A META-ANALYSIS EXPLORING THE EFFECT OF AGE ON WEIGHT LOSS FOLLOWING A LAPAROSCOPIC SLEEVE GASTRECTOMY

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Approval page

The undersigned, appointed by the dean of the Graduate School, have examined the dissertation entitled

A META-ANALYSIS EXPLORING THE EFFECT OF AGE ON WEIGHT LOSS FOLLOWING A LAPAROSCOPIC SLEEVE GASTRECTOMY

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Abstract

Obesity is a grave concern within the United States, resulting in lost productivity, increased medical costs and obesity related comorbidities with lifelong repercussions. The laparoscopic sleeve gastrectomy is a treatment option for obesity and is performed in both adolescents and adults. Outcomes in the adolescent and adult are typically reported separately. A meta-analysis was conducted combining adolescent and adult literature to determine the overall effect of the laparoscopic sleeve gastrectomy and to explore age, biological sex and baseline BMI as moderating variables. The laparoscopic sleeve was effective at facilitating weight loss postoperatively. Age, biological sex and baseline BMI were not found to influence outcomes; however, there were limitations including a paucity of adolescent data. Changes in comorbidities following weight loss after the laparoscopic sleeve gastrectomy were unable to be examined due to a lack of reporting in primary studies and inconsistent definitions. Attrition was a barrier to assessing long term outcomes across studies. Further research is warranted to investigate long term outcomes and changes in comorbidities following the laparoscopic sleeve gastrectomy. Additionally, standardization in reporting methods should occur when defining obesity related comorbidities.

Chapter 1: Introduction

Significance

Within the United States, medical care related to obesity and associated comorbidities has been estimated to cost $147 billion dollars and account for almost 10% of overall healthcare dollars spent yearly (Finkelstein et al., 2008; Centers for Disease Control and Prevention [CDC], 2018). Additionally, obesity related absenteeism was estimated to cost the United States economy between $3.38 and $6.38 billion dollars per year (CDC, 2018). Obesity increases the risk of several disorders that can lead to lifelong complications including diabetes, elevated cholesterol and/or triglyceride levels, musculoskeletal pain or discomfort, obstructive sleep apnea, liver abnormalities such as hepatic steatosis and pseudotumor cerebri (Alvarez-Blasco et al., 2006; Andrews et al., 2014; Kalra et al., 2005; Kelly et al., 2013; The GBD 2015 Obesity Collaborators, 2017; Xanthakos et al., 2015). Negative psychosocial effects have been reported in the obese adolescent including depression and eating disorders (Kim et al., 2008). Adults suffering from depression were more likely to be obese than their non-depressed counterparts and were more likely to require the use of antidepressants than depressed individuals who were not obese (Pratt & Brody, 2014). Overall obesity represents a public health concern and has been cited as the second leading cause of preventable death within the United States (Mokdad et al., 2004).

Bariatric surgery is a treatment option for obesity. Approximately 256,000 total bariatric surgeries were performed in 2019, 16.7% of which accounted for revisions (American Society for Metabolic and Bariatric Surgery [ASMBS], 2022). The laparoscopic sleeve gastrectomy accounts for over half of all bariatric surgeries performed within adults and 78.2% of bariatric surgeries in individuals less than 18 yrs of age within the United States (Khorgami et al., 2017; Kyler, Bettenhausen, Hall, Fraser & Sweeney, 2019). Historically, three bariatric procedures have been offered including laparoscopic adjustable gastric banding, the roux-en-y gastric bypass procedure and the laparoscopic sleeve gastrectomy (Khorgami et al., 2017; Mattei, 2011). The laparoscopic gastric band is a restrictive procedure in which a device is placed circumferentially around the superior aspect of the stomach, decreasing capacity of the stomach and helping to limit oral intake. The sleeve gastrectomy is a procedure in which the greater fundus of the stomach is resected, restricting the volume that the stomach can accommodate. The roux-en-y gastric bypass is a restrictive and malabsorptive procedure in which the stomach is resected and a roux limb of bowel is connected from the stomach to the jejunum, bypassing the duodenum where digestive enzymes enter the bowel (Phillips & Shikora, 2018). Weight regain has been reported and represents one reason that a revision may be required and is an indication that bariatric surgery as a treatment option for obesity can be advanced (Karasko, 2018; Kushner & Sorenson, 2015). Lower baseline BMI has been strongly associated with an increased likelihood to achieve normal weight status postoperatively following bariatric surgery in the adolescent, advocating earlier referral to bariatric surgery (Inge et al., 2010). Variability of weight loss following bariatric surgery creates difficulty for practitioners attempting to identify individuals that would benefit from a laparoscopic sleeve gastrectomy. Examining and identifying potential contributing factors that affect outcomes will result in better predictability and allow practitioners to adequately inform individuals seeking to undergo weight loss surgery.

Innovation

The following meta-analysis utilizes a unique and innovative approach to investigating weight loss following bariatric surgery by combining both adult and adolescent literature to evaluate the effect of age on weight loss. Adolescent results are typically published separately from adults and meta-analyses conducted in the past investigating the effectiveness of bariatric surgery in the adolescent combined all bariatric procedures offered. The previous meta-analyses conducted revealed that the laparoscopic sleeve gastrectomy facilitates weight loss; however, long term data were lacking and each called for further research (Black et al., 2013; Shoar et al., 2017). Meta-analyses conducted in the adult patient have found that the laparoscopic sleeve gastrectomy is effective at weight loss; however, weight regain can occur (Clapp et al., 2018; O'brien et al., 2018). Combining adolescent and adult literature to investigate age as a covariate is a novel approach to attempt to identify if outcomes following bariatric surgery are different based on the mean age of the sample.

The following dissertation seeks to evaluate the effectiveness of the laparoscopic sleeve gastrectomy as a weight loss procedure, examine age as a predictor variable for weight loss and explore variation in weight loss by sample characteristics such as biological sex and baseline BMI in the form of a meta-analysis. Examining variables that potentially affect long term weight loss will help to inform practitioners and identify any gaps in knowledge that exist, helping to guide future research. Very few studies have conducted subgroup analyses to evaluate the impact of individual factors on overall weight loss. Subgroup analyses may help to clarify the variable results that are exhibited regarding weight loss following the laparoscopic sleeve gastrectomy. Additionally, adolescent and adult populations are typically segregated in analyses and rarely, if ever, combined creating a divide within the literature when examining outcomes.

The dissertation that follows utilizes age as a covariate to determine if the age at which surgery is performed impacts long term weight loss. Chapter 1 of the dissertation introduces the topic. Chapter 2 is a published systematic review that examines existing literature regarding weight loss outcomes in adolescents following bariatric surgery. Chapter 3 discusses methods used for the dissertation, a systematic review and meta-analysis of weight loss outcomes following the laparoscopic sleeve gastrectomy across the life span. Chapter 4 reports the results of the dissertation, and Chapter 5 discusses the implications for clinical practice and future research.

Chapter 2: Literature review

Weight Loss in Adolescents after Bariatric Surgery- A Systematic Review

Karasko, D. (2019). Weight Loss in Adolescents After Bariatric Surgery: A Systematic Review. *Journal of Pediatric Health Care: Official Publication of National Association of Pediatric Nurse Associates & Practitioners*, *33*(1), 26–34. https://doi.org/10.1016/j.pedhc.2018.05.010

Abstract

Introduction: Bariatric surgery is a treatment option for the obese adolescent. There are 3 primary surgical procedures: the bypass, sleeve gastrectomy and lap band. The most recent literature was reviewed to examine changes in weight, comorbidities and complications following bariatric surgery in the adolescent.

Method: A systematic search was performed to identify original research articles published within the United States between the years of 2000-2017 with subjects between the ages of 11-21 that provided greater than 30 days of results.

Results: A total of 23 articles were identified. Weight loss, improvement in comorbidities and complications were reported following all procedures.

Discussion: Outcomes were not reported in a standardized fashion, creating much difficulty in interpreting and comparing results. The sleeve gastrectomy is increasing in incidence while the lap band is decreasing. Further research is needed to draw more definitive conclusions regarding long term results in the adolescent undergoing bariatric surgery.

Introduction

Obesity in the United States remains a concern. Rates of obesity among adolescents have failed to decline despite increased awareness. Adolescent obesity continues to be a cause for concern because extreme obesity among adolescents, defined as a BMI at or above 120% on the CDC growth charts, has increased to a rate of 9.1% from 2.6% (Ogden et al., 2016).

Obesity in children and adolescents increases the risk of developing comorbidities including: diabetes, hypertension, dyslipidemia, obstructive sleep apnea, musculoskeletal pain/joint disease, nonalcoholic hepatic steatosis, gastroesophageal reflux, and polycystic ovarian syndrome contributing to poor health outcomes (Alvarez-Blasco, Botella-Carretero, San Millan, & Escobar-Morreale, 2006; Kalra et al., 2005; Kelly et al., 2013; Xanthakos et al., 2015). Pseudotumor cerebri (increased intracranial pressure of uncertain etiology), a rare but severe condition, has also been shown to have an association with obesity (Andrews, Liu & Ko, 2014). In addition to the above comorbidities, negative psychosocial effects such as depression and eating disorders have been described in obese and overweight adolescents (Kim et al., 2008; as cited in Kalra, DeSousa, Sonavane & Shah, 2012). Finally, adolescents who are obese are more likely to remain obese into adulthood, increasing their risks for continuation of overall poor health (Ogden et al, 2012).

Bariatric surgery is a treatment option for the obese adolescent. Approximately, 968 adolescents undergo bariatric procedures yearly within the United States (Kindel, Lomelin, McBride, Kothari & Oleynikov, 2016). Three procedures are primarily utilized in the United States for adolescent bariatric surgery: laparoscopic adjustable gastric banding (lap band), laparoscopic sleeve gastrectectomy (sleeve) and the roux-en-y gastric bypass (bypass) (Mattei, 2011). The lap band is a purely restrictive procedure in which an adjustable device is positioned around the upper portion of the stomach, creating a small pouch. Saline is instilled into the band and titrated as needed to provide optimal satiety without dysphagia (Mattei, 2011). The sleeve is a procedure in which the stomach is longitudinally resected along the greater curvature (Mattei, 2011). Weight loss is thought to occur primarily from a restrictive component; however, there has been evidence to suggest that the decreased presence of ghrelin, a hormone that is secreted in the fundus of the stomach and believed to regulate hunger, may play a role (Karamanakos et al., 2008). In the bypass procedure, the stomach is resected (similar to the sleeve) and the smaller stomach is then connected directly to the jejunum, bypassing the stomach, duodenum and proximal jejunum (Mattei, 2011). Weight loss occurs due to a restrictive and malabsorbptive component (Mattei, 2011).

Concerns regarding bariatric or weight loss procedures within the adolescent focus on safety and efficacy within a vulnerable population. The purpose of this paper is to examine existing literature and primarily report weight loss, while also describing the effect of bariatric surgery on comorbid conditions and postoperative complications.

