longer recommended as they can often result in severe nutritional deficiencies. Combined restrictive/malabsorptive procedures (Roux-en-Y gastric bypass, biliopancreatic diversion) typically results in partial bypass of the small intestine and hence the risk of severe nutritional deficiency is reduced (National Institutes of Health 2004).

An alternate restrictive bariatric procedure, sleeve gastrectomy, has recently garnered substantial interest as a potential means of achieving sustained weight loss in morbidly obese patients. Sleeve gastrectomy (SG), also known as “partial gastrectomy”, “tube gastrectomy”, “longitudinal gastrectomy” and “vertical gastrectomy” is essentially a partial gastrectomy. However, the medical community has long considered the weight loss achieved by SG alone is insufficient for the treatment of morbidly obese patients. Due to this, SG has often been utilised as a first-stage procedure, to be followed with biliopancreatic diversion or gastric bypass (Frezza 2007), or part of a multi-stage procedure. However, there is increasing interest in the use of SG as a single-stage procedure.

The resulting decrease in stomach size after SG inhibits distension of the stomach and therefore causing it to become full sooner; this in turn will presumably increase the patient’s sensation of fullness/satiety and decrease their appetite. Some investigators have suggested the SG is not merely restrictive, but has a

hormonal contribution to the feeling of satiety (Frezza 2007, Langer et al. 2005). These claims will be examined in greater detail later within this report.

Description of the Technology

As with other bariatric procedures, there are some variations between the retrieved studies with regards to the actual steps utilised (number of trocars etc.) for laparoscopic SG. However, the general principle of the procedure is maintained throughout.

Under general anaesthesia, the patient is placed in the lithotomy position with the surgeon positioned between the legs. A pneumoperitoneum is induced with carbon dioxide (CO_2) and is maintained as a pressure of ~16mmHg. Five trocars[4] will be inserted into the peritoneal cavity. Following this, the gastrocolic ligament is opened adjacent to the stomach starting 7cm from the pylorus and the greater curvature of the stomach is freed up to the cardiooesophageal junction. An appropriately size bougie (usually 40Fr to 50Fr) will be inserted by the anaesthesiologist into the stomach, and is directed towards the pylorus (the bougie essentially helps determine the size of the gastric sleeve). The stomach is then divided parallel to the bougie along the lesser curvature using laparoscopic linear staplers. The excision line is then reinforced with a running 2-0 polypropylene suture. The volume of the remaining stomach is measured using a nasogastric tube filled with water. A methylene blue test is conducted to check staple line integrity and a drain is placed at the left subdiagramatic space. The resected part of the stomach is then removed via an enlarge trocar site and the trocar wounds are closed (Melissas et al. 2007).

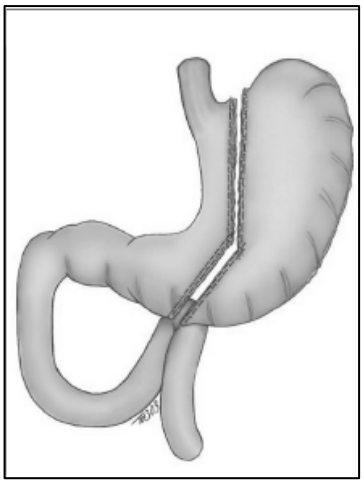

Figure 1: Sleeve gastrectomy

(Santoro et al. 2006)

Most of the studies included within the safety and effectiveness section of this report utilised laparoscopic SG (LSG), only one study (Hamoui et al. 2006) performed this procedure via laparotomy.

[4] The number of trocars utilised varies across studies, some studies utilized 7 trocars (e.g. Roa et al. 2006).

Intended purpose

As stated previously, SG was initially devised as a method of resecting stomach cancers. Over time, it became part of the bariatric arsenal but has often been utilised as part of a multi-stage bariatric procedure (Frezza 2007).The recent surge in interest on SG is related to the notion that SG is safer and less complicated compared to duodenal switch and and Roux-en-Y gastric bypass. If SG is capable of achieving adequate weight loss as a standalone bariatric procedure, it should lead to less perioperative morbidity and therefore improve patient outcome.

Clinical need and burden of disease

Obesity has been shown to place undue strain on the heart (cardiovascular disease), joints and spine (musculoskeletal disease) and is associated with type II diabetes (Australian Institute of Health and Welfare: Obesity trends in older Australians 2004). Over the last 20 years, Australians have gained a substantial amount of weight and as a result Australia is in the grip of an obesity epidemic. The proportion of adults considered overweight or obese has increased substantially from 52% to 62% in men and from 37% to 45% in women between 1994/1995 to 2004/2005; highlighting the disturbing and rapid growth of this the disease (Australian Bureau of Statistics 2006). In 2006, the Australian Bureau of Statistics estimated that 62% of men and 45% of women in Australia are overweight or obese. If overweight individuals are excluded, approximately 3.24 million Australians are considered obese (15.1% of all males and 16.8% of all females).

Among older Australians (>55 years old), the prevalence of obesity has been shown to have increased markedly in the last two decades. The Australian Institute of Health and Welfare has reported a three-fold increase in older Australians who are obese from 310,000 in 1980 to 940,000 in 2000. As older individuals are already at a greater risk of developing chronic diseases such as type II diabetes, coronary heart disease, stroke, certain cancers, osteoarthritis and kidney disease, the additional health implications from being obese can severely affect quality of life. In addition to this, the increasing number of obese older Australians will have substantial repercussions towards healthcare costs, the wellbeing of carers, and the ability of aged care services to meet the needs of the older generation (Australian Institute of Health and Welfare: Obesity trends in older Australians 2004).

International studies on the economic costs of excess body weight, including data from Australia, have shown that between 2% to 7% of total health care costs may be directly attributable to overweight and/or obesity (WHO 2000). In 2005, the estimated total financial cost of obesity was $3.767 billion. The direct cost to the health system was $873 million, while productivity costs were $1.7 billion, and carer cost was $804 million. Deadweight loss from transfers (lost tax revenue, welfare, government payments: $358 million) and other indirect costs amounted to $40 million (Access Economics 2006).

Cardiovascular disease and cancer appear to be the main sources of increased mortality in obese patients. An update of the Framingham study (Peeters et al. 2003) demonstrated that being overweight (BMI: 24 to 29.9) reduces life expectancy in 40 year-old non-smoking males and females by 3.1 and 3.3 years, respectively. Meanwhile, obese male and female (BMI>30) non-smokers life expectancies may decrease by 5.8 and 7.1 years (Peeters et al. 2003). There is some evidence that the ratios of observed death to expected deaths increase directly with the degree of obesity, this relationship appears to be stronger for individuals who are less than 50 years old, therefore suggesting that those at younger ages have a greater risk of mortality (Martin and Hunter 1995). Another study suggests that obese patients who reach the age of 70 are at no greater risk of dying compared to their non-obese counterparts. However, these individuals are more likely to spend their remaining years of life disabled (Reynolds et al. 2005).

Benefits of weight loss in obese individuals

Substantial decreases in hypertension and improvement of blood lipids can be attained even with modest weight losses of 5% to 10% (Davis et al. 1993, Dattilo and Kris-Etherton 1992). If weight loss of 15% to 20% is achieved, the patient may successfully reverse the elevated mortality risk associated with type II diabetes (Lean et al. 1990) and reduce the incidence of sleep apnea (Dixon et al. 1997). Sjostrom et al. (1995) demonstrated that a 30kg weight loss in obese patients is capable of reducing the risk of diabetes by 14-fold, hypertension, dyslipidaemia and hypertriglyceridaemia by 4-fold while achieving 60% reduction in triglyceride levels and 10% reduction of hypertension. Every 1% decrease in body weight may potentially confer a decrease of 1mmHg in systolic blood pressure and 2mmHG in diastolic pressure (Rissanen et al. 1985). In addition, it is estimated that low-density-lipoprotein cholesterol levels decrease by approximately 1% for every kilogram of weight lost (Dattilo et al. 1992). Modest weight loss has also been shown to result in increased survival and reduce total mortality rates by 25% to 50% (Singh et al. 1992, Williamson et al. 1995).

Stage of development

Laparoscopic sleeve gastrectomy (LSG) is currently offered in various obesity treatment centres in Australia. However the extent of use is not known and there is little indication of the extent of SG being utilised as a single stage bariatric procedure in Australia. Efforts to determine the safety and efficacy of SG are ongoing in Australia; a comparative study (Cohen et al. [unpublished]) is expected to be completed by 2008.

Despite the fact that bariatric surgery is the only treatment for morbid obesity with proven long-term efficacy, surgery is not widely advocated by clinicians managing severely obese patients in Australia (Talbot et al. 2005). Considering the increasing prevalence of obesity in Australia and New Zealand, it is likely that LSG will gain substantial widespread use if it is proven to be safe and effective.

