

Health Technology Assessment

Executive Summary Bariatric Surgery in Pediatric Patients

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Presented by:

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The Discipline of Science. The Integrity of Independence.

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Bariatric Surgery in Pediatric Patients

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This technology assessment report is based on research conducted by ECRI Institute, as contracted by the Washington State Health Care Authority. This report is an independent assessment of the technology question(s) described based on accepted methodological principles. The findings and conclusions contained herein are those of the investigators and authors who are responsible for the content. These findings and conclusions may not necessarily represent the views of the HCA/Agency and thus, no statement in this report shall be construed as an official position or policy of the HCA/Agency.

The information in this assessment is intended to assist health care decision makers, clinicians, patients and policy makers in making sound evidence-based decisions that may improve the quality and cost-effectiveness of health care services. Information in this report is not a substitute for sound clinical judgment. Those making decisions regarding the provision of health care services should consider this report in a manner similar to any other medical reference, integrating the information with all other pertinent information to make decisions within the context of individual patient circumstances and resource availability.

Executive Summary

This technology assessment was commissioned by the Washington State Health Technology Assessment program for use by the Health Technology Clinical Committee (HTCC). The HTCC uses evidence, primarily as assessed in this report to determine whether health technologies are safe, effective, and cost effective, and therefore should be covered by state programs that pay for health care.

This report evaluates relevant published research describing bariatric surgery in the pediatric population. ECRI Institute's technology assessment provides an independent, in-depth, formal evaluation of the strength of evidence for the safety and efficacy of bariatric surgery for treatment of co-morbid conditions associated with obesity in patients under age 21. It is based on systematic review of the published, peer reviewed scientific literature and methodological precepts described in Appendix C.

Recent years have seen substantial increases in the prevalence of morbid obesity (defined as BMI ≥ 40 kg/m² or ≥ 35 kg/m² in the presence of one or more medical comorbidities) in both the adult and pediatric populations. (1-3) Between 1988 and 1994, 2.9% of adults in the United States were morbidly obese; this percentage rose to 4.9% (10.8 million people) between 1999 and 2002. The condition was more common among women (6.4%) than among men (3.3%). Epidemiological data are not available on the percentage of the pediatric population who meet the definition of morbid obesity; however the prevalence of morbid obesity in the pediatric population is estimated at 2%-3%.

Obese individuals are at increased risk of type 2 diabetes, hypertension, coronary artery disease, stroke, gallbladder disease (cholelithiasis), osteoarthritis, sleep apnea, respiratory problems, and many types of cancer (including endometrial, breast, prostate, and colon). Obesity is also associated with pregnancy complications, menstrual irregularities, hirsutism, stress incontinence, and psychosocial impairments (e.g., binge eating, altered perception of body image, depression, social stigmatization).(1,10) These health risks contribute to obesity-related increases in all-cause mortality. Studies in pediatric populations have demonstrated the health risks of obesity in pediatric populations.(14-25), and that obesity during adolescence is highly likely to persist into adulthood and creates greater risks of adult health problems (18, 30, 31). Pediatric obesity may also be associated with reduced quality-of-life and social marginalization. (26-28)

Medical intervention for obesity is intended to promote weight loss and thereby reduce comorbid conditions associated with excess weight. Categories of treatment include diet, exercise, behavioral modifications, pharmacotherapy, and bariatric surgery. The goal of bariatric surgery in pediatric patients with morbid obesity is to halt the progression of obesity into adulthood to improve or eliminate medical conditions associated with obesity, and to improve quality of life. An individual considering whether to undergo bariatric surgery must take into consideration not only these potential improvements as compared to the risks of persistent severe obesity, but also the risks associated with the surgical procedure both in the short and long term and the need to comply with lifelong dietary and lifestyle changes. Use of bariatric surgery to treat morbid obesity has increased dramatically in recent years, from approximately 13,000 operations in 1998 to approximately 121,000 operations in 2004.(34) Patients under age 18 comprise about 0.1 - 1% of patients reported to have received bariatric surgery for morbid obesity at various centers. It is

estimated that over 2,000 pediatric patients ages 21 and younger in the United States received bariatric surgery in 2004, and based on a 2005 survey of bariatric surgeons in the United States indicating 75% were planning to perform adolescent bariatric surgery in the coming year, this number is likely to rise. Many different types of bariatric surgical procedures are performed, so “bariatric surgery” cannot be considered a single procedure. Some bariatric surgeries are purely restrictive—they cause weight loss by limiting the amount of food that can be consumed in one meal. Others are malabsorptive—they cause weight loss by reducing the amount of food that is absorbed into the body. The two most common bariatric surgical procedures are laparoscopic adjustable gastric banding (LAGB), which is a purely restrictive procedure, and Roux-en-Y gastric bypass (RYGB), which is both restrictive and malabsorptive. While the mechanism of action differs from procedure to procedure, all bariatric procedures are intended to induce weight loss, improve medical comorbidities, enhance quality of life, and (ultimately) extend survival.

Overall, data from 17 studies that enrolled a total of 553 pediatric patients are included. (Table 2) Eight studies reported outcomes after laparoscopic adjustable gastric banding (LAGB), six after Roux-en-Y gastric bypass (RYGB), two after vertical banded gastroplasty (VBG), and one after banded bypass. One study reported data separately for RYGB and VBG. Additional study characteristics and patient characteristics are listed in **Table 19** and **Table 20** of Appendix E, respectively.

Our detailed assessments of the quality (defined as internal validity) of the literature appear in **Table 21** and **Table 22** of Appendix E. Quality was addressed in the context of the specific outcome(s) being examined and the specific time points at which each outcome was measured. Briefly, only one study was clearly prospective. Although the remaining studies appeared to have collected data retrospectively, 13 studies did include data on consecutive patients. Consecutive enrollment helps ensure that authors did not specially select patients who experienced desired outcomes. Of note in regard to generalizability of the information is that the majority of studies were conducted in academic medical centers, and at least four of the centers had multidisciplinary pediatric bariatric surgery programs. Consequently, we believe that this evidence is most generalizable to similar care settings. Also, although the mean number of pediatric bariatric surgeries performed by surgeons in the studies was generally low, whether these surgeons had more extensive experience in the adult population was not reported.

The average age of patients in the included studies ranged from 15.6 years to 18.1 years, with little difference in mean age among bariatric procedures. None of the studies focused exclusively on patients aged 18-21, or on patients aged 12 or less. Four studies enrolled only patients aged 13-17: the Nadler study of LAGB, the Barnett study of RYGB and VBG, the Strauss study of RYGB, and the Capella study of banded bypass.

For pre-surgical BMI the weighted average was lower for LAGB (BMI = 45.8 kg/m²) than for RYGB (BMI = 51.8 kg/m²). This observation conforms to the conventional use of purely restrictive procedures (such as LAGB) for less obese patients, or the use of more malabsorptive procedures (such as RYGB) for those who are more obese. For reference, a 17-year-old boy of average height with a BMI of 48 kg/m² weighs approximately 334 pounds (152 kilograms), and the corresponding 17-year-old girl weighs approximately 289 pounds (131 kilograms). This report defines “clinically significant” weight loss as 7% of body weight (see *Methods* section). In the included LAGB studies, 7% of body weight in the enrolled patients corresponds to 3.5 BMI

units. For RYGB, it corresponds to 4 BMI units; for VBG or banded bypass, it corresponds to 3.9 BMI units.