Method

Studies deemed eligible for this review included works of original research published in 2000 or later focusing on bariatric surgery conducted in the United States with subjects between the ages of 11- 21 years at the time of surgery that reported weight as a main outcome measure and provided greater than 30 days of results. Two search engines were used to locate relevant articles: PubMed and Scopus. The original search was conducted in November 2016 with an updated search in December 2017. The following key terms were utilized: adolescent AND bariatric surgery. Limits placed on the search included: English language, article, and United States. The search yielded 1,466 results in Scopus. A similar number was obtained in PubMed. Most of the 1,466 articles were identified as failing to meet the inclusion criteria by reading the title and/or abstract. Ancestry searches were performed of primary research articles and review articles. Seventy articles were accessed and reviewed in full. After review, 47 articles were excluded. Fourteen of the excluded articles did not report weight as the primary outcome. The decision to exclude articles focusing on a different primary outcome than weight was made to prevent overlap in subject populations. Fourteen articles were excluded because the articles included the same patient population as an article published at a later date that was included in the review. Four articles were excluded because data did not come from an original subject population. Thirteen articles were excluded because they were conducted outside the United States. One article was excluded because it was a methodology paper. One article was excluded because it did not include results past thirty days. See figure 1 for search strategy.

Findings

Twenty-three studies were found to meet inclusion criteria and comprise the review. The number of subjects included in the studies varied, ranging from 4 to 228 subjects. The median number of subjects of all the studies was 26.5. The majority of the studies reported outcomes following the bypass procedure (Barnett et al., 2005; Capella & Capella, 2003; Collins et al., 2007; Cozacov et al., 2014; De La Cruz-Munoz et al., 2013; Ducoin, Moon, Mulatre, Teixeira, & Jawad, 2015; Inge et al., 2015; Inge et al., 2017; Lee et al., 2012; Madan, Dickson, Ternovits, Tichansky & Lobe, 2007; Nijhawan, Martinez & Wittgrove, 2012; Serrano et al., 2016; Strauss, Bradley & Brolin, 2001; Sugerman et al., 2003; Teeple, Teich, Schuster & Michalsky, 2012). Six studies reported results on more than one type of procedure (Cozacov et al., 2014; De La Cruz-Munoz et al., 2013; Inge et al., 2015; Lee et. al., 2012; Pedroso, Gander, Oh & Zitsman, 2015; Serrano et al., 2016).

Patient Demographics

Seventeen studies reported mean ages of subjects with values ranging from 15.7-19.9 years (Barnett et al., 2005; Collins et al., 2007; Cozacov et al., 2014; De La Cruz-Munoz et al., 2013; Dillard et al., 2007; DuCoin et al., 2015, Holterman et al., 2010; Inge et al., 2015; Inge et al., 2017; Jaramillo et al., 2017; Lee et al., 2012; Madan et al., 2007; McGuire, Nadler, & Qureshi, 2014; Nadler, Youn, Ren, & Fieldi, 2008; Pedroso et al., 2015; Serrano et al., 2016; Sugerman et al., 2003). Twenty studies reported gender. All but one study reported the majority undergoing bariatric surgery as being female (Barnett et al., 2005; Cozacov et al., 2014; De La Cruz-Munoz, 2013; Dillard et al., 2007; DuCoin et al., 2015; Ejaz et al., 2016; Holterman et al., 2010; Inge te al., 2015; Inge et al., 2017; Jaramillo et al., 2017; Lee et al., 2012; Madan et al., 2007; McGuire et al., 2014; Nadler et al., 2008; Pedroso et al., 2015; Serrano et al., 2016; Strauss et al., 2001; Sugerman et al., 2003; Teeple et al., 2012). The singular study that did not report a majority of female patients had an equal number of male and female patients (Horgan et al., 2005). Nine studies reported race/ethnicity. Five studies reported a majority of individuals undergoing bariatric surgery as Caucasian, 3 studies reported a majority of Hispanic subjects and 1 study reported a majority of African-American subjects (De La Cruz-Munoz et al., 2013; Ejaz et al., 2016; Holterman et al., 2010; Inge et al., 2015; Inge et al., 2017; Jaramillo et al., 2017; Nadler et al., 2008; Pedroso et al., 2015; Sugerman et al., 2003).

Weight Outcomes

Weight was reported utilizing different measures including pounds (lb), kilograms (Kg), body mass index (BMI) and percent excess weight loss (%EWL), defined as: [(preoperative weight- follow up weight)/(preoperative weight – ideal body weight)] X 100 (Montero, Stefanidis, Norton, Gersin, & Kuwada, 2011). See table 1 for weight outcomes.

Lap band

Eight studies reported results following the lap band procedure with follow up times ranging from 9-15 months (subjects included in the analysis had follow up times varying from 9-15 months) to 4 years (De La Cruz-Munoz et al., 2013; Dillard et al., 2007; Holterman et al., 2010; Horgan et al., 2005; Inge et al., 2015; Lee et al., 2012; Nadler, Youn, Ren, & Fieldi, 2008; Pedroso et al., 2015).

Preoperative mean weights ranged from 126.2 Kg to 147 Kg and 296 to 298 lbs (De La Cruz-Munoz et al., 2013; Holterman et al., 2010; Horgan et al., 2005; Nadler et al., 2008, & Pedroso et al., 2015). Preoperative mean BMI ranged from 45.3-51 (De La Cruz-Munoz et al., 2013; Dillard et al., 2007; Holterman et al., 2010; Horgan et al., 2005; Lee et al., 2006; Nadler et al., 2008; & Pedroso et al., 2015).

Studies reported weight loss and a decrease in BMI postoperatively. Mean postoperative weights ranged from 115.2 Kg at 9-15 months to 115.1 at 2 years (De La Cruz-Munoz et al., 2013, & Pedroso et al., 2015). One study reported a decrease from

298 lbs to 204 lbs over a time period of 2 years (Nadler et al., 2008). Inge et al. (2015) reported weight in terms of kilograms lost, with an average of 10.4 Kg lost over 3 years, corresponding to an 8.3% decrease in weight. Mean postoperative BMI ranged from 32.1 to 43 over 9-15 months to 4 years (De La Cruz-Munoz et al., 2013; Dillard et al., 2007; Nadler et al., 2008; & Pedroso et al., 2015). Inge et al. (2015) reported %BMI change with subjects decreasing their BMI by 8.1% over 3 years. Two studies reported changes in BMI as BMI loss in units. Results ranged from a decrease in 9.4 units after 18 months to a decrease of 3.8 units over 3 years (Holterman et al., 2010; & Inge et al., 2015). Lastly, one study reported individual weight loss ranging from 6-51 Kg, corresponding to a 15-87% EWL in four subjects over 4-30 months (Horgan et al., 2005).

Sleeve

Seven studies reported results following the sleeve procedure over 6 months to an average of 47.9 months (Cozacov et al., 2014; Ejaz et al., 2016; Inge et al., 2015; Jaramillo et al., 2017; McGuire, et al., 2014; Pedroso et al., 2015; & Serrano et al., 2016). Mean preoperative weights ranged from 132 to 144 Kg (Inge et al., 2015; Jaramillo et al., 2017; Pedroso et al., 2015; & McGuire et al., 2014). Preoperative BMI ranged from 46.2-51.0 (Cozacov et al., 2014; Ejaz et al., 2016; Inge et al., 2015; Jaramillo et al., 2017; McGuire et al., 2014; Pedroso et al., 2015; & Serrano et al., 2016). Postoperative mean weight varied from 94.2 to 105 kg, with 1 study reporting a mean weight of 196.8 lbs (Cozacov et al., 2014; Inge et al., 2015; & Pedroso et al., 2015). Percent EWL ranged from 38.6%-70.9% over a period of 6- 24 months (Ejaz et al., 2016; Jaramillo et al., 2017; McGuire et al., 2014; Pedroso et al., 2015; & Serrano et al., 2016). Post-operative mean BMI varied from 29.6- 37.4 over 12 months to a mean 47.9 months (Cozacov et al., 2014; Inge et al., 2015; Jaramillo et al., 2017; Pedroso et al., 2015; Serrano et al., 2016).

Bypass

Fifteen studies reported results following bypass in adolescent patients (Barnett et al., 2005; Capella & Capella, 2003; Collins et al., 2007; Cozacov et al., 2014; De La Cruz-Munoz et al., 2013; Ducoin, Moore, Mulatre, Teixeira & Jawad, 2015; Inge et al., 2015; Inge et al, 2017; Lee et al., 2012; Madan, Dickson, Ternovits, Tichansky & Lobe, 2007; Nijhawan, Martinez & Wittgrove, 2012; Serrano et al., 2016; Strauss, Bradley, & Brolin, 2001; Sugerman et al., 2003; Teeple, Teich, Schuster, & Michalsky, 2012). Mean pre-operative weights ranged from 293-323 lbs and 128.57-179.6 Kg (Capella & Capella, 2003; Collins et al., 2007; Cozacov et al., 2014; De La Cruz-Munoz et al., 2013; Inge et al., 2015; Inge et al., 2017; Madan et al., 2007; Strauss et al., 2001; Sugerman et al., 2003; & Teeple et al., 2012). Pre-operative mean BMI ranged from 45.7-58.8 (Barnett et al., 2005; Capella & Capella, 2003; Collins et al., 2007; Cozacov et al., 2014; De La Cruz-Munoz et al., 2013; DuCoin et al., 2015; Inge et al., 2015; Inge et al., 2017; Lee et al., 2012; Madan et al., 2007; Nijhawan et al., 2012; Serrano et al., 2016; Sugerman et al., 2003; & Teeple et al., 2012). Post-operative mean weights ranged from 97.7-122 kg over 9-15 months to 14 years (De La Cruz-Munoz, 2013; Inge et al., 2015; & Teeple et al., 2012). Cosacov et al. reported a post-operative mean weight of 189.3 lbs with an average follow up of 54.4 months. Percent EWL ranged from 54.8-83.4% over an average of 11.5 months to 9 years (Barnett et al., 2005; Capella & Capella, 2003; Collins et al., 2007; DuCoin et al., 2015; Lee et al., 2012; Madan et al., 2007; Nijhawan et al., 2012; Serrano et al., 2016; Sugerman et al., 2003; & Teeple et al., 2012). Two studies reported

BMI loss in terms of units lost, with values ranging from 15-20.7 over a time period of 12 months to 9 years (Inge et al., 2015; & Nijhawan et al., 2012).

Changes in obesity related comorbidities

Lap Band

Five studies evaluated comorbid conditions in patients undergoing lap band placement. Two of three studies evaluating dyslipidemia reported improvements postoperatively, while the third study reported improvements in one of two subjects (Holterman et al., 2010; Lee et al., 2012; & Nadler et al., 2008). Hypertension was evaluated by 2 studies with both studies reporting improvement (Holterman et al., 2010; & Nadler et al., 2008). Glucose sensitivities were evaluated in three studies, with each study measuring a slightly different outcome. Hemoglobin A1C, fasting glucose levels, glucose tolerance tests and homeostatic model assessment (defined as fasting insulin X fasting glucose/405) were all utilized to measure glucose sensitivities. All studies reported improvement within subjects following the lap band procedure (Holterman et al., 2010; Nadler et al., & Pedroso et al., 2015). Obstructive sleep apnea was evaluated by one study with 3 of 4 subjects reporting resolution of symptoms (Nadler et al., 2008). Musculoskeletal issues, categorized as back pain and musculoskeletal complaints were evaluated by 2 studies with both studies reporting improvement postoperatively (Horgan et al., 2005; & Nadler et al., 2008).