Existing comparators

At the time of writing, there is no gold-standard bariatric procedure and the selection of the operative technique is often influenced by patient characteristics and/or surgeon preference. The three main bariatric procedures utilised in Australia are:

a) Laparoscopic adjustable gastric banding (Lap-band)

Adjustable gastric banding, also known as lap-band, is the procedure of choice in more than 90% of cases in Australia (O'Brien et al. 2005). This procedure involves the use of a hollow band, made of silicone rubber, which is placed around the stomach near its upper end, creating a small pouch and a narrow passage into the rest of the stomach. The band is inflated with saline through a tube that connects the band to an access port placed under the skin. The band can be tightened or loosened over time to change the size of the passage by increasing or decreasing the amount of salt solution (National Institutes of Health 2004). The rationale of this procedure is that the small pouch created with the band fills with food quickly due to the restricted passage of food from the top of the stomach (pouch) to the bottom. This therefore induces a feeling of satiety and should result in decreased food intake.

b) Roux-en-Y gastric bypass (RYGBP)

RYGBP is the second most common bariatric procedure next to lap-band in Australia. During this procedure, a small stomach pouch is created to restrict food intake. Following this, a Y-shaped section of the small intestine is attached to the pouch to allow food to bypass the lower portion of the stomach, the duodenum, and the first portion of the jejunum. As this Y-connection is moved farther down the gastrointestinal tract, the amount of bowel capable of fully absorbing nutrients is progressively reduced. This therefore reduces the amount of calories and nutrients absorbed by the body. In some cases, a cholecystectomy is performed to avoid the formation of gallstones that may result from rapid weight loss (National Institutes of Health 2004).

c) Biliopancreatic diversion (BPD)/Duodenal switch (DS)

Biliopancreatic diversion/Duodenal switch involves the creation of a small stomach pouch (partial gastrectomy) while leaving the pyloric valve intact.

This procedure rearranges the small intestine to separate the flow of food from the flow of bile and pancreatic juices, therefore inhibiting the absorption of calories and nutrients. The duodenum is divided near the pyloric valve and the small intestine is divided as well. The portion of the small intestine that was previously connected to the large intestine is attached to the short duodenal segment next to the stomach. The remaining segment of the duodenum that is connected to the pancreas and gallbladder is attached closer to the large intestine (approximately 30 inches from the colon[5]. Meanwhile, the portion of the small intestine connected to large intestine is attached to the short duodenal segment next to the stomach. This separates the digestive enzymes and food into two different segments, preventing digestion until the final short 30 inch section of the intestine (Miller 2004).

d) Vertical banded gastroplasty

Vertical banded gastroplasty (VBG) is a restrictive procedure where the upper stomach near the oesophagus is stapled vertically to create a small pouch along the inner curve of the stomach. The outlet from the pouch to the rest of the stomach is restricted by a band, which delays the emptying of food from the pouch; therefore resulting in the feeling of satiety with smaller amounts of food.

Clinical Outcomes

Two randomised controlled trials (level II intervention evidence) and five comparative studies (level III intervention evidence) were retrieved that evaluated SG as a single-stage bariatric procedure and are presented in this report. There are also a substantial amount of case series studies (level IV intervention evidence) on SG, investigating its viability as a single-stage or part of a multi-stage bariatric procedure. For the purposes of this horizon scanning report, case series studies were not included for discussion due to the low level of evidence and the lack of direct comparisons to alternative bariatric procedures.

Safety

Complications

The randomised controlled trial by Himpens et al. (2006) compared laparoscopic sleeve gastrectomy (LSG) to lap-band (40 LSG, 40 lap-band) in obese patients and reported that both procedures were not exempt from major complications. The lap-band group experienced 7 major late complications compared. There were 2 major complications in the LSG group but these were both postoperative (Table 1). The overall complication rate was higher in lap-band patients (35%) compared to LSG patients (10%), indicating that LSG is relatively safer. However, it is

[5] This segment carriers the digestive enzymes and bile.

worth noting that the complications experienced by the LSG patients (intraperitoneal bleeding and gastric ischemia) were more severe. The case of gastric ischemia in one LSG patient was life-threatening and required total gastrectomy. The ischemia was a result of poor vascularisation to the gastric sleeve, caused by damage of the left gastric vessels during surgery (Himpens et al. 2006).

Table 1: Postoperative early and late major complications.

	Complications	No.	Treatment
Lap-band	Postoperative complications	-	
	Late complications	7	
	-pouch dilation	3	2 band removal, 1 RYGBP
	-gastric erosion	1	Conversion to RYGBP
	-disconnection	3	Reconnection
LSG	Postoperative complications	2	
	-intraperitoneal bleeding	1	Re-laparoscopy
	-gastric ischemia	1	Total gastrectomy
	Late complications	-	

Himpens et al. (2006)

Lap-band patients were associated with higher rates of minor complications (i.e. did not require reoperation) compared to LSG patients at 3-years post-surgery (Table 2). The shoulder pain experienced exclusively by lap-band patients was consequent to radiating pain from the upper left quadrant, where a port was positioned just distal to the costal margin during the procedure. Himpens and colleagues noted that 10% of LSG patients experienced mineral deficiency, specifically vitamin B12, which may have been caused by lower production of intrinsic factor and acid by the reduced stomach (Table 2).

Table 2: Postoperative minor complications.

	Complications	No.
Lap-band	**1-year:**	
	GERD (new cases)	3 (8.8%)
	Shoulder pain	3 (7.5%)
	Frequent vomiting	6 (15%)
	Poor choice alimentation	2 (5%)
	3-years:	
	GERD (new cases)	7 (20.5%)
	Shoulder pain	3 (8.5%)
	Frequent vomiting	10 (28.5%)
	Poor choice alimentation	17 (48.5%)
	Gastric ulcer	1 (2.8%)
LSG	**1-year:**	
	GERD (new cases)	7 (21.8%)
	Gastric pain	2 (5%)
	Frequent vomiting	1 (2.5%)
	Deficiency of minerals	2 (5%)

3-years:	
GERD (new cases)	1 (3.1%)
Frequent vomiting	5 (16.6%)
Poor choice alimentation	8 (26.6%)
Deficiency of minerals	3 (10%)

GERD: Gastroesophageal reflux disease

Himpens et al. (2006)

A greater proportion of LSG patients were affected with *de novo* gastroesophageal reflux disease (GERD) at 1-year post-surgery (lap-band: 8.8%; LSG: 21.8%), however this reversed at 3-years (lap-band: 20.5%; LSG: 3.1%). (Himpens et al. 2006). The relatively high incidence of GERD in LSG patients after 1-year may have been caused by the anatomical changes imposed on the angle of His during the LSG procedure where this angle is often blunted; leading to the manifestation of GERD in previously asymptomatic patients (2006).

In another randomised trial (Langer et al. 2005), the investigators highlighted that one SG patient (10%) required conversion to gastric bypass due to GERD 15 months postoperatively, while no such complication occurred in LAGB patients. No other safety data were presented.

Of the comparative studies retrieved (Table 3), one study on super-obese patients demonstrated that patients who underwent SG had substantially higher perioperative morbidity compared to duodenal switch (Hamoui et al. 2006). Meanwhile, two other comparative studies (Lee et al. 2007, Milone et al. 2005) reported that SG was relatively safe. Lee et al. (2007) compared four bariatric procedures, namely LSG, lap-band, laparoscopic RYGBP and duodenal switch; and demonstrated that patients who underwent LSG were less likely to suffer from major complications compared to laparoscopic RYGBP ($p < 0.03$) and duodenal switch ($p < 0.03$) (Table 3). In addition, the overall total complication rate for LSG patients was significantly lower compared to duodenal switch ($p < 0.01$). The results presented by Lee et al. (2007) indicate that SG has comparable morbidity rates to the popular lap-band procedure (p-value, not significant). However, it is interesting to note that reoperations for lap-band patients were almost twice to that of SG patients, but statistical tests did not detect any significance (Table 3) (Lee et al. 2007). In comparison to intragastric balloon, LSG was associated with fewer complications (Milone et al. 2005) (Table 3). However, this study is somewhat limited by the fact the comparator group was a combination of historical data from two previously published studies on intragastric balloon implantation.

Table 3: Safety outcomes (comparative studies).

Study	Study details	Safety outcomes
Hamoui et al. (2006)	Level III-2 intervention study Sleeve gastrectomy (via lapratomy)	**Intraoperative complications** Sleeve gastrectomy: One case of liver laceration. One case of splenic injury.

<table>
<tr>
<td></td>
<td>118 patients

<u>Duodenal switch</u>
701 patients</td>
<td>Perioperative complications
<u>Sleeve gastrectomy:</u>
Perioperative mortality – Two cases (30-days and 60-days post-surgery) due to cardiopulmonary failure and gastric leak (1.7%).
Late mortality – Two cases due to causes unrelated to surgery (1.7%).

Perioperative complications (overall) – 18 patients (15.3%)
<table>
<tr><th>Complications</th><th>No. of patients</th></tr>
<tr><td>Intraoperative</td><td></td></tr>
<tr><td>-myocardial infarction</td><td>1</td></tr>
<tr><td>-pancreatic tail leak</td><td>1</td></tr>
<tr><td>-bile leak (liver laceration)</td><td>1</td></tr>
<tr><td>Pulmonary</td><td></td></tr>
<tr><td>-respiratory failure</td><td>6</td></tr>
<tr><td>-pneumonia</td><td>2</td></tr>
<tr><td>GI perforations/leaks</td><td></td></tr>
<tr><td>-gastric leak</td><td>1</td></tr>
<tr><td>-perforated duodenal ulcer</td><td>1</td></tr>
<tr><td>-enterocutaneous fistula</td><td>1</td></tr>
<tr><td>Infectious</td><td></td></tr>
<tr><td>-wound dehiscence</td><td>3</td></tr>
<tr><td>-sepsis</td><td>2</td></tr>
<tr><td>Thromboembolic</td><td></td></tr>
<tr><td>-pulmonary embolism</td><td>1</td></tr>
<tr><td>-deep vein thrombosis</td><td>2</td></tr>
<tr><td>Miscellaneous</td><td></td></tr>
<tr><td>-negative exploratory laparotomy for suspected leak</td><td>1</td></tr>
<tr><td>-stroke</td><td>1</td></tr>
</table>
<u>Duodenal switch:</u>
Perioperative mortality – 1.4%

Perioperative complications (overall) – 2.9%

Note: Complication data for duodenal switch patients were limited and further details were not provided.</td>
</tr>
<tr>
<td>Lee et al. (2007)</td>
<td>Level III-2 intervention study

<u>Laparoscopic SG</u>
216 patients

<u>Lap-band</u>
271 patients

<u>Laparoscopic RYGBP</u>
303 patients

<u>Duodenal switch</u>
56 patients</td>
<td>No deaths or conversions to open procedure in any patient group.