Prior to surgery, all patients had undergone multiple unsuccessful attempts at weight loss using non-surgical methods (see studies' descriptions of prior attempts in **Table 19** of Appendix E). We believe that it is reasonable to assume that these patients would not have lost any weight if they had received additional non-surgical treatments. One of the 17 studies reported a control group of patients who were not treated with bariatric surgery; however the control group patients weighed statistically significantly less at baseline than surgical patients, and the study did not report any medical comorbidities among control group patients, as compared to surgical patients who had several comorbidities at baseline. These factors mean that the groups were not well-matched at baseline; thus we excluded the data from this control group, and included only the data from the surgical group.

We examined this evidence in the context of five clinical questions, which are listed below, along with our evidence-based conclusions. Our strength of evidence ratings take into consideration not only the individual study quality for each outcome and time point, but also the quantity, consistency, and robustness of the evidence, in addition to the magnitude of observed effects.

1. Does pediatric bariatric surgery lead to sustained and clinically significant weight loss compared to non-operative approaches?
 - a. In patients aged 21 or less
 - b. Specifically in patients aged 18-21
 - c. Specifically in patients aged 13-17
 - d. Specifically in patients aged 12 or less

ECRI Institute evidence assessments:

Laparoscopic Adjustable Gastric Banding (LAGB) for morbidly obese patients aged 21 or less does lead to sustained and clinically significant weight loss compared to non-operative approaches.

- Strength of evidence at longest followup after surgery (1.7 to 3.3 years): Weak
- Strength of evidence at one year after surgery: Moderate

Roux-en-Y Gastric Bypass (RYGB) for morbidly obese patients aged 21 or less does lead to sustained and clinically significant weight loss compared to non-operative approaches.

- Strength of evidence at longest followup after surgery (1 to 6.3 years): Weak;
- Strength of evidence at one year after surgery: Moderate

The evidence is insufficient to permit quantitative estimates of the precise amount of weight loss after any bariatric surgical procedure for pediatric patients.

The evidence is insufficient to permit any conclusions about weight loss after other bariatric surgical procedures for pediatric patients.

The evidence is insufficient to permit any conclusions about weight loss in specific age

subgroups (18-21, 13-17, 12 or less) within the pediatric population.

Five of eight LAGB studies reported BMI data that met inclusion criteria. The length of followup ranged from 1.7 to 3.3 years, and the percentage of patients in our analysis of longest-follow-up BMI was 100% in four studies and 64% in the fifth study. Our study quality assessments for this analysis indicated that the overall quality was low. All five studies observed statistically and clinically significant weight loss after surgery. We performed seven tests to confirm the robustness of the finding, including an alternate assumption that patients might lose as many as 1.7 BMI units without surgery (change in weight as measured by kilograms per meter of height squared). All analyses still indicated clinically significant weight loss. Based on the overall quality of the studies as well as the quantity, consistency, and robustness of the evidence, we rated the strength of the evidence at longest followup after LAGB as Weak. Also, three of the studies had reported BMI specifically at one year after LAGB. The overall quality of the one-year BMI data was moderate, and each reported statistically and clinically significant weight loss. All seven qualitative robustness tests analyses were passed; therefore the strength of this evidence for one-year BMI reduction after LAGB was Moderate.

Five of six RYGB studies reported BMI data that met inclusion criteria. One study's BMI data were very low quality, and consequently we excluded it from further consideration. For the remaining four studies, the percentage followup ranged from 60% to 90%, and the mean length of followup ranged from 1 year to 6.3 years. The overall quality was low. All four studies observed statistically and clinically significant weight loss after surgery, and the analysis passed all seven robustness tests. Thus, as with LAGB, we rated the strength of the evidence as Weak for longest-follow-up BMI after RYGB. Also, three of the studies had reported BMI specifically at one year after LAGB. The overall quality of the one-year BMI data was moderate, and each reported statistically and clinically significant weight loss. All seven qualitative robustness tests analyses were passed; therefore the strength of this evidence for one-year BMI reduction after RYGB was Moderate.

The evidence did not permit precise quantitative estimates of the number of BMI units lost after either LAGB or RYGB, because studies did not generally report sufficient information for us to calculate the pre-post correlation for BMI. Also, the evidence on weight loss after other bariatric procedures (e.g., VBG) did not support conclusions due to low quantity and quality of evidence. For specific age groups of pediatric patients (e.g., 13-17), there were not enough studies of any single age group to permit conclusions.

2. Does bariatric surgery for patients a-d (as above) improve comorbid conditions linked to obesity (e.g., diabetes, hypertension, obstructive sleep apnea, and musculoskeletal disorders), quality of life, or survival, as compared to non-operative approaches?

ECRI Institute evidence assessments:

Laparoscopic Adjustable Gastric Banding (LAGB) for morbidly obese patients aged 21 or less does resolve comorbid conditions linked to obesity (diabetes, hypertension) compared to non-operative approaches. (Strength of evidence for comorbidity data: Weak).

Roux-en-Y Gastric Bypass for morbidly obese patients aged 21 or less does resolve comorbid conditions linked to obesity (hypertension) compared to non-operative approaches. (Strength of evidence for comorbidity data: Weak).

The evidence is insufficient to permit quantitative estimates of the likelihood of comorbidity resolution, quality of life improvement, or survival after any bariatric surgical procedure for pediatric patients.

The evidence is insufficient to permit any conclusions about comorbidity resolution after other bariatric surgical procedures for pediatric patients.

The evidence is insufficient to permit any conclusions about comorbidity resolution in specific age subgroups (18-21, 13-17, 12 or less) within the pediatric population.

Four of eight LAGB studies met inclusion criteria for comorbidity and quality of life outcomes. The mean length of follow-up ranged from 1.3 years to 2.9 years. No studies evaluated changes in medical conditions or quality of life using validated instruments or long term survival. The evidence was sufficient to permit conclusions only for diabetes (two studies, with resolution rates of 80% and 100%) and hypertension (three studies, with resolution rates of 50%, 100%, and 100%). These are large rates, but due to the moderate quality and limited quantity, we rated the strength of evidence as Weak for these outcomes. The evidence on other comorbidities and quality of life was too sparse to permit conclusions.

Four of six RYGB studies met inclusion criteria for comorbidity and quality of life outcomes. The mean length of followup ranged from 5 months to 2.7 years. The evidence was sufficient to permit a conclusion only for hypertension (three studies, with resolution rates of 50%, 82% and 100%). Due to the moderate quality and limited quantity, we rated the strength of evidence as Weak for hypertension resolution. One other comorbidity had at least two studies (sleep apnea), but the data were of overall low quality, therefore we drew no conclusions. The evidence on other outcomes was too sparse to permit conclusions.

We drew no conclusions about other bariatric procedures or specific age groups, due to a limited quantity of evidence.

3. What are the relative safety profiles of bariatric surgery and non-operative approaches for patients a-d (as above)?

ECRI Institute evidence assessments:

Our review of the eight LAGB studies (the procedures were performed between 1996 and 2006; the individual patient follow-up times ranged from one month to 85 months) found:

No reported in-hospital or postoperative death.

The most frequently reported complication after LAGB was band slippage.

Reoperations were performed on 26 (7.92%) of the 328 LAGB patients to correct various complications.

Our review of the six RYGB studies (the procedures were performed between 1978 and 2005; the individual patient follow-up times ranged from two weeks to six years) found:

One postoperative death was reported for RYGB; no in-hospital death was reported.

The most frequently reported complication after RYGB was related to protein-calorie malnutrition and micronutrient deficiency.

Potentially life-threatening complications such as shock, pulmonary embolism, severe malnutrition, immediate postoperative bleeding, and gastrointestinal obstructions were reported in the RYGB studies.