Sleeve

Six studies reported on comorbid conditions in patients undergoing the sleeve procedure (Cozacov et al., 2014; Ejaz et al., 2016; Inge et al., 2015; Jaramillo et al., 2017;

Pedroso et al., 2015; Serrano et al., 2016). Cozacov et al., 2014 reported comorbid conditions in conjunction with subjects undergoing bypass surgery. Results could not be differentiated by procedure type and are discussed in the bypass section. Sugerman et al., 2003 reported comorbid conditions preoperatively but did not report postoperative results. Improvements in glucose levels were observed in 3 of 4 studies evaluating diabetes mellitus type II (Ejaz et al., 2016; Inge et al., 2015; Jaramillo et al., 2017; & Serrano et al., 2016). Three of 4 studies reported improvement in hypertension postoperatively (Ejaz et al., 2016; Inge et al., 2015; Jaramillo et al., 2017; & Serrano et al., 2016). Abnormal lipid levels were evaluated by four studies and reported in the following ways: hyperlipidemia, individual components (triglycerides and HDL) and dyslipidemia. All studies reported improvements with one study observing reduced levels of HDL (Ejaz et al., 2016; Inge et al., 2015; Jaramillo et al., 2017; & Pedroso et al., 2015). Three studies evaluated obstructive sleep apnea with mixed results. Two reported improvement while one did not observe any change (Ejaz et al., 2016; Jaramillo et al., 2017; & Serrano et al., 2016). Asthma was evaluated by Serrano et al., (2016) with the authors reporting a decrease to 23.5% from 35.3% of subjects experiencing symptoms.

Bypass

Thirteen articles reported comorbid conditions in subjects undergoing bypass surgery (Barnett et al., 2005; Capella & Capella, 2003; Collins et al., 2007; Cozacov et al., 2014; DuCoin et al., 2015; Inge et al., 2015; Inge et al., 2017; Lee et al., 2012; Nijhawan et al., 2012; Serrano et al., 2016; Strauss et al., 2001; Sugerman et al., 2003; & Teeple et al., 2012). Two studies reported improvement in comorbidities postoperatively but did not delineate specific comorbidities and could not be included (Capella &

Capella, 2003; DuCoin et al., 2015). Hypertension was evaluated by 12 articles with 7 reporting improvements, 3 did not report postoperative outcomes and 2 studies found no significant difference (Barnett et al., 2005; Collins et al., 2007; Cozacov et al., 2014; DuCoin et al., 2015; Inge et al., 2015; Inge et al., 2017; Lee et al., 2012; Nijhawan et al., 2012; Serrano et al., 2016; Strauss et al., 2001; Sugerman et al., 2003; & Teeple et al., 2012). Glucose abnormalities were assessed in 9 articles and reported in different manners including: diabetes mellitus type II, insulin resistance, HgA1c levels and homeostatic model assessment index. Eight studies reported improvement in glucose abnormalities while one study found no significant change in glucose levels, but a significant decrease in HgA1c (Collins et al., 2007; Cozacov et al., 2014; Inge et al., 2015; Inge et al., 2017; Lee et al., 2012; Nijhawan et al., 2012; Serrano et al., 2016; Sugerman et al., 2003; & Teeple et al., 2012). Obstructive sleep apnea was evaluated by 7 studies with 6 reporting improvements postoperatively and one did not report outcomes postoperatively (Barnett et al., 2005; Collins et al., 2007; Cozacov et al., 2014; Nijhawan et al., 2012; Serrano et al., 2016; Strauss et al., 2001; & Sugerman et al., 2003). Abnormal lipid levels were evaluated by 8 studies and categorized in different ways including: dyslipidemia, hypercholesterolemia, hypertriglyceridemia as well as evaluation of individual components (Collins et al., 2007; Cozacov et al., 2014; Inge et al., 2015; Inge et al., 2017; Lee et al., 2012; Nijhawan et al., 2012; Serrano et al., 2016; & Teeple et al., 2012). Three studies reported improvement in lipid levels postoperatively (Inge et al., 2015; Lee et al., 2012; & Nijhawan et al., 2012). Triglyceride and LDL levels significantly decreased postoperatively and HDL levels significantly increased postoperatively in 2 of 3 studies (Inge et al., 2017; Serrano et al., 2016; & Teeple et al., 2012). Four studies evaluated musculoskeletal issues with differing categories including degenerative joint disease, joint pain, lower back pain, musculoskeletal complaints and arthritic symptoms with all reporting improvements postoperatively (Barnett et al., 2005; Nijhawan et al., 2012; Serrano et al., 2016 & Sugerman et al., 2003). Improvements in symptoms were reported in 2 of 4 studies evaluating asthma (Collins et al., 2007; Cozacov et al., 2014; Nijhawan et al., 2012; & Serrano et al., 2016).

Complications

Lap band

All 8 studies reported a complication in subjects after undergoing placement of the lap band (De La Cruz-Munoz et al., 2013; Dillard et al., 2007; Holterman et al., 2010; Horgan et al., 2005; Lee et al., 2012; Nadler et al., 2008; Pedroso et al., 2015; & Inge et al., 2015). Two studies reported an overall complication rate of 15-23.4% (Nadler et al., 2008; Pedroso et al., 2015). Six studies reported complications involving the lap band device including a port leak, band removal, band displacement or band slip (Dillard et al., 2007; Holterman et al., 2010; Inge et al., 2015; Lee et al., 2012; Nadler et al., 2008; & Pedroso et al., 2015). Additional complications included bowel obstruction, esophagitis, gastric prolapse, bleeding, gastric perforation, wound infection, hiatal hernia, cholelithiasis and/or cholecystitis with cholecystectomy, enlargement of the pouch, reoperation/revision, vitamin D deficiency, reflux and nephrolithiasis (Dillard et al., 2007; Holterman et al., 2010; Horgan et al., 2005; Nadler et al., 2008; & Pedroso et al., 2015). Three studies cited removal of the lap band with 2 studies reporting weight gain with conversion to another bariatric procedure (Inge et al., 2015; Lee et al., 2012; Nadler et al., 2008 & Pedroso et al., 2015).

Sleeve

Five studies reported complications following the sleeve procedure (Cozacov et al., 2014; Ejaz et al., 2016; Inge et al., 2015; & Jaramillo et al., 2017; Pedroso et al., 2015; & Serrano et al., 2016). One study cited a previously published article as having listed complications that occurred within their subjects which is not included in this review (McGuire et al., 2014). Abdominal reoperations included the following procedures: ventral hernia repair, wound drainage, luminal stent placement (for an anastomotic leak), cholecystectomy, appendectomy, endoscopy, stricture dilatation and conversion to bypass for weight regain (Cozacov et al., 2014; & Inge et al., 2015). Pancreatitis was reported by Jaramillo et al. (2017) in a single subject that had a previous history of pancreatitis. A pulmonary embolism reported by Ejaz et al. (2016). One mortality was reported as a result of a mesenteric venous thrombosis that occurred postoperatively (Pedroso et al., 2015). Additional complications included wound infection, blood transfusion, diarrhea, abdominal pain, heartburn, nausea, vomiting and feeding intolerance (Cozacov et al., 2014; & Ejaz et al., 2016).

Bypass

Fourteen studies reported complications following bypass surgery (Barnett et al., 2005; Capella & Capella, 2003; Collins et al., 2007; Cozacov et al., 2014; De La Cruz-Munoz et al., 2013; DuCoin et al., 2015; Inge et al., 2015; Inge et al., 2017; Lee et al., 2012; Nijhawan et al., 2012; Serrano et al., 2016; Strauss et al., 2001; Sugerman et al., 2003; & Teeple et al., 2012). Complications included: bowel obstruction, internal hernia, port site hernia, stricture, gastric or bowel perforation/leak, gastrogastric fistula stomal stenosis, bleeding, nausea, vomiting, severe protein and calorie deficiency requiring total parenteral nutrition, dumping syndrome, wound infections and/or complications, electrolyte imbalances, nutritional deficiencies and/or hypoglycemia, and cholelithiasis. Procedures, when listed, included revisions of the bypass, exploration, endoscopy, lysis of adhesions, repair of internal hernia, bowel resection, stricture dilatation, colonoscopy, appendectomy, cholecystectomy, excess skin removal and repair of incisional hernia (Barnett et al., 2005; Capella & Capella, 2003; Collins et al., 2007; Cozacov et al., 2014; De La Cruz-Munoz et al., 2013; DuCoin et al., 2015; Inge et al., 2015; Inge et al., 2017; Lee et al., 2012; Nijhawan et al., 2012; Serrano et al., 2016; Strauss et al., 2001; Sugerman et al., 2003; & Teeple et al., 2012). A gastric or marginal ulcer was reported by 4 studies (Capella & Capella, 2003; Collins et al., 2007; Inge et al., 2017; & Sugerman et al., 2003). Anemia was reported by 3 studies, the majority being caused by iron deficiency (Capella & Capella, 2003; Cozacov et al., 2014; De La Cruz-Munoz et al., 2013). Lee et al. (2012) reported a gastrogastric fistula occurring in one of their subjects and Sugerman et al. (2003) reported a pulmonary embolism occurring in one subject. Additional complications included. Folic acid deficiencies, vitamin D deficiency and vitamin B6 deficiency resulting in neuropathy in a singular subject was observed (Serrano et al., 2016; Strauss et al., 2001). Inge et al., (2017) reported two deaths. One subject experienced death following infectious colitis, while another subject experienced death following events unrelated to surgery. Two studies reported overall complication rates with Teeple et al. (2012) citing a short-term complication rate of 20% and Serrano et al. (2016) citing an 8.1% complication rate in combined sleeve and bypass data.

Discussion

Trends indicate that Caucasian is the majority race/ethnicity of patients undergoing bariatric surgery as an adolescent and female is the predominating gender (Kindel et al. 2016; Messiah et al., 2013, Shoar et al., 2017; Zwintscher, Azarow & Horton, 2013). The studies in this review reported similar trends apart from 4 studies reporting a different predominating race/ethnicity (De La Cruz-Muoz et al., 2013; Ejaz et al., 2016; Jaramillo et al., 2017; Pedroso et al., 2015). A possible explanation for this discrepancy includes location of the institution and the sample failing to reflect overall trends due to a small sample size. The average and median age of adolescents undergoing bariatric surgery is around 18 years of age with a range of approximately 14-18 years, comparable to reported ages within the articles included in this review (Kindel et al., 2016; Shoar et al., 2017; & Zwintscher et al., 2013)

Weight loss was achieved following all bariatric procedures. Evaluation of weight loss was inconsistent across studies with different methods of measurements. The inconsistency in measurements used to assess weight loss make it difficult to compare studies and procedures. Statistical evaluations were often lacking with studies, a weakness when attempting to evaluate the significance and impact of weight loss following bariatric surgery. Several studies consisted of a small sample size, possibly limiting the ability to perform statistical testing. Percent EWL was utilized by multiple studies included in this review and has been reported to vary significantly depending upon the calculation method used, leading to further confusion in interpreting postoperative results (Montero, Stefanidis, Norton, Gersin, & Kuwada, 2011). While the studies included in this review demonstrate that weight loss is achievable following bariatric surgery, weight regain was reported by 6 studies with some subjects undergoing revision or conversion to another bariatric procedure. (Barnett et al., 2005; Cozacov et al., 2014; DuCoin et al., 2015; Inge et al., 2015; Pedroso et al., 2015; & Sugerman et al., 2003). Weight regain emphasizes the need for continued evaluation to determine long term effectiveness of bariatric surgery within the adolescent patient.