<u>Laparoscopic SG</u>
<table>
<tr><td>Nonoperative admissions</td><td>5 patients (2.3%)</td></tr>
<tr><td>Reoperations</td><td>6 patients (2.8%)</td></tr>
<tr><td>Major complications</td><td>10 patients (4.6%)</td></tr>
<tr><td>Total complications</td><td>16 patients (7.4%)</td></tr>
</table>
<u>Lap-band</u>
<table>
<tr><td>Nonoperative admissions</td><td>4 patients (1.5%)</td></tr>
<tr><td>Reoperations</td><td>13 patients (4.8%)</td></tr>
<tr><td>Major complications</td><td>13 patents (4.8%)</td></tr>
<tr><td>Total complications</td><td>18 patients (6.6%)</td></tr>
</table></td>
</tr>
</table>

<table>
<tr>
<td></td>
<td></td>
<td>Laparoscopic RYGBP
<table><tr><td>Nonoperative admissions</td><td>12 patients (4.0%)</td></tr><tr><td>Reoperations</td><td>26 patients (8.6%)</td></tr><tr><td>Major complications</td><td>32 patients (10.6%)</td></tr><tr><td>Total complications</td><td>69 patients (22.8%)</td></tr></table>
Duodenal switch
<table><tr><td>Nonoperative admissions</td><td>4 patients (7.1%)</td></tr><tr><td>Reoperations</td><td>18 patients (32.1%)</td></tr><tr><td>Major complications</td><td>22 patients (39.3%)</td></tr><tr><td>Total complications</td><td>27 patients (48.2%)</td></tr></table></td>
</tr>
<tr>
<td>Milone et al. (2005)</td>
<td>Level III-3 intervention evidence

Laparoscopic SG
20 patients

Intragastric balloon
57 patients</td>
<td>Postoperative complications
Laparoscopic SG
One case of trocar-site infection (5%)

Intragastric balloon
Four cases of balloon removal (7%) due to balloon dysfunction, abdominal pain, and non-compliance.

One case of spontaneous elimination of balloon in stool (1.8%).

Two complications not requiring balloon removal (3.5%): severe vomiting and skin reaction of unknown origin.</td>
</tr>
</table>

Most of the retrieved studies indicate that SG is potentially as safe as lap-band surgery (Langer et al. 2005, Lee et al. 2007), and safer than laparoscopic RYGBP (Lee et al. 2007) or intragastric balloon implantation (Milone et al. 2005). However, there is evidence that despite lower complication rates to lap-band surgery, patients undergoing SG may be associated with a higher rate of serious/major complications (Himpens et al. 2006).

There is some contention with regards to the safety of SG compared to duodenal switch. Hamoui et al. (2006) observed substantially higher perioperative SG complications compared to those who underwent duodenal switch (15.3% vs. 2.9%, no statistical tests conducted). Conversely, Lee et al. (2007) reported that patients who underwent SG experienced major and total complication rates that were significantly lower in comparison to duodenal switch patients ($p < 0.01$) (Table 3). This discrepancy may have resulted from different preoperative patient characteristics between studies, especially the fact that the patients studied by Hamoui et al. (2006) were super-obese. It is also important to note that the SG group studied by Hamoui et al. (2006) had significantly higher preoperative BMI and age compared to the duodenal switch group, therefore the complication rates may be overstated in this study.

Operative duration/hospital stay

Only one of the comparative studies retrieved evaluated the operative time and length of hospital stay for SG patients relative to RYGBP, duodenal switch and lap-band surgery (Table 4). Overall, SG is associated with significantly shorter operative times compared to RYGBP ($p < 0.01$) and duodenal switch ($p < 0.01$). In addition to this, SG patients had shorter hospital stay relative RYBGP ($p < 0.01$) and duodenal switch ($p < 0.01$), but higher hospital stay compared to lap-band patients ($p < 0.01$) (Lee et al. 2007).

Table 4: Operative time and length of stay

	Sleeve gastrectomy	Lap-band	RYGBP	Duodenal switch
Operative time (min)	90 ± 30	89 ± 25	140 ± 37	226 ± 45
Length of stay (days)	1.9 ± 1.2	1.2 ± 0.7	2.8 ± 1.4	3.2 ± 2.0

Data presented as mean ± standard deviation.
RYGBP: Roux-en-Y gastric bypass

Lee et al. (2007)

Effectiveness

a) BMI and %EWL[6]

Sleeve gastrectomy vs. lap-band

Randomised controlled trials (Himpens et al. 2006, Langer et al. 2005) comparing SG to lap-band indicates that superior weight loss is achieved with SG in obese and morbidly obese patients. Himpens et al. (2006) demonstrated that median weight loss after 1-year was significantly greater for SG patients (26 [range: 0 to 46] kg) compared to lap-band (14 [range: -5 to 38] kg) ($p < 0.0001$). After three years, median weight loss achieved by LSG patients remained significantly higher (29.5 [range: 1 to 48] kg) compared to lap-band patients (17 [range: 0 to 40] kg) ($p < 0.0001$). Similarly, the decrease in median BMI after laparoscopic SG was significantly greater relative to lap-band ($p < 0.0001$) at 1-year post-surgery and this persisted to 3-years post-surgery ($p = 0.0004$) (Table 5). Correspondingly, the median %EWL for LSG patients was significantly higher at 1-year and 3-years post-surgery ($p = 0.0001$ and $p = 0.0025$, respectively; Table 5) (Himpens et al. 2006).

Langer et al. (2005) demonstrated that at 1-month and 6-months post-surgery, %EWL was significantly higher for SG patients compared to lap-band patients ($p = 0.005$ and $p = 0.001$, respectively) (Table 5).

[6] %EWL: Percent excess weight loss

Lee et al. 2007 showed that LSG is capable of achieving similar or greater weight loss when compared to lap-band (Table 6). At 1-year post-surgery, %EWL and absolute weight loss for LSG patients was significantly greater relative to lap-band ($p < 0.05$ and $p < 0.01$, respectively); whereas the BMI of LSG patients at 1-year was significantly higher in comparison to lap-band patients ($p < 0.01$). However, it should be noted that the mean preoperative BMI for LSG patients was 5 units higher than the preoperative BMI of lap-band patients ($p < 0.01$).

Overall, there is strong evidence (Level II and III intervention evidence) that SG is capable of achieving greater weight loss compared to lap-band surgery within the same time frame (Himpens et al. 2006, Lee et al. 2007, Langer et al. 2005), and that the superior weight loss is maintained up to 3-years post-surgery (Himpens et al. 2006).

Sleeve gastrectomy vs. duodenal switch, RYGBP and intragastric balloon

Patients who underwent SG achieved significantly lower %EWL at 1-year post-surgery relative to duodenal switch patients ($p < 0.001$, Hamoui et al. 2006; $p < 0.05$, Lee et al. 2007; Table 6). Hamoui et al. (2006) reported that actual weight loss was significantly lower for SG patients ($p = 0.05$); and at 18 months post-surgery, 44.6% of SG patients had > 50% EWL, significantly lower compared to 91.6% EWL for duodenal switch patients (Table 6).

Percent EWL was significantly lower for SG patients in the study by Lee et al. (2007), indicating that duodenal switch and RYGBP achieved better weight loss results (Table 6). However, it is important to note that SG patients in this study had the higher preoperative weight and BMI compared to duodenal switch and RYGBP patients. In *absolute terms*, SG patients actually achieved similar weight loss to duodenal switch patients and significantly higher weight loss compared to RYGBP patients ($p < 0.01$). The authors claimed that %EWL was inaccurate and misleading lower for the significantly more obese SG patients in this study due to the fact that for a given weight loss, more obese patients will have a lower % EWL compared to a less obese patient (Lee et al. 2007). Nevertheless, it is difficult to objectively determine if SG was equally/more effective compared to DS and RYGBP in this study. In comparison to intragastric balloon implantation, patients who underwent LSG achieved faster and greater weight loss (Milone et al. 2005) (Table 6).

The results indicate that SG does not seem to be capable of inducing %EWL to the extent that is possible with DS and RYGBP; but is significantly more effective compared to intragastric balloon implantation. It is debatable if the results of Lee et al. (2007), particularly the higher *absolute* weight loss, for SG patients are enough to claim that the effectiveness of the procedure is on par with DS and RYGBP. However, it is notable that SG, being a substantially less invasive procedure compared to DS and RYGBP, managed to achieve commendable weight loss in morbidly obese patients (Lee et al. 2007).