The evidence is insufficient to permit any conclusions on potential impacts of bariatric surgery on growth and development of pediatric patients.

The evidence is insufficient to permit any conclusions on potential harms in specific age groups (18-21, 13-17, 12 or less).

Systematic reviews on pediatric obesity management did not provide sufficient data for the development of a safety profile of non-operative approaches.

All 17 studies were included for data on complications. The overall evidence quality was rated as Moderate for these outcomes. Given the low patient enrollment, we did not attempt to estimate the rate of any complication. For LAGB, the primary concern is the need for reoperation, which was necessary for 26 pediatric patients (7.92%) overall. Reasons for reoperation include band slippage, intragastric migration, and port/tubing problems. For RYGB, there is a different profile of complications, varying from mild events (e.g., slight malnutrition, correctable by supplements) to severe events (e.g., pulmonary embolism, severe malnutrition, immediate postoperative bleeding, and gastrointestinal obstruction).

4. What are the relative cost profiles of bariatric surgery and non-operative approaches for patients a-d (as above)?

ECRI Institute evidence assessments:

Nationally, the median inpatient hospital cost for bariatric surgeries performed in pediatric patients in 2004 was \$8,651; the median hospital charge was \$25,021.

Nationally, the median inpatient hospital cost for restrictive bariatric procedures performed in pediatric patients in 2004 was \$6,688; the median inpatient hospital cost for bypass procedures was \$8,893.

Nationally, for those aged 13-17, the median inpatient hospital cost for bariatric procedures performed in 2004 was \$7,973; the median inpatient hospital cost for those aged 18-21 was \$8,945. No conclusions can be drawn regarding the cost of patients aged 12 and less due to lack of data.

Data were not sufficient to permit a comparison of inpatient hospital cost between the State of Washington and the rest of the nation.

Data were not sufficient to permit an analysis of the costs for professional services and post-surgery care.

The evidence was not sufficient to permit the development of a comprehensive cost profile of non-operative approaches to pediatric obesity management.

Due to the inadequacy of published evidence on the costs of bariatric surgery in pediatric patients with morbid obesity, we conducted our own analyses of publicly available data to estimate inpatient hospital costs. However, due to lack of data, we were unable to conduct similar primary analyses to estimate the costs for professional services and postoperative

care.

5. Do the effectiveness, safety and cost of bariatric surgery for patients a-d (as above) vary based on patients' characteristics, including:
 - a. Chronological age
 - b. Physiologic/skeletal age
 - c. Pre-surgical BMI
 - d. Pre-surgical BMI categories (35-40, 40-50, 50+)
 - e. Sex
 - f. Race
 - g. Comorbid conditions (e.g., hypertension)
 - h. Other factors (e.g., psychosocial or socioeconomic factors)

ECRI Institute evidence assessments:

The evidence is insufficient to permit any conclusions for this question

Studies' data were included for four of the eight patient characteristics: chronological age (a), pre-surgical BMI (c), pre-surgical BMI category (d), and sex (e). However, none of these associations were addressed by more than two studies of any given bariatric procedure, and the low quantity of evidence precluded conclusions. The association between chronological age and surgical outcome was addressed by only one study of LAGB, one study of RYGB, and one study of banded bypass. Similarly, the association between sex and outcome was addressed by only one study each for LAGB, RYGB, and VBG. There were two studies of LAGB addressing the association between pre-surgical BMI and surgical outcome (and also the association between pre-surgical BMI category and surgical outcome), but the overall low quality precluded conclusions.

Overall assessment

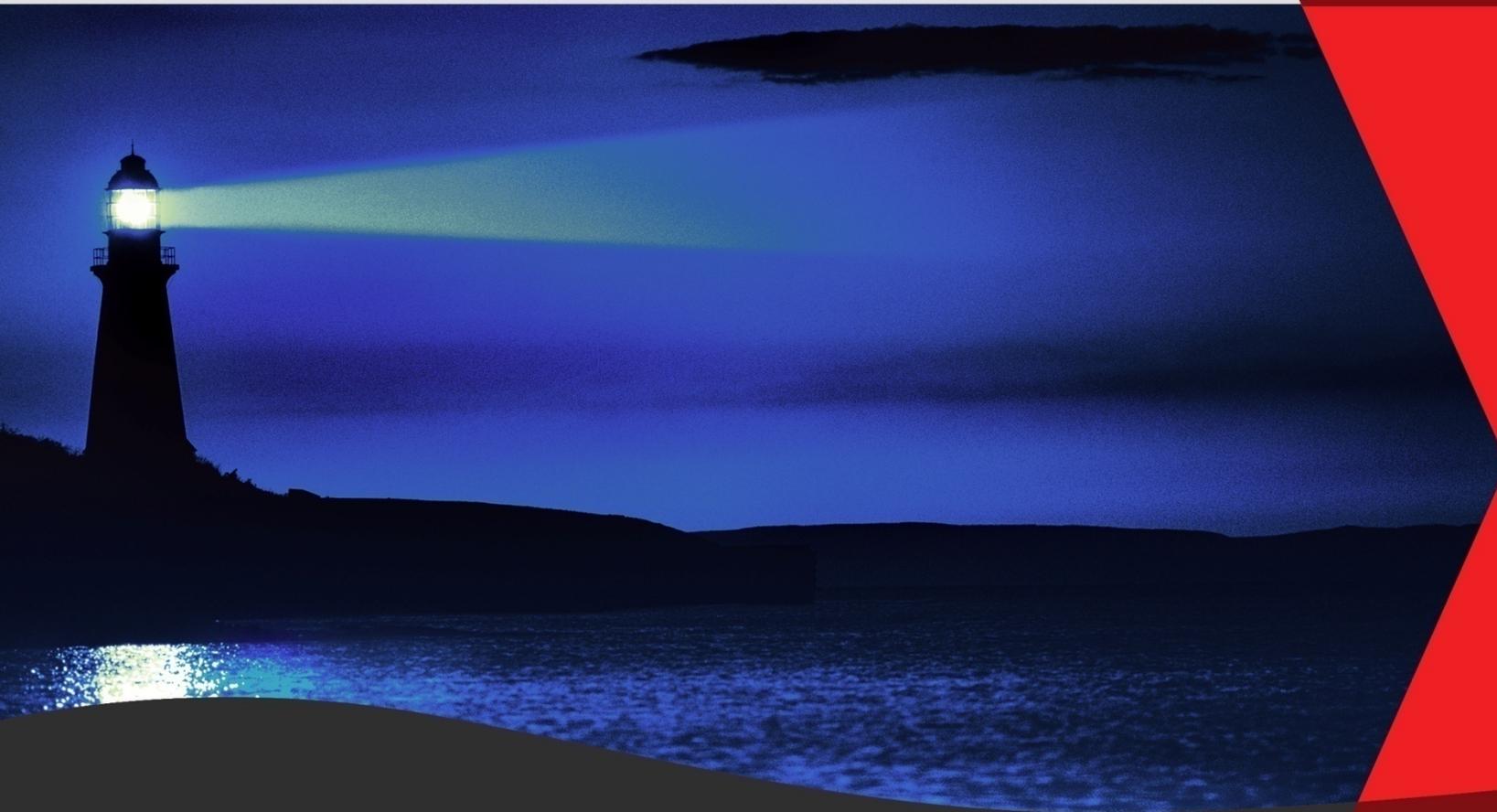
Both LAGB and RYGB led to clinically significant weight loss in morbidly obese pediatric patients over the followup times reported. While reporting of comorbid conditions was limited, there was evidence that diabetes and hypertension resolved following LAGB and that hypertension resolved after RYGB. A number of complications were reported following both procedures, including one postoperative death following RYGB. Variations in outcomes based on patient characteristics such as age, baseline BMI, sex, race or socioeconomic variables could not be determined from the available literature.