Adolescents undergoing bariatric surgery exhibit an increased prevalence of comorbid conditions associated with obesity when compared with previous years. Despite increased complexities, overall rates of complication remain low, indicating bariatric surgery in the adolescent patient is safe (Kelleher, Merrill, Cottrell, Nadler, & Burd, 2013). While comorbid conditions showed improvements postoperatively, interpretation was often subjective. Future research should include standardized, objective data for more accurate reporting and analysis. Inconsistent follow up and attrition was reported by studies in this review, further contributing to difficulty interpreting results and necessitating ongoing evaluation for safety and efficacy in the adolescent undergoing bariatric surgery (Barnett et al., 2005; Capella & Capella, 2003; Collins et al., 2007; Cozacov et al., 2014; Ejaz et al., 2016; Holterman et al., 2010; Inge et al., 2015; Inge et al., 2017; Lawson et al., 2006; Lee et al., 2012; Nadler et al., 2008; Nijhawan et al., 2012; Pedroso et al., 2015; Serrano et al., 2016; Sugerman & Sugerman, 2003; Teeple et al., 2012). .

Procedures following bariatric surgery were reported by several studies; however, additional procedures may not always constitute a direct complication. Cholecystectomies were reported by 5 studies, which is not unexpected due to the increased risk for development of cholelithiasis following weight loss (Capella & Capella, 2003; Everhart, 1993; Inge et al., 2015; Inge et al., 2017; Nadler et al., 2008; &

Strauss et al., 2001). Studies have purposed prophylactic treatment with Actigall or Ursodiol, though the incidence rate and need for prophylaxis remains controversial (Li et al., 2009).

The sleeve procedure is a newer procedure with less longitudinal data available for analysis. Recent trends indicate a decreasing number of lap band surgeries being performed and an increasing number of sleeve gastrectomies (Kindel et al., 2016). While complications overall appear to be less than with the bypass, mesenteric venous thrombosis resulting in death post-operatively was described following a sleeve gastrectomy procedure (Pedroso et al., 2015). In adults, while overall uncommon, portomesenteric vein thrombosis has been identified as a complication following the sleeve procedure (Salinas et al., 2014). Consideration for the potential risk for portomesenteric vein thrombosis should be taken seriously despite the low occurrence rate due to the severe consequence of potential death.

Despite obesity being at the forefront of medicine, rates of childhood obesity have not decreased (Ogden et al., 2016). Aspects to consider as adolescent bariatric surgery continues to be an option for weight management are the long term results and complications as well as sustained weight loss. There is a paucity of data regarding long term results and complications following bariatric surgery in the adolescent, especially regarding newer procedures such as the sleeve. Further research is needed to draw definitive conclusions regarding outcomes and complication rates. Researchers should report outcomes using a standardized approach in data collection and definitions of comorbidities should be standardized in order to facilitate comparisons across studies. Finally, multi-center studies would result in larger numbers of participants and allow for more definitive conclusions in outcomes, complications and improvement in comorbidities.

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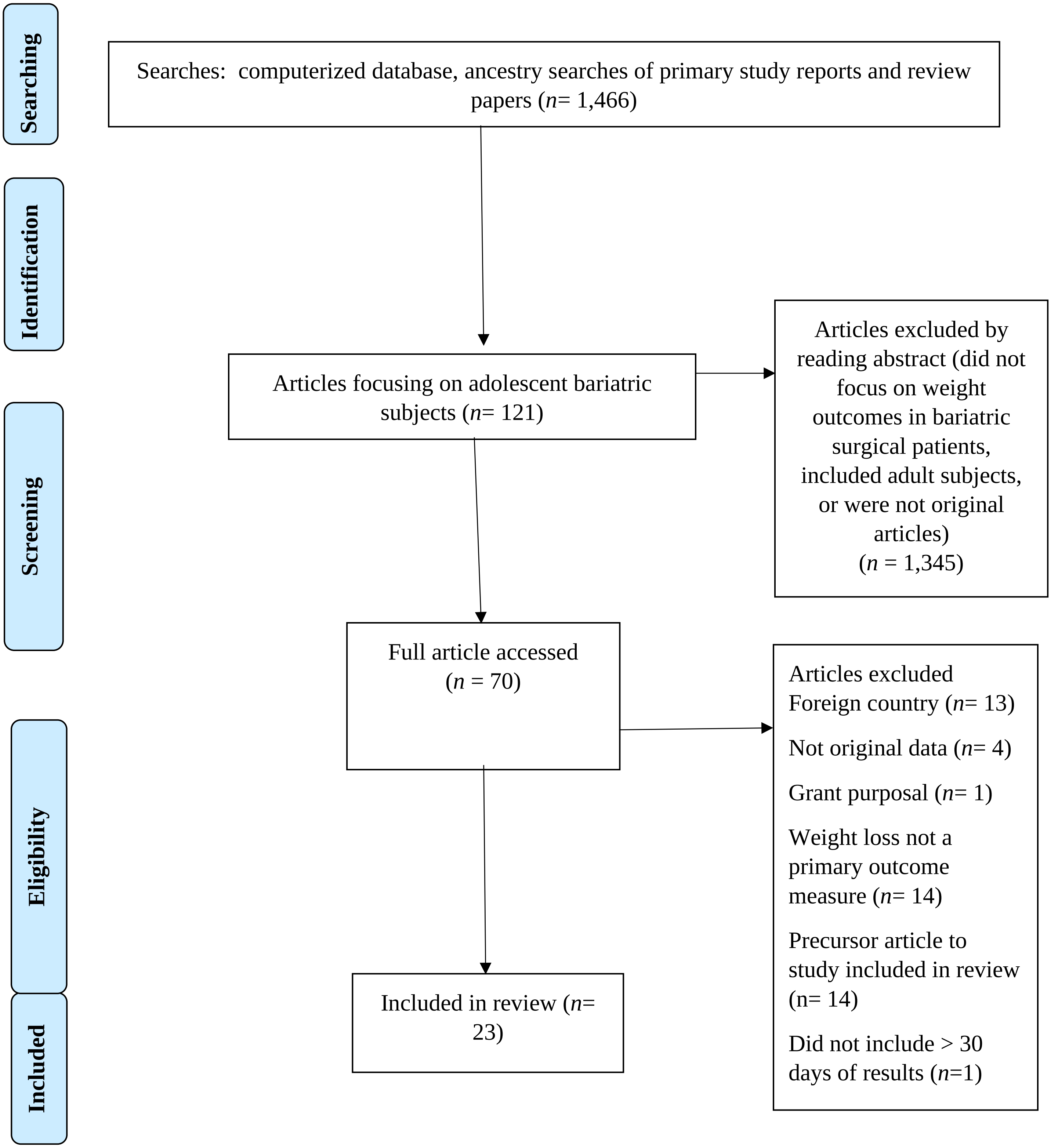
Figure 1. Flow diagram for Adolescent bariatric surgery



Note: *n* denotes the number of research reports

Studies

TABLE 1
Weight loss results by procedure type

Study	Length of Follow up	Total # of patients/# of patients for which results are reported	Pre-op weight (SD)	Post op weight (SD)	Pre-op BMI (SD)	Post-op BMI (SD)	%EWL (SD)
Lap Band							
De La Cruz-Munoz et al.	9-15 months	6/---	126.2(9.99)	115.2(12.1)	45.3(3.1)	41.4(3.8)	---
Dillard et al.	4 years	24/2	---	---	49(10)	43(14)	42(30)
Holterman et al.	18 months	20	296(78)lbs	---	50(10)	---	41 (27)
Horgan et al. #	30 months	4/1	147(25)	---	51(9)	---	---
Lee et al.	2 years	23/7	---	---	47(7.4)	---	29.7(18.9)
Nadler et al.	2 years	73/16	298(55)lbs	204(41)lbs	47.6(7)	32.1(6.4)	60.9(20.5)
Pedroso et al.	2 years	137/80	136.1(26.9)	115.1(31.2)	48.3(8.3)	40.5(10.9)	35.5(28.6)
Inge et al. ^(2015)	3 years	14/11	---	---	---	---	---
Sleeve Gastrectomy							
Cozacov et al.	47.9 months~	10/9	280.9 lbs	196.8 lbs	46.2	32.5	---
Ejaz et al.	2 years	18/2	---	---	48.6(7.2)	37.4	40
Inge et al. (2015)	3 years	67/52	144	105	50	37	---
Jaramillo et al.	12 months	38/25	132.0(24.6)	---	46.7(5.7)	35.5	47.7
McGuire et al.	6 months	59/---	144	---	50.6	---	38.6
Pedroso et al.	2 years	37/6	138.2(25.4)	94.2(20.1)	50.1(9.4)	33.0(6.2)	70.9(20.7)
Serrano et al.	3 years	17/---	---	---	51.0(9.5)	29.6(6.8)	59.0
Roux en Y gastric bypass							
Barnett et al.	6 years~	14/---	----	---	55.1(14.8)	---	64
Capella et al.	5.5 years~	19	133	---	49	28	80
Collins et al.	11.5 months~	11	149.9(7.1)	---	50.5(2.0)	---	60.8
Cozacov et al.	54.4 months~	8	308.4 lbs	189.3 lbs	48.5	28.9	---
De La Cruz-Munoz et al.	9-15 months	65/---	128.57(2.06)	97.7(2.6)	46.2(0.6)	34.9(0.8)	---

DuCoin et al.	15.7 months~	14	---	---	47.2(11.1)	33.8(8.3)	54.8(8.5)
Inge et al. (2015)	3 years	161/131	151	109	54	39	---
Inge et al. (2017)	8.0 years~	55/74	170.8(37.0)	122(37.6)	58.5(10.5)	41.7(12.0)	---
Lee et al.	2 years	32/5	---	---	50.6(7.0)	---	83.4(20.5)
Madan et al.	34 months~	5	323 lbs	---	48	---	77
Nijhawan et al.	9 years	25/4	---	---	45.7	28.6	77.7
Serrano et al.	36 months	37/---	---	---	51.8(9.7)	31.0(4.4)	61.8
Strauss et al.#	10 yrs	10/9	148(37)	---	---	---	---
Sugerman et al.	14 years	33/6	150(40)	114(5.6)	52(11)	38(16)	33(68)
Teeple et al.	2 years	15/9	179.6(42.5)	104.9(25.8)	58.8(10.7)	34.9(5.6)	62.2(14.6)

All weight is given in Kg unless otherwise specified, weight loss and BMI are presented as means and (SD), post operative results are given for the longest length of follow up time or the mean length of follow up as specified in column 2. ~ = mean follow up time

Chapter 3: Methods

Approach

This study aims to **1) determine the overall effect of the sleeve gastrectomy on weight loss, 2) evaluate the effect of age at the time surgery on weight loss and 3) describe and explore variation in weight loss by sample characteristics.** A meta-analysis was conducted to address Aim 1. A meta-analysis allows for synthesis of data across studies to examine the overall effect size of weight loss following the laparoscopic sleeve gastrectomy. Moderator analyses of sample characteristics and how these characteristics affect weight loss was conducted to address Aims 2 and 3.