Table 5: Efficacy outcomes (Level II intervention evidence)

Study details	Patient numbers	Patient demographics	Preoperative co-morbidities	Weight reduction achieved (%EWL, BMI, absolute weight)	Satiety/ghrelin levels	Postoperative co-morbidities	Other reported outcomes
Himpens et al. (2006) Level II intervention evidence Size of gastric sleeve/bougie size 34Fr bougie	LSG 40 patients (9 males, 31 females) Lap-band 40 patients (7 males, 33 females)	LSG **BMI** 39 (30-53) kg/m^2 **Age** N/A Lap-band **BMI** 37 (30-47) kg/m^2 **Age** N/A	Not reported	Median (range) decrease of BMI and %EWL: **BMI** Lap-band: 1 year: 15.5 (5 to 39) kg/m^2; 3 years: 18 (0 to 39) kg/m^2 LSG: 1 year: 25 (0 to 45) kg/m^2; 3 years: 27.5 (0 to 48) kg/m^2 **% EWL** Lap-band: 1 year: 41.4 (-11.8 to +130.5)%; 3 years: 48 (0 to 124.8)% LSG: 1 year: 57.7 (0 to 125.5)%; 3 years: 66 (-3.1 to +152.4)%	LSG Loss of feeling of hunger: **1 year:** 75% **3 years:** 46.7% Loss of craving for sweet eating: **1 year:** 50% **3 years:** 23.3% Lap-band Loss of feeling of hunger: **1 year:** 42.5% **3 years:** 2.9% Loss of craving for sweet eating: **1 year:** 35% **3 years:** 2.9%	Not reported	Not reported
Langer et al. (2005) Level II intervention evidence Size of gastric sleeve/bougie size 48Fr bougie	LSG 10 patients (9 females, 1 male) Lap-band 10 patients (9 females, 1 male)	LSG **BMI** 48.3±5.7 kg/m^2 **Age** 39.3±11.7 years Lap-band **BMI** 46.7±3.5 kg/m^2 **Age** 38.5±13.6 years	LSG Diabetes: 1 patient (10%) Hypertension: 3 patients (30%) Dyslipidaemia: 8 patients (80%) Hyperuricemia: 4 patients (40%) Lap-band Diabetes: 3 patients (30%) Hypertension: 5 patients (50%) Dyslipidaemia: 7 patients (70%) Hyperuricemia: 2 patients (20%)	LSG **%EWL** 1-month: 29.8±12.8% 6-months: 61.4±16.3% Lap-band **%EWL** 1-month: 16.7±6.5% 6-months: 28.7±10.6%	LSG **Plasma ghrelin** 1-day: Decrease from 109.6±32.6 to 35±12.3 fmol/ml (p=0.005) 6-months: 44.8±13.2 fmol/ml Lap-band **Plasma ghrelin** 1-day: From 73.7±24.8 to 71.8±35.3 fmol/ml 1-month: 101.9±30.3 fmol/ml (p=0.028 compared to preop) 6-months: 104.9±51.1 fmol/ml (p=0.012, compared to preop)	Not reported	Not reported

Data expressed as mean ± SEM/(range) unless stated otherwise. LSG: laparoscopic SG; BMI: body mass index; %EWL: percent excess weight loss.

Table 6: Efficacy outcomes (Level III intervention evidence)

Study details	Patient numbers	Patient demographics	Preoperative co-morbidities	Weight reduction achieved (%EWL, BMI, absolute weight)	Satiety/ghrelin levels	Postoperative co-morbidities	Other reported outcomes
Cohen et al. (unpublished, ongoing) Level III-2 intervention evidence Size of gastric sleeve/bougie size 40Fr and 50Fr bougies	LSG 307 patients (201 females, 69 males) Lap-band 343 patients (289 females, 54 males)	LSG **BMI** 41 (26-75) kg/m^2 **Age** 43 years Lap-band **BMI** 39 (29-70) kg/m^2 **Age** 43 years	LSG Diabetes: 41 patients (13.4%) Lap-band Not available at the time of writing	LSG **% EWL** 1-year: 56±21% 2-years: 60±20% **Weight loss** 1-year: 32±17.7% 2-years: 41±31.5kg Lap-band **% EWL** 1-year: 38±17% 2-years: 47±19% **Weight loss** 1-year: 19±10.8% 2-years: 23±11.7kg	Not available at the time of writing	LSG 21 diabetic patients experienced complete resolution (6.8%). 9 diabetic patients reduced medication dosage (2.9%).	Not available at the time of writing
Hamoui et al. (2006) Level III-2 intervention evidence Size of gastric sleeve/bougie size Not reported	Sleeve gastrectomy 118 patients (99 females, 19 males) Duodenal switch 701 patients (553 females, 148 males)	Sleeve gastrectomy **BMI** 55 (37-108)kg/m^2 **Age** 47(16-70) years Duodenal switch **BMI** 51 (34-95) kg/m^2 **Age** 42(16-71) years *Note: Both BMI and age significantly different between groups (p<0.001)*	Sleeve gastrectomy Diabetes: 49 patients (41.5%) Hypertension: 79 patients (66.9%) Sleep apnoea: 53 patients (44.9%) Duodenal switch Not stated	Sleeve gastrectomy **%EWL** Median: 49.4% (26.8-79.6) at 1-year **Weight loss** 48.6 (10.5-115.5) kg at 1-year Duodenal switch **%EWL** Median: 67.3% (30.4-117) at 1-year **Weight loss** 53.6 (17.7-148.6) kg at 1-year	Not reported	Sleeve gastrectomy 23 diabetic patients experienced complete resolution (46.9%) 11 diabetic patients reduced medication dosage (22.4%) 12 hypertensive patients experienced disease resolution (15.2%) 13 hypertensive patients experienced improvement (16.5%)	Sleeve gastrectomy At 1-year, proportion of patients with normal levels of: Serum albumin 100% Serum haemoglobin 86.1% Serum calcium 87.2% Duodenal switch At 1-year, proportion of patients with normal levels of: Serum albumin 94.1% Serum haemoglobin 63.7% Serum calcium 79.3%

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Study	Patient numbers	Patient demographics	Preoperative co-morbidities	Weight reduction achieved (%EWL, BMI, absolute weight)	Satiety/ghrelin levels	Postoperative co-morbidities	Other reported outcomes
Lee et al. (2007) Level III-2 intervention evidence Size of gastric sleeve/bougie size 60-80ml 32Fr bougie	LSG 216 patients (173 females, 43 males) Lap-band 271 patients (237 females, 34 males) Lap RYGBP 303 patients (257 females, 46 males) Duodenal switch 56 patients (49 females, 7 males)	LSG **BMI** 49±11 kg/m^2 **Age** 43±11 years Lap-band **BMI** 42±5 kg/m^2 **Age** 42±12 years Lap RYGBP **BMI** 46±6 kg/m^2 **Age** 43±19 years Duodenal switch **BMI** 47±6 kg/m^2 **Age** 42±8 years	Not reported	At 1-year: LSG **BMI:** 37±9 kg/m^2 **%EWL:** 59±17% **Weight Lost:** 129±51 lbs Lap-band **BMI:** 32±5 kg/m^2 **%EWL:** 47±20% **Weight Lost:** 58±27 lbs Lap RYGBP **BMI:** 28±5 kg/m^2 **%EWL:** 75±16% **Weight Lost:** 110±37 lbs Duodenal switch **BMI:** 27±4 kg/m^2 **%EWL:** 79±12% **Weight Lost:** 120±24 lbs	Not reported	Not reported	Not reported
Milone et al. (2005) Level III-3 intervention evidence Size of gastric sleeve/bougie size 150-200ml 60Fr bougie	LSG 20 patients (13 males, 7 females) Intragastric balloon 57 patients (33 males, 24 females) *[Historical controls from two studies]*	LSG **BMI** 68.8 (60.0-85.1) kg/m^2 **Age** 43 (27-63) years Intragastric balloon **BMI** a) 60.2 (58.0-72.0) kg/m^2 b) 58.4±6.6 kg/m^2 **Age** a) 38 (20-56) years b) 43 (33-54) years	LSG Hypertension: 11 patients (55%) Sleep apnoea: 12 patients (60%) Diabetes: 6 patients (30%) Osteoarthritis: 19 patients (95%) Gastroesophageal reflux: 5 patients (25%) Hypercholesterolaemia: 6 patients (30%) Depression: 14 patients (70%)	At 6-months post-treatment: LSG **BMI loss:** 15.9 kg/m^2 **%EWL:** 34.9% **Weight loss:** 46 kg Intragastric balloon **a)** **BMI loss:** 6.4 kg/m^2 **%EWL:** 21% **Weight loss:** 18 kg **b)** **BMI loss:** 9.4 kg/m^2 **%EWL:** 26.1% **Weight loss:** 26 kg	Not reported	Investigators stated that each patient from LSG and intragastric balloon group experienced improvement of co-morbidities such as hypertension, osteoarthritis and sleep apnoea. No actual data presented for either treatment groups.	Not reported