Individuals who work with morbidly obese children and adolescents have expressed concern about the appropriateness of bariatric surgery in this population. In particular, many question the ability of pediatric patients to give informed consent not only to an invasive procedure, but also to the long-term lifestyle and dietary changes necessary following the surgery. Future research should examine methods of presenting the complex information necessary for truly informed consent in pediatric individuals considering bariatric surgery. More evidence is needed on outcomes such as physical growth and

quality of life. Longer term prospective collection of data on weight loss, persistence or resolution of comorbid conditions, and long-term survival would be valuable for understanding more fully the role of these surgical procedures in treating morbidly obese pediatric patients. Data collection on a large population (e.g., a national registry) could provide enough data to improve our ability to identify individuals most likely to benefit long term from a surgical approach, and to determine which surgical approach is best suited to individuals with specific characteristics.

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ECRI Institute - Who We Are

- Nonprofit health services research agency in existence since the 1960's; 300 interdisciplinary staff
- Evidence-based Practice Center, Agency for Health Care Research and Quality (since 1997)
- Collaborating Center, World Health Organization for Patient Safety, Risk Management and Healthcare Technology
- National Guideline Clearinghouse and National Quality Measures Clearinghouse
- Pennsylvania Patient Safety Reporting System

The Integrity of Independence

Our conflict-of-interest rules

- Were developed to create an environment that maximizes objectivity, productivity, and integrity of process.
- We accept no advertising revenues from any source.
- Our employees are not permitted to own stock shares in medical device or pharmaceutical firms, and we verify this by examining each employee's federal income tax return.
- We go beyond the industry norm to ensure that you receive unbiased guidance.

Definitions

- Morbid obesity: BMI ≥ 40 kg/m², or BMI ≥ 35 kg/m² with comorbidity, e.g.,
 - Diabetes, hypertension, sleep apnea, GERD, hyperlipidemia
 - Polycystic Ovary Syndrome
 - Musculoskeletal disorders
- Pediatric: Age ≤ 21

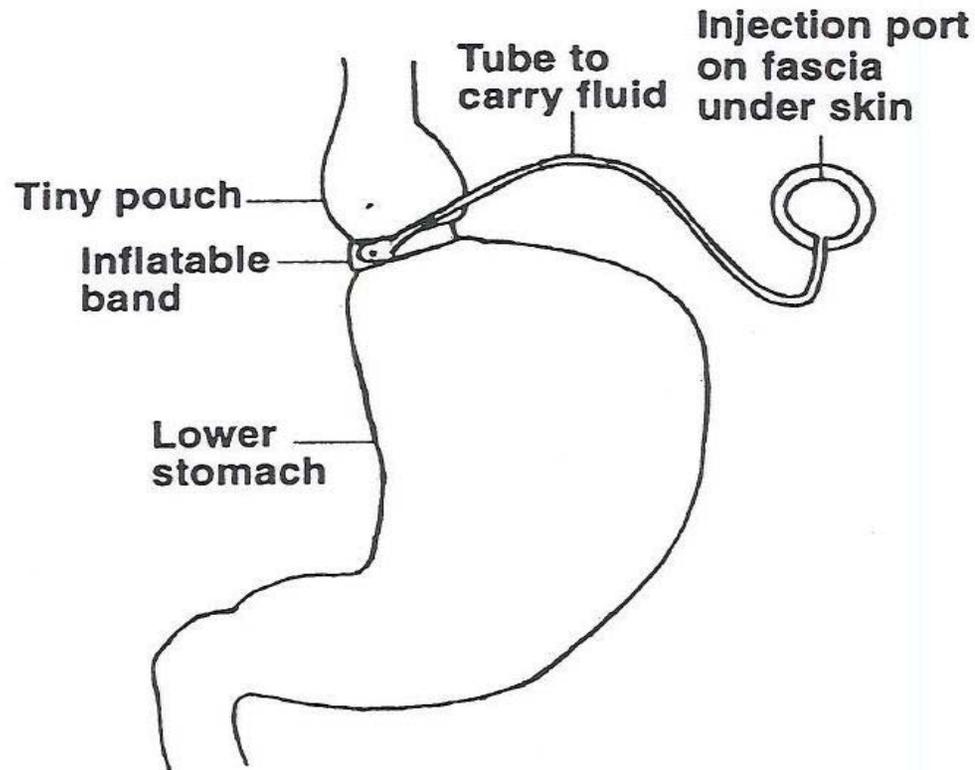
Example Weights at Average Height

Age and Sex	BMI =40	BMI =50
13 year old girl	217 lbs.	272 lbs.
13 year old boy	215 lbs.	268 lbs.
17 year old girl	234 lbs.	292 lbs.
17 year old boy	270 lbs.	338 lbs.

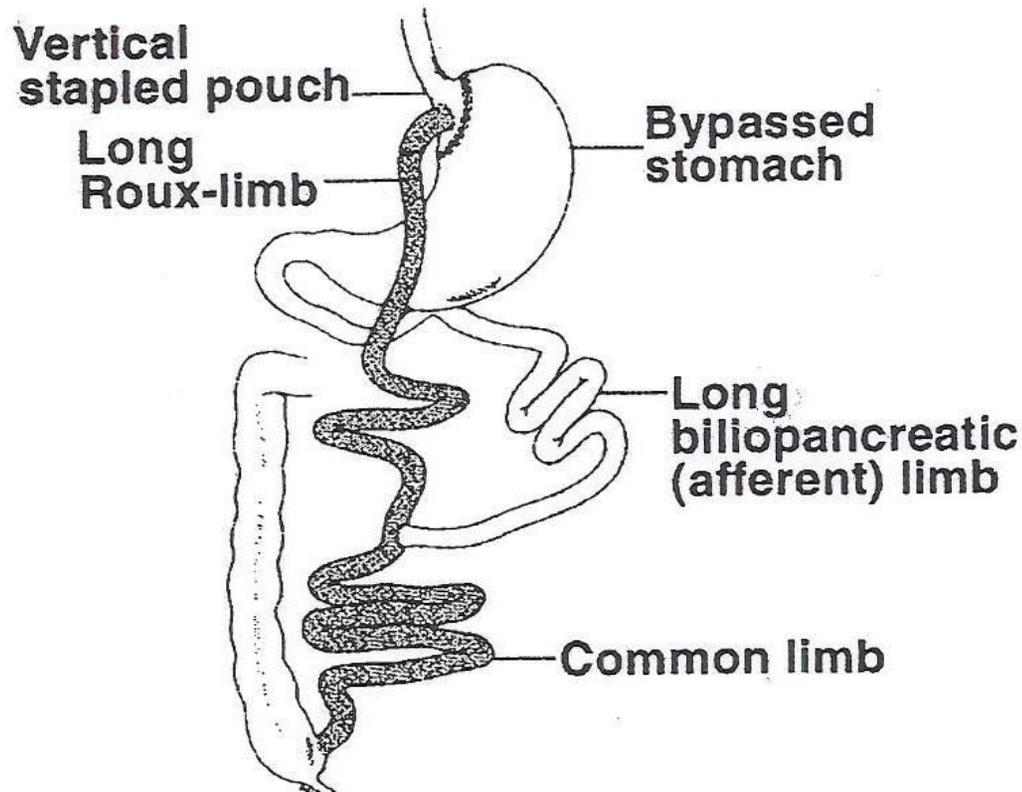
Epidemiology

- ~15% of adolescents are “overweight”
- Estimated prevalence of morbid obesity in the pediatric population is ~2-3%

Laparoscopic Adjustable Gastric Banding (LAGB)



Roux-en-Y Gastric Bypass (RYGB)



Key Questions

1) Does pediatric bariatric surgery lead to sustained and clinically significant weight loss compared to nonoperative approaches?