Inclusion criteria

Inclusion criteria for the meta-analysis on laparoscopic sleeve gastrectomy included all published original studies reporting weight as an outcome published in the year 1999 or later in English. The cutoff for the year 1999 was decided upon due to the evolution of the sleeve gastrectomy. Previously, the sleeve gastrectomy was part of a staged procedure combining two surgeries: sleeve gastrectomy and roux-en-Y gastric bypass. The sleeve gastrectomy has since evolved to become a stand-alone weight loss procedure. Studies eligible for inclusion were published or unpublished reports of primary studies such as unpublished dissertation work, conference abstracts or presentations. The minimum age of study participants was 14 years or older; there was no upper age limit for included studies. Fourteen years was selected as the minimum age because many pediatric bariatric centers require patients to be 14 years or older to be a candidate for bariatric surgery. Studies conducted outside of the United States were excluded. The decision to exclude foreign countries stems from an effort to isolate a population of interest and eliminate confounding variables that may affect outcomes, such as societal norms, differences that may exist in selection of patients, differences in technical aspects of the procedure and selection biases due to language barriers. Studies were required to provide adequate data to calculate an effect size including sample size and outcome statistics, such as mean weight loss and standard deviation. Studies were required to have a minimum number of 5 subjects. The decision was made to include a minimum number of subjects due the processes of the meta-analysis utilizing group means and standard deviations as the primary statistical method.

Definitions

The laparoscopic sleeve gastrectomy procedure is defined as a primary surgical procedure in which part of the stomach is resected to facilitate weight loss. Weight was defined as the body's relative mass. Accepted measurements of weight included pounds (lbs.), kilograms (Kg), body mass index (BMI), change in BMI (initial BMI-postoperative BMI), change in Kg (initial weight in Kg-postoperative weight in Kg) and change in lbs. (initial weight in lbs.- postoperative weight in lbs).

Procedure

Potential studies were located through the rigorous search strategies discussed below. Abstracts were first reviewed for eligibility for inclusion. If, after reading the abstract, the study was deemed to be potentially eligible for inclusion, the article was saved to an electronic reference manager (Zotero) to be reviewed in full and categorized as eligible or not eligible. Studies were then more thoroughly evaluated to screen for information required for analyses including weight outcomes, SD and age of the sample. Following the initial screening, studies were evaluated for overlapping populations as authors have published multiple papers on the same sample. Screening for overlapping populations consisted of identifying the years that data collection occurred, the location of the study and any authors that bear the same name. If any of the factors listed above were identified to be suspect, further evaluation occurred by examining the article for key phrases such as "previously reported" as well as closely examining the methodology section for similarities that may indicate that the population is identical. The majority of articles were able to be identified as having overlapping populations by evaluating the years that data were collected as well as the location. The articles with overlapping populations were classified as companion articles. When evaluating companion articles, the following hierarchy was utilized to decide which article to include: number of time points the article included, number of subjects, and pertinence of study purpose. For articles that included the same number of time points, the article providing the longest time point was chosen as long term outcomes are of interest to this meta-analysis. If all time points were the same, the number of subjects was identified, if both articles had greater than 10 subjects, the purpose of each article was examined, and the article with the closest matching purpose was chosen to be included in the analysis. Most companion articles were able to be eliminated following the first or second criteria, with only a handful of articles progressing to the third criteria of consideration.

Once an article was identified as meeting the inclusion criteria for the study, pertinent data was extracted using the codebook described in further detail below. Data collection and management will be discussed in further detail in following sections. Once data was extracted, an overall mean effect size across studies was calculated utilizing standard meta-analytic procedures. A second analyses was performed with age as a covariate. Biological sex and baseline BMI were also evaluated to identify if either factor influenced postoperative weight loss.

Literature Search

Searches were conducted during the dates of 09/2019-1/20/2020 utilizing the following databases: PubMed, Scopus, EMBASE, Medline, GoogleScholar, CINAHL and ProQuest Dissertations and Theses for the years 1999 to current. Pediatric and adult literature is typically published separately, therefore, two separate searches within each database were conducted to identify both pediatric and adult articles. The following terms were used in the database to search for pediatric studies within articles, abstracts and keywords: child or pediatric or paediatric or adolescent or youth or childhood AND sleeve gastrectomy or laparoscopic sleeve gastrectomy or sleeve or LSG. Limits of English language and journal article were placed on results. Results ranged from 1,245 to 1,720 articles for the different databases. The following terms were used to search within the databases for studies with adult populations: laparoscopic sleeve gastrectomy or sleeve gastrectomy or LSG or sleeve AND weight loss or weight outcome or long-term outcomes(s). Limits of English language and journal article were placed on results. Results ranged from 1,451- 2,070 articles for the different databases. Ancestry searches were conducted of primary articles as well as review articles to identify any additional studies that were not identified in the primary search. The journal of *Obesity Surgery* was hand searched online from the year 1999 to present to identify potential articles. An updated search was performed on 9/17/2021 to identify any additional articles published since the original search resulting in 68 new articles which were screened for inclusion.

Most articles were eliminated based on titles and a review of the abstract. If an article could not be eliminated by the title or a review of the abstract, the article's reference information was saved to Zotero for further review. A total of 1,118 references were saved to Zotero after elimination of duplicate references. A detailed review of the abstract was performed, resulting in elimination of 335 additional articles. The remaining 783 articles were accessed in full and reviewed. Articles were first examined to determine the location in which the study took place, thus studies excluded for taking place in a foreign country represent the largest reason for exclusion at 496 articles. Seventy-five articles were excluded because they did not report data required to meet inclusion criteria such as weight outcomes or age of the sample. Forty-nine articles were excluded for lacking data needed to calculate a meta-analysis such as mean, standard deviation (SD) or number of subjects. Forty-two articles were excluded because outcome data or demographic data was combined with data from another bariatric procedure limiting ability to isolate outcomes following the laparoscopic sleeve gastrectomy. Thirty-five articles accessed did not provide original subject data and were excluded. Examples of articles lacking original data included letters to editors, review articles, poster presentations and abstracts. Thirteen articles reported %EWL as the outcome measure and were eliminated from the analysis as a standardized mean difference could not be accurately computed. Eleven articles utilized a database or registry that encompassed different health care systems, making it impossible to identify subject overlap with other included articles. Eight articles studied individuals in organ failure undergoing a laparoscopic sleeve gastrectomy. Organ failure represents severe disease progression and the effect of a laparoscopic sleeve gastrectomy in individuals with organ failure has the potential to be significantly different than in healthy individuals. The population of interest includes healthy individuals not in organ failure, thus, the 8 articles were excluded for representing a different population. Seven articles reported on individuals undergoing a different or additional procedure such as an endoscopic sleeve gastrectomy, removal of a gastric band or revisional laparoscopic sleeve gastrectomy and were excluded from the analyses. Three articles had less than 5 subjects and were excluded from the analysis. Twenty-nine articles were identified as companion articles and were excluded. Management and identification of companion articles is discussed in more detail in the following paragraphs. Fifteen individual articles and 1 unpublished data set were included in the final analysis. See figure 3.1.

Codebook

A code book was created to guide the coder in extracting study data. A thorough and systematic review of the literature was conducted by the author and pertinent data for extraction was identified with special consideration given to the study's specific aims. The codebook was utilized to convert information into numerical form to allow entry into statistical software for analyses. The codebook was developed to be exhaustive of information that may be included in any analyses. The codebook was piloted tested on 10 individual studies to identify any possible missing data points and necessary changes were implemented with the resulting codebook being satisfactory to the author.

Data Collection

Data regarding individual studies was collected utilizing the codebook described above and included the year of the study, design of the study, location, number of subjects, length of follow up, companion papers, and years that data were collected. Demographic information obtained from each study included mean age, biological sex, ethnicity of subjects, presence of comorbidities and baseline weight reported as body mass index (BMI), Kg and lbs. Outcome measures included weight and resolution of comorbidities. Weight outcomes were described in the following ways: BMI, Kg, lbs, BMI change, Kg change, lb change. Due to the nature of a meta-analysis and the process with which data are converted to a standardized measurement, percent excess weight loss (%EWL), defined as: [(preoperative weight-follow up weight)/(preoperative weight-ideal body weight)] X 100, was not able to be accepted as an outcome measurement (Montero, Stefanidis, Norton, Gersin & Kuwada, 2011). Percent excess weight loss lacks a standardized approach as the ideal body weight can be defined differently (Montero et al., 2011). Additionally, %EWL lacks a pre intervention measurement, limiting the ability of the comprehensive meta-analysis software (CMA) to calculate a standardized mean difference (Borenstein et al., 2014). If multiple values were provided, BMI took precedence as this value is clearly defined and often reported. Weight loss was recorded for the following data points after undergoing a laparoscopic sleeve gastrectomy as provided by the study: 1 month, 3 months, 6 months, 12 months, 18 months and yearly until the completion of the data provided by the individual study. The time points were selected after a rigorous search within the literature identified the above time points to be consistent intervals for reporting outcomes among studies. The following comorbidities were included for review as they have been found to be commonly reported: hypertension, dyslipidemia, diabetes mellitus and obstructive sleep apnea.

Data Management

A reference manager, Zotero, was utilized to manage articles. An all-inclusive folder was created and titled "Dissertation Search." Notes were used in Zotero after evaluating each study. Articles were given a "yes" or "no" note followed by any other pertinent information such as "no-accessed full- foreign country." After evaluating each study and giving each study a note, all articles identified as meeting inclusion criteria were transcribed into an Excel spreadsheet and assigned an individual identifying number. The Excel spreadsheet consisted of the following information: the unique identifying number of the article, year the article was published, location that the study took place, years over which the data was collected, full citation of the article and a column with which to list companion articles. The Excel spreadsheet was carefully examined to identify any overlapping dates and locations. The articles identified to possibly overlap were then closely evaluated to determine if they were companion articles. Groups of articles deemed to be companion articles reporting on the same population were handwritten into a notebook with the corresponding unique identifying number of each article. Each group of companion articles were carefully evaluated to choose which would serve as the primary (or index article) utilizing the hierarchy previously described. The rationale for choosing each article was then transcribed into the notebook and the unique identifying number corresponding to the article that served as the index article was then circled. Companion article numbers were listed in the Excel spreadsheet under the column titled "companion" and the articles not identified as primary were then moved to a different tab within the worksheet titled "companion." A new note was then entered into Zotero on each companion article identifying them as such "Yes-but companion article."

The Excel spreadsheet consisting of all the index articles with their full citation served as a "master sheet." A blank codesheet was created and printed for each article. See figure 3.2. Each article was hand coded and values obtained were written on the codesheet. For articles that reported on two different cohorts or subgroups, separate codesheets were utilized for each group, with the unique article identifying number followed by a ".1" or ".2." On the coding sheet the name of the group as referenced in the article was handwritten to provide identification such as "12.2- Cefazolin group." The group identification was also transcribed onto the Excel master sheet. If an article was excluded during coding for missing information, the article was crossed off the Excel master sheet, "excluded" was written on the codesheet and a note was made in Zotero documenting why the study was excluded. All codesheets that were started but unable to be completed due to lack of data were saved, placed together and titled "excluded during coding."

To ensure accuracy of the extracted data, a second coder familiar with meta-analytic procedures individually reviewed studies and extracted 100% of study effect size data. The second coders' work was cross-checked to ensure reliability. The second coder utilized the codesheet and codebook provided. Once coding was complete, the codesheet was scanned and emailed. Both code sheets were then compared side by side. Differences were discussed between the two coders until a consensus was met regarding the correct value. All codesheets provided by the second coder were saved, placed together and labeled as "Sharon's coded articles." Data from the primary coder's codesheets was transcribed to an Excel spreadsheet that representing the data that was entered into CMA. Each code sheet was entered and checked at two separate intervals to ensure accuracy.