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Study	Patient numbers	Patient demographics	Preoperative co-morbidities	Weight reduction achieved (%EWL, BMI, absolute weight)	Satiety/ghrelin levels	Postoperative co-morbidities	Other reported outcomes
		Note: (a) Weiner et al. (b) Busetto et al. *Data presented as mean (range)*	Intragastric balloon Hypertension: 30 patients (69.8%) Sleep apnoea: 29 patients (67.4%) Diabetes: 19 patients (44.2%) Osteoarthritis: 30 patients (69.8%) Gastroesophageal reflux: None Hypercholesterolaemia: 12 patients (27.9%) Depression: 6 patients (14%)	*Note: (a) Weiner et al. (b) Busetto et al.*			
Vidal et al. (2007) Level III-2 intervention evidence Size of gastric sleeve/bougie size 46-50Fr bougie	LSG 35 patients (15 males, 20 females) Lap RYGBP 50 patients (17 males, 33 females) *Note: all patients had type II diabetes mellitus*	LSG **BMI** 52.0 ± 1.2 kg/m^2 **Age** 48.3 ± 1.6 years Lap RYGBP **BMI** 47.6 ± 0.7 kg/m^2 **Age** 46.6 ± 0.6 years	LSG Hypertension: 65.7% Dyslipidaemia: 34.0% Metabolic syndrome: 91.4% Lap RYGBP Hypertension: 72.0% Dyslipidaemia: 48.0% Metabolic syndrome: 94.0%	At 4-months post-surgery: LSG Weight loss (% from baseline): 20.6 ± 0.7% Excess BMI loss: 41.4 ± 1.8% Lap RYGBP Weight loss (% from baseline): 21.0 ± 0.6% Excess BMI loss: 45.3 ± 1.3%	Not reported	LSG T2DM resolved: 51.4% Lap RYGBP T2DM resolved: 62%	Various metabolic changes reported. *-Detailed tables reproduced within relevant sections of text-*

Data expressed as mean ± SEM/(range) unless stated otherwise.
LSG: laparoscopic SG; Lap RYGBP: laparoscopic roux-en-Y gastric bypass; BMI: body mass index; %EWL: percent excess weight loss.

b) Satiety/appetite outcomes and ghrelin levels

The randomised trial by Himpens et al. (2006) reported that 75% of SG patients experienced the loss of feeling of hunger (abolished or diminished in questionnaire) after 1-year, significantly greater in comparison to 42.5% for lap-band patients ($p = 0.003$). After 3-years, this decreased to 46.7% for SG patients and 2.9% for lap-band patients ($p < 0.0001$). The investigators noted that a greater proportion of SG patients experienced a loss of craving for sweet eating (abolished or diminished in questionnaire) compared to lap-band patients at 1-year (50% vs. 35%,) and 3-years (23% vs. 2.9%) post-surgery, but the differences were not statistically significant (Table 6).

It is postulated that ghrelin, a peptide hormone mainly produced in the stomach fundus, is involved in the regulation of appetite. Circulating ghrelin levels decrease with feeding and increase before meals, achieving concentrations sufficient to stimulate hunger and food intake. Previous studies on ghrelin have shown that ghrelin levels increase significantly after diet-induced weight loss and appear to play a role in weight regain (Langer et al. 2005). However, the available evidence on ghrelin levels after bariatric surgery is somewhat limited and conflicting. Some studies have demonstrated significant reductions of plasma ghrelin levels following RYGBP (Cummings et al. 2001, Geloneze et al. 2003). Other studies found no change in plasma ghrelin levels in weight-stable RYGBP patients, but a significant increase in actively weight-losing RYGBP patients (Faraj et al. 2003, Holdstock et al. 2003). With regards to lap-band surgery, some investigators have observed no changes in ghrelin levels (Hanusch-Enserer et al. 2003), while others described significant increases (Schindler et al. 2004, Stoekli et al. 2004). One proposed explanation to the observation that RYGBP decreases ghrelin levels while lap-band may increase ghrelin levels is that ghrelin producing cells within the gastric fundus does not have contact with ingested nutrients resulting in override suppression after RYGBP (Cummings et al. 2001). Conversely, lap-band surgery does not bypass the ghrelin producing cells; therefore the cells remain functioning and result in compensatory ghrelin secretion and therefore elevated serum ghrelin levels after surgery.

In the only SG comparative study retrieved which measured plasma ghrelin levels (Langer et al. 2005), SG patients demonstrated a significant decrease in plasma ghrelin levels one day post-surgery compared to preoperative levels (35.8 fmol/ml vs. 109.6 fmol/ml; $p = 0.005$), while lap-band patients experienced no change. During the 1- and 6-month follow up, plasma ghrelin levels for SG patients remained stable at 43.7 fmol/ml and 44.8 fmol/ml, respectively. With regards to lap-band patients, significant *increases* of plasma ghrelin levels were observed at 1-month ($p = 0.028$) and 6-months ($p = 0.012$) compared to preoperative levels (Table 6). Because the restrictive effect on food intake is comparable between SG and lap-band, it is highly plausible that the superior weight loss observed in LSG patients are attributable to the permanently lower ghrelin levels which prevent an increase in appetite as a compensatory mechanism.

e) Co-morbidities

Considering the weight loss that can be achieved by SG (Table 5, Table 6), it is therefore reasonable to expect that that it should translate to decreased co-morbidities, such as diabetes and hypertension. Vidal et al. (2007) conducted a 4-month prospective comparative trial and found that both LSG and RYGBP patients achieved similar weight loss (20.6% vs 21.0%, respectively) and resolution of type II diabetes mellitus (51.4% vs. 62.0%, respectively; $p = 0.332$) (Table 6). The changes in clinical and metabolic variables are presented in Table 7 and are clearly comparable between the two bariatric procedures. The proportion of subjects requiring oral hypoglycaemic agents and/or insulin declined significantly for both LSG and RYGBP patients as well (28.6% [$p < 0.05$] and 34% [$p < 0.05$], respectively) (Vidal et al. 2007).

Table 7: Change in clinical and metabolic variables in morbidly obese patients who underwent LSG or RYGBP.

	Sleeve gastrectomy (n=35)	RYGBP (n=50)
Weight loss (% from baseline)	20.6 ± 0.7	21.0 ± 0.6
Excess BMI loss (%)	41.4 ± 1.8	45.3 ± 1.3
Δ Waist circumference (%)	-13.8 ± 1.3	-13.5 ± 1.1
Δ Fasting plasma glucose (%)	-32.9 ± 3.1	-32.3 ± 2.6
Δ HbA1c (%)	-22.9 ± 2.5	-23.5 ± 1.8
Δ HDL-cholesterol (%)	-16.7 ± 2.8	-12.5 ± 2.8
Δ Triglycerides (%)	-19.8 ± 5.4	-22.3 ± 4.2
Δ Systolic blood pressure (%)	-9.4 ± 1.6	-5.3 ± 1.7
Δ Diastolic blood pressure (%)	-7.9 ± 3.8	-4.2 ± 2.3
Δ Metabolic syndrome score (%)	-12.8 ± 4.8	-11.6 ± 3.9
Δ HOMA-IR (%)	-51.6 ± 7.3	-60.8 ± 3.2
Δ C-reactive protein (%)	-11.1 ± 9.5	-17.9 ± 6.3

Data expressed as mean ± SEM
RYGBP: Roux-en-Y gastric bypass; Δ indicates 'change'; BMI: body mass index; HbA1c: glycosylated haemoglobin; HOMA-IR: homeostasis model assessment of insulin resistance.

Vidal et al. (2007)

Hamoui et al. (2006) observed complete resolution of diabetes in 46.9% (23/49 patients) of patients who were diagnosed preoperatively, while an additional 22.4% (11/49 patients) managed to reduce medication dosage 1-year after SG. Meanwhile, 15.2% (12/79 patients) of patients with hypertension achieved complete resolution and 16.5% (13/79 patients) experienced improvement of symptoms.

The evidence demonstrates that SG is associated with a high resolution rate of type II diabetes mellitus within 4-months after surgery and the rate of resolution was comparable to the more invasive and complicated RYGBP (Vidal et al. 2007). However, the two patient groups in the study by Vidal et al. (2007) were not matched for preoperative BMI (SG patients were significantly more obese

compared to RYGBP patients, $p < 0.01$). Nevertheless, this does not adversely alter the interpretation of the results presented.

e) Gastric sleeve dilatation

One particular concern relating to the use of SG is the potential for gastric sleeve dilatation over time, which may limit the restrictive effect of the procedure therefore resulting in weight regain. The case series by Langer et al. (2006) is the first and only study available at the time of writing which investigated this issue specifically. At a mean follow-up of 20 months, dilatation of the gastric sleeve was noted in one patient (4.3%) while weight regain after initial successful weight loss was observed in 13% (3/23 patients) of patients. Although these results indicate that gastric sleeve dilatation is a relatively uncommon event, it is important to note the limitations of this study; particularly the small patient cohort and the short follow-up duration. Pending the publication of further studies, the incidence of sleeve dilatation and its potential contribution as a limiting factor to weight loss remains unresolved.

Potential Cost Impact

Cost Analysis

There are no studies available at the time of writing that examines the cost-effectiveness of SG. The actual total cost of SG is not known, however the cost of all instruments and disposables is less than AU$3000. In comparison to lap-band, currently the most used procedure is Australia, which costs AU$3500 for the band itself, the cost of equipment for SG appears attractive. The potentially lower complication rates for SG patients (Himpens et al. 2006, Lee et al. 2007, Langer et al. 2005) may contribute to further savings, however this may be offset by the occurence of more severe complications (Himpens et al. 2006).

Long-term studies evaluating the durability of weight loss from SG and safety of the procedure compared to lap-band and other existing bariatric procedures are required before more detailed analysis of cost can be conducted.

Ethical Considerations

Informed Consent

Patients who choose to undergo SG should be made aware of the risks associated with this procedure, particularly the fact that it is a relatively new/emerging technique with limited long-term safety data. The patient should be informed that the evidence on the long-term durability of weight loss is currently limited although its relative efficacy to lap-band appears promising. In addition, clinicians

should clarify that sleeve gastrectomy involves the removal of a large portion of the stomach and is not reversible. In the event of serious complications, the patient should be informed that total gastrectomy may be required.