Key Questions

2) Does bariatric surgery for pediatric patients improve co-morbid conditions linked to obesity (diabetes, hypertension, dyslipidemia, obstructive sleep apnea, asthma, GERD, musculoskeletal disorders), quality of life, or survival, as compared to non-operative approaches?

Key Questions

3) What are the relative safety profiles of bariatric surgery and nonoperative approaches for pediatric patients?

Key Questions

4) What are the relative cost profiles of bariatric surgery and non-operative approaches for pediatric patients?

Key Questions

5) Do the effectiveness, safety and cost of bariatric surgery for pediatric patients vary based on patients characteristics?

Inclusion Criteria

- Morbid obesity
- Age ≤ 21 , N ≥ 3
- Weight or BMI at ≥ 1 year after surgery
- $\geq 85\%$ had the same bariatric procedure
- $\geq 50\%$ completion
- Current procedure

Literature Search

- Medical librarians searched 15 databases
- Last search date 8/6/07
- 153 articles identified
- 38 retrieved
- 24 included (17 unique studies)
- 8 LAGB, 5 RYGB, 2 VBG, 1 RYGB or VBG, 1 BB

Strength of Evidence

- Quality, quantity, consistency, robustness, and magnitude of effect
- Strong, Moderate, Weak, or Inconclusive
- Separately assessed for different outcomes and different timepoints

Studies in Brief - LAGB

Study	Country	Design
Al-Qahtani (2007)	Saudi Arabia	Case series, retrospective, consecutive
Nadler (2007)	USA	Case series, prospective, consecutive
Yitzhak (2006)	Israel	Case series, retrospective, consecutive
Silberhumer (2006)	Austria	Case series, ? pro/retro ,consecutive
Angrisani (2005)	Italy	Case series, retrospective, consecutive
Fielding (2005)	Australia	Case series, retrospective, consecutive
Horgan (2005)	USA	Case series, retrospective, consecutive
Abu-Abeid (2003)	Israel	Case series, retrospective, ? consecutive

Studies in Brief – RYGB

Study	Country	Surgery	Design
Collins (2007)	USA	RYGB	Case series, retrospective, consecutive
Lawson (2006)	USA	RYGB	Case series, retrospective, consecutive
Barnett (2005)	USA	RYGB or VBG	Case series, retrospective, consecutive
Sugerman (2003)	USA	RYGB	Case series, retrospective, consecutive
Strauss (2001)	USA	RYGB	Case series, retrospective, consecutive
Rand (1994)	USA	RYGB	Case series, retrospective, nonconsecutive

Studies in Brief – VBG, BB

Study	Country	Surgery	Design
Greenstein (1995)	USA	VBG	Case series, retrospective, nonconsecutive
Mason (1995)	USA	VBG	Case series, retrospective, nonconsecutive
Capella (2003)	USA	BB	Case series, retrospective, consecutive

VBG = Vertical Banded Gastroplasty

BB = Banded Bypass

Studies of LAGB

- 8 studies, 328 patients
- Only 2/8 conducted in the USA
- Nonsurgical methods had failed
- Average age 16.6
- Average BMI 45.8
- 6 studies used the LAP-BAND[®], 1 used the SAGB band, and 1 used mostly SAGB (74%)

Studies of RYGB

- 6 studies, 125 patients
- All 6 conducted in the USA
- Nonsurgical methods had failed
- Average age 16.8
- Average BMI 51.8
- 3 studies of open; 2 laparoscopic bypass; 1 predominantly open (94%)

Internal validity

- 1 prospective, 15 retrospective, 1 unclear
- 13 consecutive, 3 nonconsecutive, 1 unclear
- For longest follow-up BMI, 6 of 10 studies had at least 85% of patients in the analysis
- No independent outcome assessment reported
- Funding sources not reported

Generalizability

- Patients: Age 16-17, BMI 45-55
- Surgeon's experience (range): 4 – 60 cases
- Surgical techniques: LAGB or RYGB most commonly performed
- Care setting: Academic centers, several with multidisciplinary programs
- Country: LAGB mostly non-USA; RYGB all USA

Studies of Nonoperative Approaches: Diet, Exercise, Pharmacologic Agents, and Behavioral Modification

- Rarely follow patients as long as one year
- Enroll a younger population
- Enroll a population with lower mean BMI

Key Questions

1) Does pediatric bariatric surgery lead to sustained and clinically significant weight loss compared to non-operative approaches?

LAGB: BMI at Longest Follow-Up

Study	n/N (%) in analysis	Mean follow-up (range)	Mean BMI before	Mean BMI after
Yitzhak (2006)	60/60 (100%)	3.1 yr (2.1-5.4)	43	30
Silberhumer (2006)	50/50 (100%)	2.9 yr (0.3-7.2)	45.2	32.6
Angrisani (2005)	37/58 (64%)	3.0 yr (3.0-3.0)	46.1	37.8
Fielding (2005)	17/17 (100%)	1.7 yr (1.0-2.0)	43.1	30.2
Abu-Abeid (2003)	11/11 (100%)	1.9 yr (1.0-3.0)	46.5	32.5

LAGB: BMI at Longest Follow-Up

Study	n/N (%) in analysis	Mean follow-up (range)	Mean BMI before	Change in BMI in kg/m ² (95% CI)
Yitzhak (2006)	60/60 (100%)	3.1 yr (2.1-5.4)	43	- 13.0 (-14.8 to -11.2)
Silberhumer (2006)	50/50 (100%)	2.9 yr (0.3-7.2)	45.2	- 12.6 (-14.4 to -10.8)
Angrisani (2005)	37/58 (64%)	3.0 yr (3.0-3.0)	46.1	- 8.3 (-11.2 to -5.4)
Fielding (2005)	17/17 (100%)	1.7 yr (1.0-2.0)	43.1	- 12.9 (-15.5 to -10.3)
Abu-Abeid (2003)	11/11 (100%)	1.9 yr (1.0-3.0)	46.5	- 14.0 (-16.5 to -11.5)

LAGB: BMI at One Year

Study	n/N (%) in analysis	Mean BMI before	Change in BMI in kg/m² (95% CI)
Angrisani (2005)	48/58 (83%)	46.1	-10.2 (-12.1 to -8.3)
Fielding (2005)	17/17 (100%)	43.1	-10.1 (-12.7 to -7.5)
Abu-Abeid (2003)	11/11 (100%)	46.5	-12.5 (-14.9 to -10.1)

RYGB: BMI at Longest Follow-Up

Study	n/N (%) in analysis	Mean follow-up (range)	Mean BMI before	Mean BMI after
Collins (2007)	3/4 (75%)	1.8 yr (1.7-1.8)	52	28
Lawson (2006)	30/30 (77%)	1.0 yr (1.0-1.0)	56.5	35.8
Sugerman (2003)	20/33 (61%)	5.0 yr (5.0-5.0)	52	33
Strauss (2001)	9/10 (90%)	6.3 yr (1.0-13.0)	52	35.2