Lastly, all reference citations were reviewed in Zotero to ensure that all articles were evaluated and had corresponding notes documenting reasons for eligibility or ineligibility. Four folders were created within Zotero for accurate categorization of each article. Titles of the folders consisted of “foreign country,” “no-accessed full- other reason,” “yes BUT” and “yes.” Every note attached to each reference was evaluated and the article was then placed within the appropriate folder. Categorizing each article allowed for a final review of all 1,119 citations and an accurate count for reasons of exclusions.

Data Analysis

Statistical analysis of data was completed using Comprehensive Meta-Analysis (CMA) software. CMA is a computer program specifically designed for meta-analyses computations, graphing and plots (Borenstein et al., 2014). Standard meta-analytic procedures were used to derive statistics as required from each of the studies (Borenstein et al., 2021). Outcome data was converted to a standardized measure to facilitate comparisons. Hedges’ g is a standardized measure that is defined as the sample estimate of the standardized mean difference (Borenstein et al., 2021). Each cohort analyzed consisted of at least one study that had less than 20 subjects, necessitating the use of Hedges’ g instead of Cohen’s d due to the tendency of Cohen’s d to overestimate the standardized mean difference in small samples (Borenstein et al., 2021; Higgins et al., 2021). A random-effects model was used to calculate all mean effects. A random-effects model was chosen because an assumption of the random-effects is that different effect sizes exist in different studies related to differences in technique, implementation and participants (Higgens et al., 2021; Borenstein et al., 2021). The articles included within the meta-analysis consisted of different surgeons, resulting in slightly different surgical techniques, and different participants in different bariatric programs. While there is generally a consensus among treatment centers regarding patient selection, the selection process cannot be assumed to be completely identical in each center and may differ between adolescents and adults. The random-effects model better accounted for the heterogeneity among the participants, programs, and technique. Additionally, studies were weighted more equally regardless of sample size in the random effects model, a better model for the analysis given that multiple studies had small sample sizes, helping to prevent skewed results (Higgens et al., 2021; Borenstein et al., 2021).

Heterogeneity statistics including Cochran's *Q* along with its p-value and *I*-squared (I^2) were calculated for each statistical analysis. Cochran's *Q* assesses for heterogeneity among studies and uses a test of significance to denote if differences exist, either rejecting or accepting the null hypothesis. I^2 can be defined as the measure of variances between studies that is related to true variability (Borenstein et al., 2021). I^2 gives values based on a scale, or percentage. When interpreting I^2, values of 0-24%, 25-49%, 50-74% and 75-100% were considered to represent no heterogeneity, mild heterogeneity, moderate heterogeneity and severe heterogeneity respectively (Borenstein et al., 2021). Cochran's *Q* is sensitive to the number of studies with decreased power when there is a low number of studies and increased power with a large number of studies, a bias of the statistical measure. Given that there were only 16 individual data sets analyzed, evaluating a second measure to assess heterogeneity among studies was essential to provide a comprehensive analysis. I^2 is not sensitive to the number of studies or the metric of the effect size, making this method a beneficial second measure to assess heterogeneity (Borenstein et al., 2021). To assess for publication bias, a funnel plot was analyzed. In the absence of publication bias, studies were expected to be evenly distributed around the total overall estimate of the meta-analysis (Borenstein et al., 2021). In addition to the funnel plot, Egger's regression intercept was calculated. Egger's regression intercept is defined as a linear regression of the intervention effect estimates on their standard errors weighted by inverse variance (Borenstein et al., 2021; Egger et al., 1997). Egger's test assesses for asymmetry of the funnel plot and if asymmetry is present, the slope of the regression line will be significantly different than 0, which is measured by a p-value. Significance was defined as a p-value < 0.05 (Borenstein et al, 2021; Egger et al., 1997). If the p-value was significant, or neared significant, Orwin's fail-safe *N* was then calculated to provide an estimated number of studies with an effect size of zero that would need to be added to the analysis to result in a nonsignificant cumulative effect, helping to determine if the overall observed effect is robust. To calculate Orwin's fail-safe *N*, a value of 0.2 was utilized to represent trivial standard difference in means (Borenstein et al., 2021). While there is no standardized approach to assess for publication bias, multiple different methods were chosen to create a thorough assessment for publication bias.

Specific Aim 1

The first aim of the meta-analysis is to **determine the overall mean effect of the laparoscopic sleeve gastrectomy on weight loss in patients 14 years and older**. To address the first aim, the researcher employed standardized mean difference as the statistic to evaluate effect size. The mean for the entire sample was utilized to calculate the standardized mean difference in the form of Hedges' *g* (Borenstein et al., 2021; Higgens et al., 2021). This method is most appropriate for the proposed study because weight is a continuous variable and the values being assessed are paired (preoperative weights and postoperative weights). Preoperative values and postoperative values of weight were subtracted to obtain the mean difference and converted to Hedges' *g*. The following correction factor was used to ultimately calculate Hedges' *g*: *J= 1 – [(3)/(4df-1)]*. Hedges *g* was then calculated utilizing the following formula: *J X d* (Borenstein et al., 2021). Standard deviations, if not provided, were calculated using the following formula: *SD= [(Sdifference)/(the square root of (2(1-the correlation between pairs of observations))]* (Borenstein et al., 2021).

After evaluating data, the decision was made to group outcome measures into proximal and latter time points. The proximal group consisted of data collected at or between 3-6 months. The second group, consisting of latter data points included data collected between 12-36 months. Grouping outcome measures in this manner allowed for a more thorough and accurate analyses as meta-analyses tend to have decreased accuracy with a smaller number of studies (Borenstein et al., 2021). A separate analysis and effect size was calculated for the proximal and distal points. If a study provided multiple data points within the range (i.e. outcomes were reported at both 3 month and 6 months), the most distal timepoint (6 months) was chosen to be included in the analysis. Heterogeneity statistics of Cochran's *Q* and I^2 were calculated for each analysis. Cochran's *Q* is distributed using chi-square statistics and is calculated by taking the weighted sum of squared differences between individual study effects (Borenstein et al., 2021). I^2 was assessed utilizing the following formula: $[(Q\text{-}df)/(Q)]\ X\ 100$ (Borenstein et al., 2021). Publication bias statistics consisting of a funnel plot, Egger's intercept regression and Orwin's fail safe *N* were conducted on the 12-36 month analysis. Evaluation of publication bias was conducted on the 12-36 month group only to increase accuracy. Analyses assessing publication bias are more accurate with a larger number of studies and the 12-36 month analysis had more studies and represented the complete data set (Borenstein et al., 2021).

Specific Aim 2

The second aim of the meta-analysis was **to evaluate the effect of age at the time of surgery on weight loss for individuals undergoing the laparoscopic sleeve gastrectomy**. The second aim was conducted utilizing standardized mean difference on a continuous scale. Standardized mean difference was chosen because the data is of a paired and continuous nature (Borenstein et al., 2021). Preoperative values and postoperative values of weight were subtracted to obtain the mean difference and converted to Hedges' *g* using the formula listed above. Standard deviations were calculated using the method previously described. Initially, a meta-regression was planned to be conducted; however, upon evaluation of the data, the mean age of the samples centered around two points: the second decade of life and the fourth decade of life, rendering a meta-regression that evaluates data of a continuous nature of less benefit. Instead, studies were grouped two groups: those with a mean age less than or equal to 21 yrs of age or those with a mean age greater than 21 yrs of age to allow for exploration of a age as a dichotomous moderator variable. The 12-36 month data range was utilized to conduct the analysis as this data range contained a greater number of studies. A greater number of studies is more likely to show a change in effect (Borenstein et al., 2021).

The overall effect size was calculated for each study. Each study was then placed into its appropriate group. A mixed effects analysis (random effects analysis with pooled estimate of T^2) was completed utilizing CMA. A random effects analysis was chosen as the two groups were still assumed to vary on characteristics such as differences in surgical technique, selection process and implementation of the intervention. A fixed effects analysis between subgroups was chosen because the subgroups in the analysis were not randomly chosen. A pooled estimate was employed as the group of studies in the group less than or equal to 21 yrs of age consisted of 4 studies and variance estimates are not likely to be reliable when there are 5 or less studies per subgroup; therefore T^2 was computed within groups and then pooled across groups (Borenstein et al., 2021). T^2, a statistic used to calculate variance between groups, can be defined as $[(Q-df)/C]$. A p-value was then assessed to evaluate if a difference in effect size was noted between the two subgroups with a p-value of < 0.05 to indicating a significant difference. Cochran's Q and I^2 were assessed utilizing methods previously described to evaluate heterogeneity in the two subgroups.

Specific Aim 3:

Describe and explore variation in weight loss by sample characteristics. Baseline BMI and biological sex were examined to evaluate their impact on weight loss. Additional characteristics including comorbidities and ethnicity were not able to be analyzed due to a lack of reporting in the primary studies. A meta-regression was utilized to explore the impact of baseline BMI on weight loss after laparoscopic sleeve gastrectomy. A meta-regression was chosen because baseline BMI is a continuous variable. Standardized mean difference was utilized to evaluate effect size because data is of a paired and continuous nature (Borenstein et al., 2021). Preoperative values and postoperative values of weight (BMI or Kg) were subtracted to obtain the mean difference and converted to Hedges' *g* using the formula previously described in specific aim 1 and listed in table 3.1. Hedges' *g* was chosen because the analysis included studies with fewer than 20 subjects and Cohen's *D* is not as accurate with fewer subjects (Borenstein et al., 2021). Standard deviations were calculated utilizing the methods previously described.

A meta-regression was conducted to evaluate the effect of baseline BMI on postoperative weight loss. The 12-36 month dataset was utilized because this data point consisted of the most studies. The slope of the relationship and significance of the slope was evaluated based on the *Z*-distribution and the following formula: $Z=[(B)/(SE_B)]$. A *p*-value of 0.05 indicated that the slope and relationship are statistically significant (Borenstein et al., 2021). Cochran's *Q* and I^2 were calculated using the formulas previously listed to assess heterogeneity. In addition, goodness of fit tests were conducted including R^2 analog defined as the proportion of total between study variance explained by the model and Q_{model}, which evaluates the amount of dispersion that can be explained by the covariate (Borenstein et al., 2021). Goodness of fit tests help validate if differences seen are greater than expected by chance and thus, more likely to be related to the covariate evaluated in the model.

Biological sex was assessed via a meta-regression utilizing the methods described above. Two separate analyses were run: one utilizing the percentage of male participants as a covariate and one utilizing the percentage of female participants as a covariate to evaluate the effect of biological sex on weight loss postoperatively. Calculations were conducted on the 12-36 month data set. The slope of the relationships and significance of the slope were evaluated utilizing the same formula and *p*-value described above. Cochran's Q and I^2 were calculated to assess for heterogeneity and goodness of fit test were conducted utilizing the same methods described above.

Limitations

Research and statistical methods always have limitations, and a meta-analysis is no exception. Meta-analyses face the following biases: selection biases, publication biases and search biases (Walker, Hernandez, & Kattan, 2008). Selection biases is a broad term used to describe any biases that may exist when selecting data to be included within a study. Selection bias within a meta-analysis may be limited by clearly defining criteria a priori and having an additional researcher evaluate data (Walker et al., 2008). The researcher of this meta-analysis identified criteria for inclusion a priori, a second coder familiar with meta-analyses techniques was recruited to help facilitate data extraction and resolve differences in opinion regarding effect size data. Publication bias refers to the likelihood that published data is more likely to reveal differences than unpublished data (Borenstein et al., 2008). The researcher attempted to obtain multiple unpublished data sets and successfully acquired one unpublished data set, helping to mitigate publication bias. Additionally, a rigorous search method was implemented as described above and attempts made to identify unpublished literature. Lastly, a funnel plot, Egger's test of regression and Orwin's fail safe *N* were conducted to identify the presence of any publication bias. Search bias can be defined as biases that exist within the search method (Walker et al., 2008). The researcher consulted a librarian to assist with selection of search terms and a rigorous search method was employed in an effort to identify all eligible data sets. Additionally, a journal was hand searched, further decreasing risks of search biases.