In all circumstances, patients should receive adequate counselling before undergoing any form of bariatric surgery. The clinical guidelines for the treatment of obesity clearly states that patients should only receive bariatric surgery after attempts of weight loss with dietary, behavioural and pharmacological interventions have failed (NHMRC 2003). Furthermore, patients should be aware of the fact that there is no single, effective treatment for *all* overweight and obese individuals and therefore should have realistic expectations before receiving bariatric surgery.

In some situations, the health benefits that can be derived from weight loss may not actually outweigh the excessive costs in terms of the effort required and the disruption of quality of life, such as elderly adults.

Access Issues

Bariatric surgery is conducted in specialist medical centres under trained clinicians; therefore it is likely that SG will be confined to major cities.

Training and Accreditation

Training

As SG is a relatively new bariatric surgery technique and it is not widely practised in Australia or New Zealand, adequate training is required before a surgeon is allowed to perform this procedure. Training and accreditation is current being addressed by the Obesity Surgery Society of Australia and New Zealand and the Royal Australasian College of Surgeons.

Clinical Guidelines

The clinical practice guidelines for the management of overweight and obesity in adults (NHMRC 2003) acknowledges that bariatric surgery is the most effective treatment for severe obesity currently available. However, sleeve gastrectomy, being a relatively new procedure, was not specifically mentioned within these guidelines. The NHMRC recommends that clinicians should be aware of the following provisos issued by the US National Institutes of Health:

- Severely obese patients seeking therapy for the first time should be considered for treatment in a non-surgical program with integrated components of a dietary regimen, appropriate exercise, and behaviour

modification and support. Surgery should be considered only if non-operative measures for weight loss have failed.

- Bariatric surgery should be considered only for well-informed, motivated patients with acceptable operative risks.
- Candidates for surgical procedures should be selected after careful evaluation by a multi-disciplinary team with medical, surgical and nutritional expertise.
- The operation should be performed by a surgeon who has substantial experience with the procedure and is working in a clinical setting with adequate support for all aspects of managements and assessment.
- Lifelong medical surveillance after surgical therapy is essential.

Limitations of the Assessment

Methodological issues and the relevance or currency of information provided over time are paramount in any assessment carried out in the early life of a technology.

Horizon Scanning forms an integral component of Health Technology Assessment. However, it is a specialised and quite distinct activity conducted for an entirely different purpose. The rapid evolution of technological advances can in some cases overtake the speed at which trials or other reviews are conducted. In many cases, by the time a study or review has been completed, the technology may have evolved to a higher level leaving the technology under investigation obsolete and replaced.

A Horizon Scanning Report maintains a predictive or speculative focus, often based on low level evidence, and is aimed at informing policy and decision makers. It is not a definitive assessment of the safety, effectiveness, ethical considerations and cost effectiveness of a technology.

In the context of a rapidly evolving technology, an Horizon Scanning Report is a 'state of play' assessment that presents a trade-off between the value of early, uncertain information, versus the value of certain, but late information that may be of limited relevance to policy and decision makers.

This report provides an assessment of the current state of development of sleeve gastrectomy, its present and potential use in the Australian public health system, and future implications for the use of this technology.

Search Strategy used for the Report

The sources utilised in this assessment are listed in Table 8. The medical literature was searched with the search terms outlined in Table 9 to identify relevant studies up to April 2007 in English only. In addition to this, major international health technology assessment databases and clinical trial registers were searched.

Table 8: Literature sources utilised in assessment

Source	Location
Electronic databases	
AustHealth	University of Adelaide library
Australian Medical Index	University of Adelaide library
CINAHL	University of Adelaide library
Cochrane Library – including Cochrane Database of Systematic Reviews, Database of Abstracts of Reviews of Effects, the Cochrane Central Register of Controlled Trials (CENTRAL), the Health Technology Assessment Databese, the NHS Economic Evaluation Database	University of Adelaide library
Current Contents	University of Adelaide library
Embase	Personal subscription
Pre-Medline and Medline	University of Adelaide library
PyscINFO	Personal subscription
RACS electronic library	Personal subscription
Internet	
Blue Cross and Blue Shield Association's Technology Evaluation Center	http://www.bcbs.com/tec/
Canadian Agency for Drugs and Technologies in Health	http://www.cadth.ca
Current Controlled Trials metaRegister	http://www.controlled-trials.com/
EuroScan	http://www.euroscan.bham.ac.uk/
Health Technology Assessment International	http://www.htai.org/

International Network for agencies for Health Technology Assessment	http://www.inahta.org
Medicines and Healthcare products Regulatory Agency (UK)	http://www.mhra.gov.uk/
US Food and Drug Administration, Center for Devices and Radiological Health	http://www.fda.gov/cdrh/index.html
US Food and Drug Administration, Manufacturer and User Facility Device Experience Database	http://www.fda.gov/cdrh/maude.html
UK National Research Register	http://www.nrr.nhs.uk/
Websites of specialty organisations	http://www.health.gov.au/ (Obesity guidelines) or http://www.obesityguidelines.gov.au

Table 9: Search terms utilised

Search terms
MeSH Obesity/surgery*; obesity, Morbid/surgery; weight loss; gastrectomy/methods*; gastrectomy*/adverse effects; weight loss. **Text words** Sleeve gastrectomy; vertical gastrectomy; ghrelin; bariatric surgery. **Limits** English, human

Availability and Level of Evidence

Two randomised controlled trials (Level II screening evidence) and five comparative studies (Level III intervention evidence) were retrieved for discussion in this horizon scanning report. The profiles of the included studies are summarised in Appendix B.

The medical literature (Table 12) was searched utilising the search terms outlined in Table 13 to identify relevant studies and reviews, up to September 2007. In addition, major international health assessment databases were searched.

Sources of Further Information

The following is a list of future/ongoing studies on sleeve gastrectomy:

Comparison of Laparoscopic Sleeve Gastrectomy and Roux-Y-Gastric Bypass in the Treatment of Morbid Obesity

This study aims to compare sleeve gastrectomy and RYGBP in a prospective randomized study. Primary outcome measures are effectiveness in terms of weight loss, reduction in co-morbidity and quality of life, secondary outcome measures are early morbidity, duration and cost of the operation, late morbidity, re-operations (for complications, for insufficient weight loss), postoperative changes of gastrointestinal hormones. Expected completion date: August 2011. (ClinicalTrials.gov identifier: NCT00356213).

Laparoscopic Sleeve Gastrectomy with and without omentectomy

This study aims to determine the clinical and metabolic effects of sleeve gastrectomy with or without omentectomy in the treatment of morbid obesity. The investigators hypothesize that the endocrine suppression of ghrelin (appetite hormone) and resistin (insulin antagonist) provided by sleeve gastrectomy and omentectomy (omentum or intra-abdominal fat removal) will provide clinical and metabolic benefits for morbidly obese patients. Expected completion date: N/A (study began April 2007) (ClinicalTrials.gov identifier: NCT00434525).

A Trial of Advanced Medical Therapy vs. Advanced Medical Therapy Plus Bariatric Surgery for the Resolution of Type 2 Diabetes

The aim of the study is to compare the relative clinical outcomes between advanced medical therapy alone or advanced medical therapy combined with bariatric surgery (either Roux-en-Y gastric bypass (RYGBP) or laparoscopic sleeve gastrectomy) in patients with type 2 diabetes and a body mass index (BMI) between 30 and 40 kg/m2. The study will examine the short and long term effects of each intervention on biochemical resolution of diabetes, diabetic complications and end-organ damage. Expected completion date: N/A (study began February 2007) (ClinicalTrials.gov identifier: NCT00432809).

Neuroendocrine Brake for Type 2 Diabetes Mellitus

Evaluate safety and efficacy of the illeal interposition associated with a sleeve gastrectomy and the illeal interposition associated with a diverted sleeve gastrectomy. Expected completion date: N/A (Study began March 2006) (ClinicalTrials.gov identifier: NCT00450710).

Laparoscopic Gastric Banding Versus Sleeve Gastrectomy

This study aims to determine the clinical and metabolic outcomes of two available bariatric restrictive procedures: laparoscopic adjustable gastric banding and laparoscopic sleeve gastrectomy for the treatment of morbidly obesity (BMI>35

with comorbidities or BMI>40). Expected completion date: N/A (Study began April 2007) (ClinicalTrials.gov identifier: NCT00434655).

Australian comparative study (Cohen et al., personal communication)

Preliminary results from the ongoing comparative study by Cohen et al. (personal communication) indicates that %EWL for LSG patients is substantially greater at 1 and 2-years post-surgery in comparison to lap-band patients (Table 10). However, considering the absence of statistical tests at this point of time and the ongoing nature of this study, it is not possible to state conclusively that %EWL achieved by LSG is significantly greater relative to lap-band for this study. This study is expected to be completed in 2008.

Table 10: Preliminary results Cohen et al. (personal communication)

Study details	Patient numbers	Patient demographics	Preoperative co-morbidities	Weight reduction achieved (%EWL, BMI, absolute weight)	Postoperative co-morbidities
Cohen et al. (unpublished, ongoing) Level III-2 intervention evidence Size of gastric sleeve/bougie size 40Fr and 50Fr bougies	LSG 307 patients (201 females, 69 males) Lap-band 343 patients (289 females, 54 males)	LSG **BMI** 41 (26-75) kg/m^2 **Age** 43 years Lap-band **BMI** 39 (29-70) kg/m^2 **Age** 43 years	LSG Diabetes: 41 patients (13.4%) Lap-band Not available at the time of writing	LSG **% EWL** 1-year: 56±21% 2-years: 60±20% **Weight loss** 1-year: 32±17.7% 2-years: 41±31.5kg Lap-band **% EWL** 1-year: 38±17% 2-years: 47±19% **Weight loss** 1-year: 19±10.8% 2-years: 23±11.7kg	LSG 21 diabetic patients experienced complete resolution (6.8%). 9 diabetic patients reduced medication dosage (2.9%).