RYGB: BMI at Longest Follow-Up

Study	n/N (%) in analysis	Mean follow-up (range)	Change in BMI in kg/m² (95% CI)
Collins (2007)	3/4 (75%)	1.8 yr (1.7-1.8)	-24.0 (-35.1 to -12.9)
Lawson (2006)	30/ 38 (77%)	1.0 yr (1.0-1.0)	-20.7 (-23.6 to -17.8)
Sugerman (2003)	20/33 (61%)	5.0 yr (5.0-5.0)	-19.0 (-23.3 to -14.7)
Strauss (2001)	9/10 (90%)	6.3 yr (1.0-13.0)	-16.8 (-24.3 to -9.3)

RYGB: BMI at One Year

Study	n/N (%) in analysis	Mean BMI before	Change in BMI in kg/m² (95% CI)
Lawson (2006)	30/30 (100%)	56.5	-20.7 (-23.6 to -17.8)
Sugerman (2003)	32/33 (97%)	52	-16 (-19.3 to -12.7)
Strauss (2001)	9/9 (100%)	52	-18 (-21.6 to -15.1)

Sensitivity Analyses

- BMI reduction of 0.55 to 1.7 units without surgery
- Removal of each single study
- Removal of all studies with <75% completion
- Cumulative meta-analysis by year
- Pre-post correlation range: 0.36 to 0.76

All tests passed, indicating robustness of the conclusions

Conclusions for Weight Loss

- LAGB and RYGB: sufficient evidence to permit conclusion that **BMI** is reduced at **longest follow-up** by a clinically significant amount (Strength of evidence: Weak)
- LAGB and RYGB: sufficient evidence to permit conclusion that **BMI** is reduced at **one year** follow-up by a clinically significant amount (Strength of evidence: Moderate)

Key Questions

2) Does bariatric surgery for pediatric patients improve co-morbid conditions linked to obesity (diabetes, hypertension, dyslipidemia, obstructive sleep apnea, asthma, GERD, musculoskeletal disorders), quality of life, or survival, as compared to non-operative approaches?

Resolution of Diabetes and Hypertension

	Diabetes	Hypertension
LAGB	<p>2 studies: N=12 Followup: 1.3 and 2.9 yrs. Resolution: 80% (4/5) and 100% (7/7)</p>	<p>3 studies: N=21 Followup: 1.3 , 2.9, and 3.3 yrs. Resolution: 50% (6/12), 100% (6/6) & 100% (3/3)</p>
RYGB	<p>1 study: N=6 Followup: 0.96 yrs. Resolution: 50% (3/6)</p>	<p>3 studies: N=20 Followup: 0.96, 1, and 2.7 yrs. Resolution: 50% (3/6) ,82% (9/11) & 100% (3/3)</p>

Diabetes and Hypertension

- LAGB: sufficient evidence to permit conclusions for the resolution of **diabetes** and **hypertension** (Strength of evidence: Weak)
- RYGB: sufficient evidence to permit conclusions for the resolution of **hypertension** (Strength of evidence: Weak)

Other Comorbidities

- Dyslipidemia
- Sleep apnea
- Asthma
- GERD
- Musculoskeletal problems
- Polycystic Ovary Syndrome/Amenorrhea

Key Questions

5) Do the effectiveness, safety and cost of bariatric surgery for pediatric patients vary based on patients characteristics?

Key Question 5: Patient Characteristics Predictive of Outcomes

- 5 studies reported sufficient data
- 2 of LAGB, 1 of RYGB, 1 of VBG, 1 of BB

Insufficient evidence to permit evidence-based conclusions

Key Questions

3) What are the relative safety profiles of bariatric surgery and nonoperative approaches for pediatric patients?

Key Question 3: Safety Profile - LAGB

- Eight studies (11 publications), 328 cases
 - Procedures performed between 1996 - 2006.
 - Average follow-up (overall study level) range: 13.4 -39.5 months (reported in 6 studies)
 - At individual case level, follow-up range: 1 - 85 months
- No in-hospital or postoperative deaths reported
- Reoperations performed on 26 (7.92%) of 328 LAGB patients

Reported post-LAGB complications in 328 cases

- Band-related
 - Band slippage (12)
 - Intra-gastric migration (erosion) (3)
 - Port/tubing problems (2)
- Other
 - Gastric pouch dilatation (2)
 - Gastroesophageal reflux (1)
 - Iron deficiency (8)
 - Mild hair loss (5)
 - Hiatal hernia (2)
 - Nephrolithiasis and cholelithiasis (2)
 - Wound infection (1)

Key Question 3: Safety Profile - RYGB

- Six studies (9 publications) included, 125 cases
 - Procedures performed between 1978 – 2005
 - Average follow-up (overall study level) range: 11.5 – 72 months
 - At individual case level, follow-up range: 0.5 – 72 months
- No in-hospital deaths reported
- One postoperative death reported (9 months postop)
- Number of reoperations for RYGB not calculable

Reported post-RYGB complications in 125 cases probably/possibly requiring surgical intervention

- Immediate postoperative bleeding (1)
- Gastrostomy revision (≥ 1)
- Staple line leak (≥ 1)
- Internal hernia (≥ 1)
- Cholecystectomy (6)
- Anastomotic stricture/gastrojejunostomy stricture (≥ 1)
- Stomal stenoses and food obstruction (≥ 5)
- Small bowel obstruction (2)
- Pouch dilation (5)
- Incisional hernia (7)
- Wound infection (≥ 6)

Reported post-RYGB complications in 125 cases probably treated medically

- Protein-calorie malnutrition and micronutrient deficiency including iron deficiency, vitamin deficiency, hypokalemia, hypoglycemia, and beriberi (16)
- Dumping syndrome (≥ 3)
- Dehydration (≥ 1)
- Shock (≥ 1)
- Other complaints including nausea and diarrhea (≥ 2)
- Pulmonary embolism (1)
- Deep vein thrombosis (≥ 1)
- Marginal ulcer (6)
- Melena (≥ 1)

Key Question 3: Safety Profile

- The evidence is insufficient to permit any conclusions on potential impact of bariatric surgery on growth and development of pediatric patients.
- The evidence is insufficient to permit any conclusions on potential harms in specific age groups.
- Systematic reviews on pediatric obesity management did not yield sufficient safety data on nonoperative approaches.

Key Questions

4) What are the relative cost profiles of bariatric surgery and non-operative approaches for pediatric patients?

Key Question 4: Cost Profile

- Published evidence on the costs of bariatric surgery in pediatric patients was inadequate
- Analyses of HCUP data* were conducted to estimate inpatient hospital costs.
- Full cost for bariatric surgery was not estimated due to lack of data, e.g.,
 - Surgeons' and other clinicians' professional fees
 - Costs for regular follow-up care and supplements
 - Costs for treatment of complications
 - Potential savings from comorbidity resolution

*Healthcare Cost and Utilization Project (HCUP) 2004 Nationwide Inpatient Sample (NIS). Agency for Healthcare Research and Quality, Rockville, MD.
www.hcup-us.ahrq.gov/databases.jsp

Inpatient Cost and Charge, 2004

		Charges	Cost
Case number		415	391
Mean		\$30,594	\$10,913
Median		\$25,021	\$8,651
Maximum		\$245,579	\$72,641
Minimum		\$7,913	\$1,987
Percentiles	25 th	\$19,182	\$6,976
	75 th	\$37,390	\$12,379

Healthcare Cost and Utilization Project (HCUP) 2004 Nationwide Inpatient Sample (NIS). Agency for Healthcare Research and Quality, Rockville, MD. www.hcup-us.ahrq.gov/databases.jsp

Insurance Coverage Policies

- Third-party payers
 - Medicaid
 - Private insurers
 - Medicare
 - Other
- Age-related restrictions
- Commonly covered procedures

Pediatric Bariatric Procedures in HCUP NIS 2004, by Coverage

	Frequency*	Percent
Medicare	2	0.5
Medicaid	38	9.2
Private insurance	322	77.6
Self-pay	33	8.0
No charge	1	0.2
Other	19	4.6
Total	415	100.0

*This represents the sample in NIS for 2004, not a national estimate of cases

Unique Issues to Consider with Bariatric Surgery

- Informed consent
- Long term compliance with postoperative instructions:
 - Diet
 - Lifestyle changes
 - Supplements

Data Needed for Operative and Nonoperative Treatment in Morbidly Obese Pediatric Patients

- Impact on physical growth
- Quality of life outcomes
- Very long term (> 10 yr) outcomes (survival, duration of weight loss, duration of comorbidity improvement/resolution)

Questions?