Availability of information is a limitation of any meta-analysis. The information provided within the data sets is typically mean information and limits flexibility of statistical analyses (Walker et al., 2008). The researcher made attempts to contact authors if there were questions regarding the data provided, or if there was a perception that additional data may be available and useful to include for analysis (i.e. ethnicities were mentioned as being collected but results were not reported). Additionally, differences in reporting methods with a lack of standardized reporting methods exists and is a limitation of the meta-analyses. As stated above, the researcher attempted to contact the authors with any questions regarding data. Converting means to a standardized measure (Hedges' *g*) presents the data on a standardized scale, allowing for comparisons between data sets. Additional data may not be able to be converted to a standardized scale. For example, after completing a review of the literature, it is evident that comorbidities are reported differently among studies, creating challenges when attempting to categorize and analyze comorbidities. When categories were not clearly defined and accepted by the two coders, the information was summarized in paragraph form and statistical analyses were performed. Additional limitations that the researcher encountered regarding availability of information included attrition of subjects with the tendency to have less subjects at latter time points, no standardized reporting of time points, and missing data. The researcher chose common time points reported across studies to help alleviate the issues of a lack of standardization and the researcher attempted to contact authors to obtain missing data. Attrition of subjects was a limitation of the meta-analysis with no ability to overcome. An additional limitation that was not able to be improved upon, involved a gap in the mean ages of subjects within the adolescent literature and the adult literature. Typically, the mean ages of adults undergoing the sleeve gastrectomy is around 40-45 years of age, while the mean age of adolescents undergoing the sleeve gastrectomy is around 16-18 years of age, generating a gap in the statistical analyses. The researcher chose to analyze the data with a dichotomous analysis instead of a meta-regression to help mitigate the gap in age. Lastly, there was an under-representation of adolescent studies available for analyses. The researcher attempted to mitigate this unfortunate limitation by contacting three separate adolescent bariatric programs in an effort to obtain data that was known to exist but remained unpublished. The researcher was successful in obtaining data from one of the centers and included the data set in the analyses.

Figure 3.1

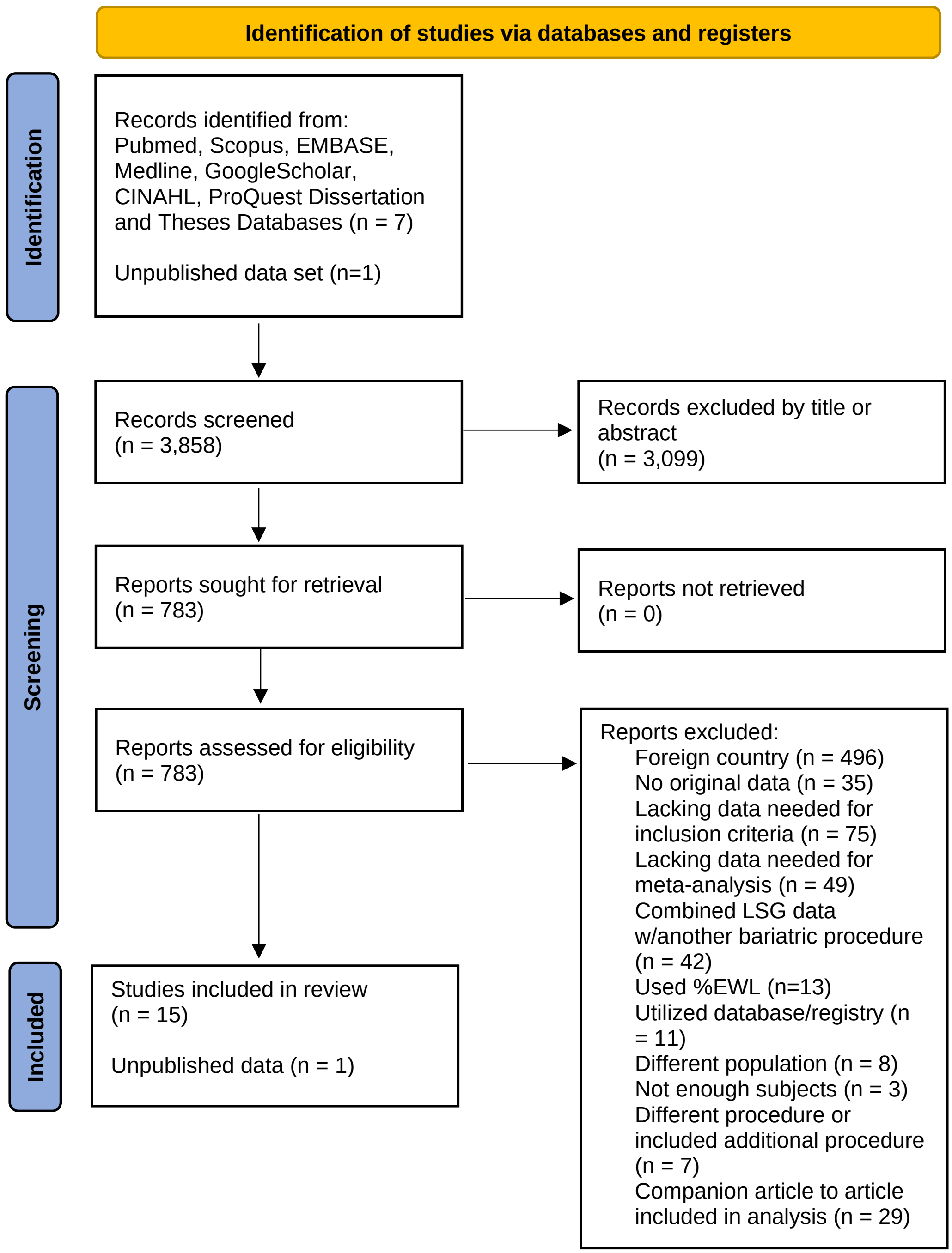


Figure 3.1- PRISMA diagram for literature search (Page et al., 2021)

Table 3.1: Codebook

Laparoscopic Sleeve Gastrectomy: A Meta-Analysis evaluating the impact of age on weight loss postoperatively

DATA	INSTRUCTIONS
1 Report numbers *Report*	• The report numbers are marked on the right top page of the report. • All reports have unique report numbers. • Some research projects are reported in multiple articles (e.g. the first article includes data 1 yr postoperatively and another includes data 2 yrs postoperatively, etc). If the research project is reported in multiple papers, add a period and then number, the first published article will be "1", the second "2" and so on and so forth (e.g. 1.01, 1.02). There may be multiple reports using the same population of patients
2 Year of publication, appearance, presentation or report *Year*	• Four-digit year • Enter the current year for articles that are released prior to publication • If there are multiple reports, use the year of the report that contains the most recent data (e.g. the report that gives the longest outcome data). • Record as '-' if you can't determine a year.
3 Companion papers *Comp*	• List the study numbers for any companion papers linked to this research article
4 Study design *Design*	• There are no blinded studies in this subject matter and there are minimal randomized studies • Code "1" for prospectively collected data (i.e. prospective database, the subject population was identified pre-intervention and prospectively entered into a database for the purpose of the study) • Code "2" for retrospectively collected data (i.e. chart review) • Code "3" for randomized design • Note: code "2" for retrospective review of a prospectively collected database
5 Study Center *Center*	• Code "1" for a single center study • Code "2" for a multicenter study
7 Years that data were collected *DataYRS*	• Record the years for which the data were collected and analyzed. For example, if data were collected from 2000-2005 and included in statistical analyses code "2000-2005"
8 Length of follow up *LastFollowUP*	• Record the most distal point in time after surgery for which data was collected using months as the unit of measurement
9 Follow up time points *TimePoints*	• Record all data collection points for which results are provided in months. Convert all time periods to months (ex: 3, 6, 9, 12, 24 months)
Sample Characteristics	• Code only the sample characteristics for those undergoing the Laparoscopic Sleeve Gastrectomy. If other procedures were included within the study- they do not need to be coded
10 Sample size *SampleSize*	• Record the number of subjects in the sample in the sample at the beginning of the study

11 Sample w/complete data *Complete*	• Record the number of subjects in the sample with data recorded at the last data collection point reported
12 Mean age of sample *meanAge*	• Record the overall mean age of the sample of patients. • If there are multiple reports, use the year of the report that contains the most recent data (e.g. the report that gives the longest outcome data). • If the mean age is not provided code as '-'
13 Low Age *LowAge*	• Record the age of the youngest subject included in the study • If there are multiple reports, use the year of the report that contains the most recent data (e.g. the report that gives the longest outcome data) • If the range of ages are not provided code as '-'
14 High Age *HighAge*	• Record the age of the oldest subject included in the study • If there are multiple reports, use the year of the report that contains the most recent data (e.g. the report that gives the longest outcome data) • If the range of ages are not provided code as '-'
15 Baseline weight measure *meanWeight*	• Record the baseline weight measure of the entire sample (if multiple weight measures are given, only code 1 unit of measurement-BMI is the preferred unit of measurement and should be used when possible) • Compute the mean if individual values are not given • Code '-' if not available and stop coding study as this is a necessary value
16 Baseline body weight measure standard deviation *SDbaseWeight*	• Record the standard deviation for the baseline weight measure of the entire sample • Compute the standard deviation if it is not given and able to be computed • Code '-' if not available and stop coding study as this is a necessary value
17 Type of baseline body weight measure *BaseWeightType*	• Code the type of baseline weight measure provided by the study (BMI is the default/preferred unit of measurement" • Code "1" for BMI • Code "2" for KG • Code "3" for Lbs • Code "4" for other and list the unit of measurement
18 Female Gender *FGender*	• Record the percent of female subjects in the study • If one gender is provided, do not calculate the percent of the other gender as this may not be binary data • If gender is not provided code '-'
19 Male Gender *MGender*	• Record the percent of male subjects in the study • If one gender is provided, do not calculate the percent of the other gender as this may not be binary data • If gender is not provided code '-'
20 Caucasian *Caucasian*	• Record the percent of Caucasian subjects in the study • Do not calculate this value if not given as it may not be possible to accurately determine the number of possible responses • If ethnicity is not provided code '-'
21 African American *AfricanAmerican*	• Record the percent of African American subjects in the study • Do not calculate this value if not given as it may not be possible to accurately determine the number of possible responses