Conclusions

The prevalence of obesity has risen to alarming levels. In Australia, approximately 62% of men and 45% of women are overweight or obese, a situation that places substantial strain to the healthcare system and the economy. Various treatment strategies have been devised and implemented as a means of treating obesity. At first glace, the problem appears to be easy to rectify; reduce caloric intake and increase physical activity. However, medical research has proven that the treatment of obesity, particularly in patients who are morbidly obese and beyond, is not an easy task. Merely 25% of patients are able to maintain lost weight 4-years afters a caloric restriction program, and this is with the caveat that the program is run well enough to attain high participation rates for a minimum of 12 months. Pharmacological interventions although effective to an extent are associated with side effects and the relative effectiveness between these weight-loss drugs is not known (Shekelle et al. 2004). Furthermore, it has been established that dietary, behavioural and pharmacological treatments are not effective for extreme forms of obesity (BMI≥40). The NHMRC and US National Institutes of Health has acknowledged that bariatric surgery is the most effective treatment option for achieving adequate and sustained weight loss in morbidly obese patients. There is no gold standard bariatric procedure at the time of writing, however lap-band is the procedure of choice in Australia; accounting for >90% of cases (O'Brien et al. 2005).

A relatively new procedure, sleeve gastrectomy, has recently emerged as a potential alternative to existing techniques. In the strictest sense, SG is technically not a new procedure, it was utilised as a method to resect gastric cancers before being considered as a bariatric procedure. Until recently, it was widely believed that the weight loss than can be achieved with SG is insufficient and therefore it is often performed as part of a multi-stage bariatric procedure (Frezza 2007). SG is often performed laparoscopically and is essentially a partial gastrectomy where the greater curvature of the stomach is removed to reduce the size of the stomach. The resulting decrease in stomach size induces the feeling of satiety sooner with less amount of food; therefore restricting caloric intake and decreasing the patient's appetite.

Randomised trials (Himpens et al. 2006, Langer et al. 2005) and comparative studies (Lee et al. 2007, Cohen et al. [unpublished]) are generally supportive of the effectiveness of SG in inducing superior weight loss compared to lap-band. Both of the included randomised controlled trials highlighted that %EWL was significantly higher for SG patients (Himpens et al. 2006, Langer et al. 2005), and this was sustained up to 3-years post-surgery (Himpens et al. 2006). When SG was compared to duodenal switch and RYGBP, the %EWL achieved was significantly lower (Lee et al. 2007, Hamoui et al. 2006). This was expected considering the fact that duodenal switch and RYGBP are substantially more invasive procedures that employ malabsorptive techniques. However, one study

(Vidal et al. 2007) reported that LSG induced similar weight loss to RYGBP. This indicates that SG has the potential to achieve comparable results to RYGBP. None of the studies included presented longer term data which would provide some insight as to whether SG patients eventually attain the similar extent of weight loss as duodenal switch. Despite the fact that weight loss was less impressive relative to duodenal switch and perhaps RYGBP, the results attained with the use of SG is commendable in light of the relative ease and simplicity of the procedure.

One of the most interesting aspects of SG is the fact that plasma ghrelin levels decrease significantly following surgery (Langer et al. 2005). Studies have postulated that circulating ghrelin levels decrease with feeding and increase before meals, indicating a role in appetite regulation. A high concentration of ghrelin stimulates hunger and therefore leads to excess consumption of food. Langer et al. (2005) pointed out that the main sources of ghrelin, the gastric fundus and the greater curvature, are completely resected during SG. This therefore explains the significant reduction in ghrelin concentrations compared to lap-band patients where an increase was observed (Langer et al. 2005). It therefore appears that SG is not merely a restrictive procedure, but is augmented by hormonal effects as well. The reduced ghrelin levels may have contributed substantially to the significantly greater weight loss observed in SG patients compared to lap-band patients (Langer et al. 2005, Himpens et al. 2006, Lee et al. 2007, Cohen et al. [unpublished]).

The weight loss induced by SG should translate to decreased co-morbidities, as confirmed by Vidal et al. (2007) where 50% patients with type II diabetes experienced complete resolution while 28.6% required less medication at 4-months post-surgery. This was comparable to RYGBP patients, a predictable outcome based on the fact that both patient groups had similar weight loss for this study. One of the factors that may limit the efficacy of SG is the incidence of gastric sleeve dilatation. To date, only one case series study has specifically examined this issue and found that only one patient (3%) experienced sleeve dilatation (Langer et al. 2006). However, further long-term studies with larger patient cohorts are required before a more accurate estimate of the incidence of sleeve dilatation can be determined.

As with all bariatric procedures, SG has risks associated with its utilisation; the majority of studies indicate that SG has comparable/lower complication rates relative to lap-band (Himpens et al. 2006, Langer et al. 2005) and substantially safer compared to RYGBP (Lee et al. 2006) and intragastric balloon implantation (Milone et al. 2005). Although complication rates were similar/lower relative to lap-band, the complications experienced by SG patients were more severe (Himpens et al. 2006). Meanwhile, the safety of SG compared to duodenal switch is debatable (Lee et al. 2007, Hamoui et al. 2006). Hospital stay and operating time is comparable to lap-band patients, and is significantly shorter in contrast to RYGBP and duodenal switch (Lee et al. 2007).

Overall, the evidence from randomised trials and comparative studies suggest the weight loss achievable with SG is commendable and provides some support with regards to its use as a stand-alone procedure. Its effectiveness in super-obese patients (BMI≥50) compared to established bariatric procedures was not explored in the included studies, but some encouraging evidence exists with regards to its use as a 1st stage procedure prior to more invasive procedures (RYGBP) (Sauerland et al. 2005). It is important to note that the long-term safety and durability of weight loss for SG remains unknown, with one randomised trial demonstrating that SG patients experienced more severe complications (Himpens et al. 2006) and the evidence for the incidence of sleeve dilation is lacking (Langer et al. 2006). Further randomised trials would be required before the efficacy of SG relative to existing bariatric procedures (particularly RYGBP and DS) can be determined. The effects of SG on plasma ghrelin levels and the subsequent effect on appetite warrants further investigation as well.

Appendix A: Levels of Evidence

Designation of levels of evidence according to type of research question

Level	Intervention [§]	Diagnosis [**]	Prognosis	Aetiology [†††]	Screening
I [*]	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies	A systematic review of level II studies
II	A randomised controlled trial	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, [§§] among consecutive patients with a defined clinical presentation [††]	A prospective cohort study [***]	A prospective cohort study	A randomised controlled trial
III-1	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)	A study of test accuracy with: an independent, blinded comparison with a valid reference standard, [§§] among non-consecutive patients with a defined clinical presentation[††]	All or none [§§§]	All or none [§§§]	A pseudorandomised controlled trial (i.e. alternate allocation or some other method)
III-2	A comparative study with concurrent controls: Non-randomised, experimental trial [†] Cohort study Case-control study Interrupted time series with a control group	A comparison with reference standard that does not meet the criteria required for Level II and III-1 evidence	Analysis of prognostic factors amongst untreated control patients in a randomised controlled trial	A retrospective cohort study	A comparative study with concurrent controls: Non-randomised, experimental trial Cohort study Case-control study
III-3	A comparative study without concurrent controls: Historical control study Two or more single arm study [‡] Interrupted time series without a parallel control group	Diagnostic case-control study [††]	A retrospective cohort study	A case-control study	A comparative study without concurrent controls: Historical control study Two or more single arm study
IV	Case series with either post-test or pre-test/post-test outcomes	Study of diagnostic yield (no reference standard) [‡‡]	Case series, or cohort study of patients at different stages of disease	A cross-sectional study	Case series

Tablenotes

* A systematic review will only be assigned a level of evidence as high as the studies it contains, excepting where those studies are of level II evidence.

§ Definitions of these study designs are provided on pages 7-8 *How to use the evidence: assessment and application of scientific evidence* (NHMRC 2000b*)*.

† This also includes controlled before-and-after (pre-test/post-test) studies, as well as indirect comparisons (ie. utilise A vs B and B vs C, to determine A vs C).

‡ Comparing single arm studies ie. case series from two studies.

** The dimensions of evidence apply only to studies of diagnostic accuracy. To assess the effectiveness of a diagnostic test there also needs to be a consideration of the impact of the test on patient management and health outcomes. See *MSAC (2004) Guidelines for the assessment of diagnostic technologies*. Available at: www.msac.gov.au .

§§ The validity of the reference standard should be determined in the context of the disease under review. Criteria for determining the validity of the reference standard should be pre-specified. This can include the choice of the reference standard(s) and its timing in relation to the index test. The validity of the reference standard can be determined through quality appraisal of the study. See Whiting P, Rutjes AWS, Reitsma JB, Bossuyt PMM, Kleijnen J. The development of QADAS: a tool for the quality assessment of studies of diagnostic accuracy included in systematic reviews. *BMC Medical Research Methodology*, 2003, 3: 25.