Washington State HCA Health Technology Assessment for Bariatric Surgery in Pediatric Patients



Allergan Public Comments

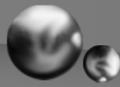
Dr. Deirdre Monroe
Sr. Manager, Medical Affairs



Health Technology Assessment

- Support the need for clinical judgment balanced with evidence-based medicine
- Better outcomes in ACS or ASBS certified facilities
- Agree that obese adolescents suffer from same co-morbidities as obese adults
 - over 70% of obese children become obese adults
- Positive short and moderate-term outcomes
- Agree long-term data on clinical outcomes is still needed

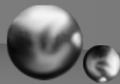
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LAPBAND System

- Manufacturer – Allergan (acquired Inamed in 2006)
- Approved by FDA in 2001
- Adjustable and reversible procedure
- Low complication and morbidity
- Physician certification process
 - required by FDA label
- Lapband device – AP generation

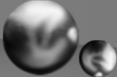
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Assessment Sub-Group Pediatric Categories

- Lapband system is FDA-approved for 18- up to 65 years of age
- HTA defines “pediatric” as ≤ 21 years of age per American Association of Pediatrics (AAP)
- HTA cited reference #4 does not support pediatric definition
- AHRQ TEC Assessment 2004 for adolescent bariatric surgery:
 - Adolescent = Age 13 to 17
 - Pediatric = 12 and younger

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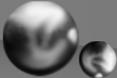
Co-morbidities Severely Obese Adolescents

- Adult – strong evidence

- Pediatric
 - Self esteem
 - QOL

- Post-bariatric surgery resolution of comorbidities

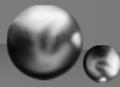
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LAP-BAND: Outcomes and Results

Changes in comorbidities after LAP-BAND surgery	
Type 2 Diabetes	Complete remission in 64% of patients Improvement in another 32% of patients
Insulin resistance	Improved from 37.5% to 62% in 254 patients during the first year
GERD	Resolved in 89% if patients
Obstructive Sleep Apnea	Rate decreased from 33% to 2%
Depression	Significant and sustained fall in Beck Depression Index (BDI) scores
Quality of Life	Dramatic and sustained improvement in all measures of SF-36

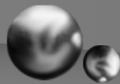
O'Brien P, Dixon J. Journal of Laparoendoscopic and Advanced Surgical Techniques. 2003; 13(4): 265-67.
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Bariatric Surgery Literature

- Reconsider exclusion of Tsai, et al 2007
 - 90% received RYGB, met criteria that 85% of patients must have received one procedure
- Clinical
 - Dolan, K et al. 2003 *Obesity Surgery* (LAGB)
- Cost-Effectiveness
 - Christou, N et al. 2004 *Ann Surg*
 - Haby, M et al. 2006 *Int J of Obesity*
 - Monk, J et al. 2004 *Obes Surg*

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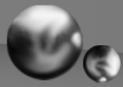


Current LAPBAND Adolescent Clinical Trial

Effectiveness and Safety Study of LAP-BAND Treatment for Obese Adolescents

- Outcome: Percent of subjects who attain clinically successful weight loss at one year post LAP-BAND implantation
- Inclusion
 - Between age 14 and 17 at time of enrollment
- BMI ≥ 40 kg/m² (with or without obesity-related co-morbid conditions)
- BMI ≥ 35 kg/m² with one or more severe co-morbid conditions
- History of obesity for at least 2 years and
 - Failed more conservative weight-reduction alternatives, such as supervised diet, exercise and behavior modification programs

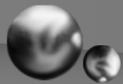
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Summary

- Exclude age group (b) 18-21 in literature searches
- Add clinical and cost-effectiveness articles
- NIH Consensus and International data provide strong evidence for resolution of co-morbidities in adults
- Consider changing “weak” to “moderate” evidence for Key question 2.

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Supplement

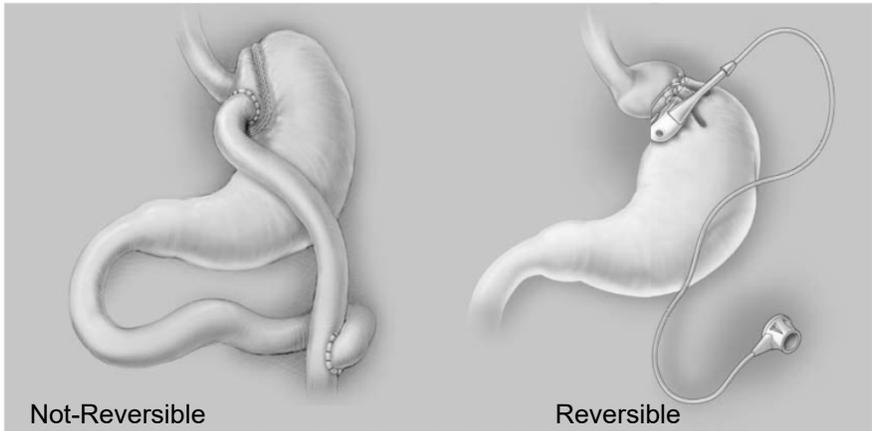
- See next slide

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Two Major Bariatric Surgeries Performed in the US:

Roux-en-Y Gastric Bypass

Adjustable Gastric Banding



*Gastric bypass is performed as an irreversible procedure, in a small number of cases, surgeons have reattached the stomach

Steinbrook R. NEJM. 2004. 350(11) 1075-59

HTCC Coverage and Reimbursement Determination Analytic Tool

HTA's goal is to achieve *better health care outcomes* for enrollees and beneficiaries of state programs by paying for proven health *technologies that work*.

To find best outcomes and value for the state and the patient, the HTA program focuses on these questions:

1. Is it safe and effective?
2. Is it more effective or safer?
3. Is it equally effective and safe, and more cost-effective?

The principles HTCC uses to review evidence and make determinations are:

Principle One: Determinations are Evidence based

HTCC requires scientific evidence that a health technology is safe, effective and cost-effective¹ as expressed by the following standards.²

- Persons will experience better health outcomes than if the health technology was not covered and that the benefits outweigh the harms.
- The HTCC emphasizes evidence that directly links the technology with health outcomes. Indirect evidence may be sufficient if it supports the principal links in the analytic framework.
- Although the HTCC acknowledges that subjective judgments do enter into the evaluation of evidence and the weighing of benefits and harms, its recommendations are not based largely on opinion.
- The HTCC is explicit about the scientific evidence relied upon for its determinations.