†† Well-designed population based case-control studies (eg population based screening studies where test accuracy is assessed on all cases, with a random sample of controls) do capture a population with a representative spectrum of disease and thus fulfil the requirements for a valid assembly of patients. These types of studies should be considered as Level II evidence. However, in some cases the population assembled is not representative of the use of the test in practice. In diagnostic case-control studies a selected sample of patients already known to have the disease are compared with a separate group of normal/healthy people known to be free of the disease. In this situation patients with borderline or mild expressions of the disease, and conditions mimicking the disease are excluded, which can lead to exaggeration of both sensitivity and specificity. This is called spectrum bias because the spectrum of study participants will not be representative of patients seen in practice.

‡‡ Studies of diagnostic yield provide the yield of diseased patients, as determined by an index test, without confirmation of accuracy by a reference standard. These may be the only alternative when there is no reliable reference standard.

*** At study inception the cohort is either non-diseased or all at the same stage of the disease.

§§§ All or none of the people with the risk factor(s) experience the outcome. For example, no smallpox develops in the absence of the specific virus; and clear proof of the causal link has come from the disappearance of small pox after large-scale vaccination.

††† If it is possible and/or ethical to determine a causal relationship using experimental evidence, then the 'Intervention' hierarchy of evidence should be utilised. If it is only possible and/or ethical to determine a causal relationship using observational evidence (ie. cannot allocate groups to a potential harmful exposure, such as nuclear radiation), then the 'Aetiology' hierarchy of evidence should be utilised.

Note 1: Assessment of comparative harms/safety should occur according to the hierarchy presented for each of the research questions, with the proviso that this assessment occurs within the context of the topic being assessed. Some harms are rare and cannot feasibly be captured within randomised controlled trials; physical harms and psychological harms may need to be addressed by different study designs; harms from diagnostic testing include the likelihood of false positive and false negative results; harms from screening include the likelihood of false alarm and false reassurance results.

Note 2: When a level of evidence is attributed in the text of a document, it should also be framed according to its corresponding research question eg. level II intervention evidence; level IV diagnostic evidence; level III-2 prognostic evidence etc.

Hierarchies adapted and modified from: NHMRC 1999; Lijmer et al 1999; Phillips et al 2001; Bandolier editorial 1999)

Appendix B: Profiles of studies

Study	Location	Study design	Study population	Patient demographics	Outcomes assessed
Cohen et al. (unpublished)	Australia	Level III-2 intervention evidence (expected)	LSG 307 patients Lap-band 343 patients	LSG BMI 41 (26-75) kg/m^2 Age 43 years Lap-band BMI 39 (29-70) kg/m^2 Age 43 years	%EWL, weight loss, complications, comorbidities.
Hamoui N, Anthone GJ, Kaufman HS, Crookes PF. (2006)	United States	Level III-2 intervention evidence	SG: 118patients Lap-band: 701 patients	Sleeve gastrectomy BMI 55 (37-108)kg/m^2 Age 47(16-70) years Duodenal switch BMI 51 (34-95) kg/m^2 Age 42(16-71) years	Weight loss, %EWL, complications, comorbidities, serum albumin, haemoglobin and calcium.
Himpens J, Dapri G, Cadiere GB. (2006)	Belgium	Level II intervention evidence	LSG: 40 patients Lap-band: 40 patients	LSG BMI 39 (30-53) kg/m^2 Age N/A Lap-band BMI 37 (30-47) kg/m^2 Age N/A	Median decrease in BMI and %EWL, GERD, complications, reoperations.
Langer FB, Hoda R, Bohdjalian A, Felberbauer FX, Zacherl J, Wenzl E, Schindler K, Luger A, Ludvik B, Prager G. (2005)	Austria	Level II intervention evidence	LSG: 10 patients Lap-band: 10 patients	LSG BMI 48.3±5.7 kg/m^2 Age 39.3±11.7 years Lap gastric banding BMI 46.7±3.5 kg/m^2 Age 38.5±13.6 years	%EWL, plasma ghrelin levels, complications.
Lee CM, Cirangle PT, Jossart GH. (2007)	United States	Level III-2 intervention evidence	LSG 216 patients Lap-band 271 patients Lap RYGBP 303 patients Duodenal switch 56 patients	LSG BMI 49±11 kg/m^2 Age 43±11 years Lap-band BMI 42±5 kg/m^2 Age 42±12 years Lap RYGBP	BMI, %EWL, weight loss, complications.

				BMI 46±6 kg/m^2 Age 43±19 years Duodenal switch BMI 47±6 kg/m^2 Age 42±8 years	
Milone L, Strong V, Gagner M. (2005)	United States	Level III-3 intervention evidence	LSG 20 patients Intragastric balloon 57 patients *[Historical controls from two studies]*	LSG BMI 68.8 (60.0-85.1) kg/m^2 Age 43 (27-63) years Intragastric balloon BMI a) 60.2 (58.0-72.0) kg/m^2 b) 58.4±6.6 kg/m^2 Age a) 38 (20-56) years b) 43 (33-54) years	BMI loss, %EWL, weight loss, complications, comorbidities.
Vidal J, Ibarzabal A, Nicolau J, Vidov M, Delgado S, Martinez G, Balust J, Morinigo R, Lacy A. (2007)	Spain	Level III-2 intervention evidence	LSG 35 patients (15 males, 20 females) Lap RYGBP 50 patients (17 males, 33 females) *Note: all patients had type II diabetes mellitus*	LSG BMI 52.0 ± 1.2 kg/m^2 Age 48.3 ± 1.6 years Lap RYGBP BMI 47.6 ± 0.7 kg/m^2 Age 46.6 ± 0.6 years	Type II diabetes mellitus resolution, medication reduction, metabolic and clinical measures of glucose sensitivity etc.

Appendix C: HTA Internet Sites

AUSTRALIA

- Centre for Clinical Effectiveness, Monash University
  http://www.med.monash.edu.au/healthservices/cce/evidence/

- Health Economics Unit, Monash University
  http://chpe.buseco.monash.edu.au

AUSTRIA

- Institute of Technology Assessment / HTA unit
  http://www.oeaw.ac.at/ita/welcome.htm

CANADA

- Agence d'Evaluation des Technologies et des Modes d'Intervention en Santé (AETMIS) http://www.aetmis.gouv.qc.ca/en/

- Alberta Heritage Foundation for Medical Research (AHFMR)
  http://www.ahfmr.ab.ca/publications.html

- Canadian Coordinating Office for Health Technology Assessment (CCOHTA)
  http://www.cadth.ca/index.php/en/

- Canadian Health Economics Research Association (CHERA/ACRES) – Cabot database http://www.mycabot.ca

- Centre for Health Economics and Policy Analysis (CHEPA), McMaster University http://www.chepa.org

- Centre for Health Services and Policy Research (CHSPR), University of British Columbia http://www.chspr.ubc.ca

- Health Utilities Index (HUI) http://www.fhs.mcmaster.ca/hug/index.htm

- Institute for Clinical and Evaluative Studies (ICES) http://www.ices.on.ca

DENMARK

- Danish Institute for Health Technology Assessment (DIHTA)
  http://www.dihta.dk/publikationer/index_uk.asp

- Danish Institute for Health Services Research (DSI)
  http://www.dsi.dk/engelsk.html

FINLAND

- Finnish Office for Health Technology Assessment (FINOHTA)
  http://finohta.stakes.fi/FI/index.htm

FRANCE

- L'Agence Nationale d'Accréditation et d'Evaluation en Santé (ANAES)

  http://www.anaes.fr/

GERMANY

- German Institute for Medical Documentation and Information (DIMDI) / HTA

  http://www.dimdi.de/dynamic/en/

THE NETHERLANDS

- Health Council of the Netherlands Gezondheidsraad
  http://www.gr.nl/adviezen.php

NEW ZEALAND

- New Zealand Health Technology Assessment (NZHTA)
  http://nzhta.chmeds.ac.nz/

NORWAY

- Norwegian Centre for Health Technology Assessment (SMM)

  http://www.kunnskapssenteret.no/

SPAIN

- Agencia de Evaluación de Tecnologias Sanitarias, Instituto de Salud "Carlos III" / Health Technology Assessment Agency (AETS)

  http://www.isciii.es/htdocs/investigacion/Agencia_quees.jsp

- Catalan Agency for Health Technology Assessment (CAHTA)
  http://www.aatrm.net/html/en/dir394/index.html

SWEDEN

- Swedish Council on Technology Assessment in Health Care (SBU)

  http://www.sbu.se/www/index.asp

- Center for Medical Health Technology Assessment

  http://www.cmt.liu.se/

SWITZERLAND

- Swiss Network on Health Technology Assessment (SNHTA)

http://www.snhta.ch/

UNITED KINGDOM

- NHS Quality Improvement Scotland
  http://www.nhshealthquality.org

- National Health Service Health Technology Assessment (UK) / National Coordinating Centre for health Technology Assessment (NCCHTA)
  http://www.hta.nhsweb.nhs.uk/

- University of York NHS Centre for Reviews and Dissemination (NHS CRD)
  http://www.your.ac.uk/inst/crd/

- National Institute for Clinical Excellence (NICE)
  http://www.nice.org.uk/

UNITED STATES

- Agency for Healthcare Research and Quality (AHRQ)
  http://www.ahrq.gov/clinic/techix.htm

- Harvard School of Public Health – Cost-Utility Analysis Registry
  http://www.tufts-nemc.org/cearegistry/index.html

- U.S. Blue Cross / Blue Shield Association Technology Evaluation Center (TEC)
  http://www.bcbs.com/tec/index.html

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