Principle Two: Determinations result in health benefit

The outcomes critical to HTCC in making coverage and reimbursement determinations are health benefits and harms.³

- In considering potential benefits, the HTCC focuses on absolute reductions in the risk of outcomes that people can feel or care about.
- In considering potential harms, the HTCC examines harms of all types, including physical, psychological, and non-medical harms that may occur sooner or later as a result of the use of the technology.
- Where possible, the HTCC considers the feasibility of future widespread implementation of the technology in making recommendations.
- The HTCC generally takes a population perspective in weighing the magnitude of benefits against the magnitude of harms. In some situations, it may make a determination for a technology with a large potential benefit for a small proportion of the population.
- In assessing net benefits, the HTCC subjectively estimates the indicated population's value for each benefit and harm. When the HTCC judges that the balance of benefits and harms is likely to vary substantially within the population, coverage or reimbursement determinations may be more selective based on the variation.
- The HTCC considers the economic costs of the health technology in making determinations, but costs are the lowest priority.

¹ Based on Legislative mandate: See RCW 70.14.100(2).

² The principles and standards are based on USPSTF Principles at: <http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm>

³ The principles and standards are based on USPSTF Principles at: <http://www.ahrq.gov/clinic/ajpmsuppl/harris3.htm>

HTCC Evaluation Factors

HTCC implements the program mandate and key principles that the decision be evidence based and that it be weighted most importantly on whether a given technology is safe and improves health through a decision tool.

Using Evidence as the basis for a Coverage Decision

Evaluate the primary coverage question by identifying for each primary factor (Safety, Effectiveness, and Cost) whether (1) evidence is available, (2) the confidence in the evidence, and (3) applicability to decision.

1. **Availability of Evidence:**

Committee members decide whether information is available - Yes/No

2. **Confidence in the Evidence:**

Committee members decide how confident they are in the scientific evidence by identifying the type and quality of evidence⁴ for consideration such as:

- Type of evidence as reported in the technology assessment or other evidence presented to committee (randomized trials, observational studies, case series, expert opinion);
- the amount of evidence (sparse to many number of evidence or events or individuals studied);
- consistency of evidence (results vary or largely similar);
- recency (timeliness of information);
- directness of evidence (link between technology and outcome);
- relevance of evidence (applicability to agency program and clients);
- bias (likelihood of conflict of interest or lack of safeguards).

Not Confident	Confident
Appreciable uncertainty exists. Further information is needed or further information is likely to change confidence.	Very certain of evidentiary support. Further information is unlikely to change confidence

3. **Factors for Consideration - Importance**

Committee members also consider the degree of importance that particular evidentiary information has to the policy and coverage decision. Factors used to assess level of importance are topic specific but most often include, for areas of safety, effectiveness, and cost:

- risk of event occurring;
- the degree of harm associated with risk;
- the number of risks; the burden of the condition;
- burden untreated or treated with alternatives;
- the importance of the outcome (e.g. treatment prevents death vs relief of symptom);
- the degree of effect (e.g. relief of all, none, or some symptom, duration, etc.);
- value variation based on patient preference.

⁴ Based on GRADE recommendation: <http://www.gradeworkinggroup.org/FAQ/index.htm>

THERAPEUTIC TECHNOLOGY

Safety

Morbidity

- Does scientific evidence show that use of the technology is free of, or unlikely to produce, significant morbidity?
Significant morbidity: Frequent adverse effect on health, but unlikely to result in lasting harm or be life-threatening, or adverse effect on health that can result in lasting harm or can be life-threatening.
 - Yes
 - No
 - Not Studied/No Evidence

- In terms of morbidity, level of confidence that the evidence confirms use of the technology is safe:
 - Not confident
 - Confident

Mortality

- Does scientific evidence show that use of the technology is not likely to increase mortality?
 - Yes
 - No
 - Not Studied/No Evidence

- In terms of mortality, level of confidence that the evidence confirms use of the technology is safe:
 - Not confident
 - Confident

Overall

- Does scientific evidence confirm that use of the technology is safe?
 - Yes
 - No

- Level of confidence that the evidence confirms that use of the technology is safe?
 - Not confident
 - Confident

THERAPEUTIC TECHNOLOGY

Effectiveness

Use of the technology compared to no or placebo treatment:

- Is there scientific evidence confirming that use of the technology improves health outcomes, compared to no treatment or placebo treatment?
 - Yes
 - No

- Level of confidence that the evidence confirms that the technology improves outcomes compared to no treatment or placebo treatment:
 - Not confident
 - Confident

If use of the technology improves outcomes compared to no treatment:

- Is there scientific evidence that confirms that use of the technology results in significantly better health outcomes than alternative treatments?
 - Yes
 - No

- Level of confidence that the evidence confirms that use of the technology results in better health outcomes than alternative treatments:
 - Not confident
 - Confident

If use of the technology does not improve outcome more than alternative treatments:

- Is there scientific evidence confirming that use of the technology results in equivalent health outcomes as using alternative treatments?
 - Yes
 - No

- Level of confidence that the evidence confirms that use of the technology results in equivalent health outcomes as alternative treatments:
 - Not confident
 - Confident

THERAPEUTIC TECHNOLOGY

Cost Impact

- Are independent cost analyses (cost benefit; cost effectiveness; or other cost analysis) identified?

- Yes
- No

If Yes:

- Do the cost analyses show that use of the new technology will result in costs that are greater, equivalent or lower than management without use of the technology?

- Greater
- Equivalent
- Lower
- Not applicable: No independent cost analysis identified

If No:

- Does the evidence available to the committee indicate that use of the new technology will result in costs that are greater, equivalent or lower than management without use of the technology?

- Greater
- Equivalent
- Lower

THERAPEUTIC TECHNOLOGY

Benefit Evaluation

- Based on the current level of evidence regarding the technology's safety and effectiveness relative to currently available treatments, is use of the technology likely to have:

- Net Benefit
- Equivalent Benefit
- Less Benefit
- Net Harm
- The available evidence does not permit a conclusion

- Based on the current level of evidence regarding the technology's cost impact relative to currently available treatment, is use of the technology likely to:

- Increase Cost
- Equivalent Cost
- Lower Cost

Relative to currently available treatment, into which category does the evidence indicate use of the new technology will fall?

Less Benefit Increased Cost	Equivalent Benefit Increased Cost	Net Benefit Increased Cost
Less Benefit Equivalent Cost	Equivalent Benefit Equivalent Cost	Net Benefit Equivalent Cost
Less Benefit Reduced Cost	Equivalent Benefit Reduced Cost	Net Benefit Reduced Cost

THERAPEUTIC TECHNOLOGY
Coverage Determination

The HTCC has reviewed and considered the technology assessment and information provided by the administrator, reports and/or testimony from an advisory group, and submissions or comments from the public. The committee has given greatest weight to the evidence it determined, based on objective factors, to be the most valid and reliable.

- Based on the evidence regarding the technology’s safety, effectiveness, and cost-effectiveness, the use of the technology should be covered?
 - No. Evidence is insufficient to conclude that the health technology is safe, efficacious, and cost-effective or the evidence is sufficient to conclude that the health technology is unsafe, ineffectual, or not cost-effective

or

- Yes. The evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective for all indicated conditions

or

- Yes, under certain conditions. Coverage is allowed with special conditions (e.g. population, conditions, timing, adjunct services, qualifications, etc.) because the evidence is sufficient to conclude that the health technology is safe, efficacious, and cost-effective only when:

This determination is consistent with the identified Medicare decisions and expert guidelines.

Based on the evidence, this determination is inconsistent with either the identified Medicare decisions or expert guidelines.