	• If ethnicity is not provided code '-'
22 Hispanic *Hispanic*	• Record the percent of Hispanic subjects in the study • Do not calculate this value if not given as it may not be possible to accurately determine the number of possible responses • If ethnicity is not provided code '-'
23 Other *Other*	• Code the percent of subjects classified as "other" ethnicity • Do not calculate this value if not given as it may not be possible to accurately determine the number of possible responses • If ethnicity is not provided code '-'
24 % of sample with hypertension preoperatively *HTNpre*	• Record the % of the sample reported to have hypertension preoperatively • If able you may calculate this value • If not provided code '-'
25 % of sample with dyslipidemia preoperatively *DYSlipidPRE*	• Record the % of the sample reported to have dyslipidemia preoperatively • If able you may calculate this value • If not provided code '-'
26 % of sample with obstructive sleep apnea preoperatively *OSApre*	• Record the % of the sample reported to have obstructive sleep apnea preoperatively • If able you may calculate this value • If not provided code '-'
Outcome Measures-Weight	
27 Mean length of follow up *MeanLOF*	• Some studies provide a mean length of follow up instead of individual time points • Record the mean length of follow up for all subjects using months as the time point • If not provided code '-'
28 Sample size for mean length of follow up *SampleSizeMeanLOF*	• Record the number of subjects for studies that report data in the form of mean length of follow up • If not provided code '-'
29 Weight loss at mean length of follow up *WtLossMeanLOF*	• Weight loss may be reported using different measures across studies and some studies may report more than one measurement • Only record one weight loss measurement • The order of preference is as follows (BMI, Kg, Lbs, %EWL, %TWL, ΔBMI, ΔKg, ΔLbs) • Record postoperative weight loss at the mean length of follow up for all subjects • If not provided code '-'
30 Mean length of follow up standard deviation *MeanFuSD*	• Record the standard deviation for the mean length of follow up • If not provided code '-'
31 Unit of measurement used to calculate weight loss *TypeMeanLOF*	• Code "1" for BMI • Code "2" for Kg • Code "3" for Lbs • Code "4" for %EWL

	• Code "5" for %TWL • Code "6" for ΔBMI • Code "7" for ΔKg • Code "8" for ΔLbs • Code "9" for %WL • Code "10" for other and write in unit of measurement • If not provided code '-'
32 Sample size 1 month postop *1mSamplePostop*	• Record the number of subjects for which data is reported at 1 month after undergoing a sleeve gastrectomy • If not included code '-'
33 Weight loss 1 month postop *1mWtLossPost*	• Weight loss may be reported using different measures across studies and some studies may report more than one measurement • Only record one weight loss measurement • The order of preference is as follows (BMI, Kg, Lbs, %EWL, %TWL, ΔBMI, ΔKg, ΔLbs) • Record postoperative weight loss at 1 month for all subjects • If not included code '-'
34 Standard deviation 1 month postop *1mWtLossPostSD*	• Record the standard deviation for 1 month postop • If not provided code '-'
35 Unit of measurement used to calculate weight loss *Type1mWtLossPost*	• Code "1" for BMI • Code "2" for Kg • Code "3" for Lbs • Code "4" for %EWL • Code "5" for %TWL • Code "6" for ΔBMI • Code "7" for ΔKg • Code "8" for ΔLbs • Code "9" for %WL • Code "10" for other and write in unit of measurement • If not provided code '-'
36 Sample size 3 months Postop *3mSamplePostop*	• Record the number of subjects for which data is reported 3 months after undergoing a sleeve gastrectomy • If not included code '-'
37 Weight loss 3 months postop 3mWtLossPost	• Weight loss may be reported using different measures across studies and some studies may report more than one measurement • Only record one weight loss measurement • The order of preference is as follows (BMI, Kg, Lbs, %EWL, %TWL, ΔBMI, ΔKg, ΔLbs) • Record postoperative weight loss at 3 months postop for all subjects • If not included code '-'
38 Standard deviation 3 months postop	• Record the standard deviation for 3 months postop • If not provided code '-'

3mWtLossPostSD	
39 Unit of measurement used to calculate weight loss *Type3mWtLossPost*	• Code “1” for BMI • Code “2” for Kg • Code “3” for Lbs • Code “4” for %EWL • Code “5” for %TWL • Code “6” for ΔBMI • Code “7” for ΔKg • Code “8” for ΔLbs • Code “9” for %WL • Code “10” for other and write in unit of measurement • If not provided code ‘-‘
40 Sample size 6 months *6mSamplePostop*	• Record the number of subjects for which data is reported at 6 months after undergoing a sleeve gastrectomy • If not included code ‘-‘
41 Weight loss 6 months postop *6mWtLossPost*	• Weight loss may be reported using different measures across studies and some studies may report more than one measurement • Only record one weight loss measurement • The order of preference is as follows (BMI, Kg, Lbs, %EWL, %TWL, ΔBMI, ΔKg, ΔLbs) • Record postoperative weight loss at 6 months for all subjects • If not included code ‘-‘
42 Standard deviation 6 months postop *6mWtLossPostSD*	• Record the standard deviation for 6 months postop • If not provided code ‘-‘
43 Unit of measurement used to calculate weight loss *Type6mWtLossPost*	• Code “1” for BMI • Code “2” for Kg • Code “3” for Lbs • Code “4” for %EWL • Code “5” for %TWL • Code “6” for ΔBMI • Code “7” for ΔKg • Code “8” for ΔLbs • Code “9” for %WL • Code “10” for other and write in unit of measurement • If not provided code ‘-‘
44 Sample size 12 months (1 yr) postop *12mSamplePostop*	• Record the number of subjects for which data is reported at 12 months (1 yr) after undergoing a sleeve gastrectomy • If not included code ‘-‘

45 Weight loss 12 months (1 yr) postop *12mWtLossPost*	• Weight loss may be reported using different measures across studies and some studies may report more than one measurement • Only record one weight loss measurement • The order of preference is as follows (BMI, Kg, Lbs, %EWL, %TWL, ΔBMI, ΔKg, ΔLbs) • Record postoperative weight loss at 12 months (1 yr) for all subjects • If not included code '-'
46 Standard deviation 12 months (1 yr) postop *12mWtLossPostSD*	• Record the standard deviation for 12 months (1 yr) postop • If not provided code '-'
47 Unit of measurement used to calculate weight loss *Type12mWtLossPost*	• Code "1" for BMI • Code "2" for Kg • Code "3" for Lbs • Code "4" for %EWL • Code "5" for %TWL • Code "6" for ΔBMI • Code "7" for ΔKg • Code "8" for ΔLbs • Code "9" for %WL • Code "10" for other and write in unit of measurement • If not provided code '-'
48 Sample size 24 months (2 yrs) postop *24mSamplePostop*	• Record the number of subjects for which data is reported at 24 months (2 yrs) after undergoing a sleeve gastrectomy • If not included code '-'
49 Weight loss 24 months (2 yrs) postop *24mWtLossPost*	• Weight loss may be reported using different measures across studies and some studies may report more than one measurement • Only record one weight loss measurement • The order of preference is as follows (BMI, Kg, Lbs, %EWL, %TWL, ΔBMI, ΔKg, ΔLbs) • Record postoperative weight loss at 24 months (2 yrs) for all subjects • If not included code '-'
50 Standard deviation 24 months (2 yrs) postop *24mWtLossPostSD*	• Record the standard deviation for 24 months (2 yrs) postop • If not provided code '-'
51 Unit of measurement used to calculate weight loss *Type24mWtLossPost*	• Code "1" for BMI • Code "2" for Kg • Code "3" for Lbs • Code "4" for %EWL • Code "5" for %TWL • Code "6" for ΔBMI • Code "7" for ΔKg

	• Code “8” for ΔLbs • Code “9” for %WL • Code “10” for other and write in unit of measurement • If not provided code ‘-‘
52 Sample size 36 month (3 yrs) postop *36mSamplePostop*	• Record the number of subjects for which data is reported at 36 months (3 yrs) after undergoing a sleeve gastrectomy • If not included code ‘-‘
53 Weight loss 36 month (3 yrs) postop *36mWtLossPost*	• Weight loss may be reported using different measures across studies and some studies may report more than one measurement • Only record one weight loss measurement • The order of preference is as follows (BMI, Kg, Lbs, %EWL, %TWL, ΔBMI, ΔKg, ΔLbs) • Record postoperative weight loss at 36 months (3 yrs) for all subjects • If not included code ‘-‘
54 Standard deviation 36 months (3 yrs) postop *36mWtLossPostSD*	• Record the standard deviation for 36 months (3 yrs) postop • If not provided code ‘-‘
55 Unit of measurement used to calculate weight loss *Type36mWtLossPost*	• Code “1” for BMI • Code “2” for Kg • Code “3” for Lbs • Code “4” for %EWL • Code “5” for %TWL • Code “6” for ΔBMI • Code “7” for ΔKg • Code “8” for ΔLbs • Code “9” for %WL • Code “10” for other and write in unit of measurement • If not provided code ‘-‘
56 Sample size 48 months (4 yrs) postop *48mSamplePostop*	• Record the number of subjects for which data is reported at 48 months (4 yrs) after undergoing a sleeve gastrectomy • If not included code ‘-‘
57 Weight loss 48 months (4 yrs) postop *48mWtLossPost*	• Weight loss may be reported using different measures across studies and some studies may report more than one measurement • Only record one weight loss measurement • The order of preference is as follows (BMI, Kg, Lbs, %EWL, %TWL, ΔBMI, ΔKg, ΔLbs) • Record postoperative weight loss at 48 months (4 yrs) for all subjects • If not included code ‘-‘
58 Standard deviation 48 months (4 yrs) postop *48mWtLossPostSD*	• Record the standard deviation for 48 months (4 yrs) postop • If not provided code ‘-‘

59 Unit of measurement used to calculate weight loss *Type48mWtLossPost*	• Code “1” for BMI • Code “2” for Kg • Code “3” for Lbs • Code “4” for %EWL • Code “5” for %TWL • Code “6” for ΔBMI • Code “7” for ΔKg • Code “8” for ΔLbs • Code “9” for %WL • Code “10” for other and write in unit of measurement • If not provided code ‘-‘
60 Sample size 60 months (5 yrs) postop *60mSamplePostop*	• Record the number of subjects for which data is reported at 60 months (5 yrs) after undergoing a sleeve gastrectomy • If not included code ‘-‘
61 Weight loss 60 months (5 yrs) postop *60mWtLossPost*	• Weight loss may be reported using different measures across studies and some studies may report more than one measurement • Only record one weight loss measurement • The order of preference is as follows (BMI, Kg, Lbs, %EWL, %TWL, ΔBMI, ΔKg, ΔLbs) • Record postoperative weight loss at 60 months (5 yrs) for all subjects • If not included code ‘-‘
62 Standard deviation 60 months (5 yrs) postop *60mWtLossPostSD*	• Record the standard deviation for 72 months (6 yrs) postop • If not provided code ‘-‘
63 Unit of measurement used to calculate weight loss Type60mWtLossPost	• Code “1” for BMI • Code “2” for Kg • Code “3” for Lbs • Code “4” for %EWL • Code “5” for %TWL • Code “6” for ΔBMI • Code “7” for ΔKg • Code “8” for ΔLbs • Code “9” for %WL • Code “10” for other and write in unit of measurement • If not provided code ‘-‘
64 Sample size 72 months (6 yrs) postop *72mSamplePostop*	• Record the number of subjects for which data is reported at 72 months (6 yrs) after undergoing a sleeve gastrectomy • If not included code ‘-‘

65 Weight loss 72 month (6 yrs) postop *72mWtLossPost*	• Weight loss may be reported using different measures across studies and some studies may report more than one measurement • Only record one weight loss measurement • The order of preference is as follows (BMI, Kg, Lbs, %EWL, %TWL, ΔBMI, ΔKg, ΔLbs) • Record postoperative weight loss at 72 months for all subjects • If not included code '-'
66 Standard deviation 72 months (6 yrs) postop *72mWtLossPostSD*	• Record the standard deviation for 72 months (6 yrs) postop • If not provided code '-'
67 Unit of measurement used to calculate weight loss *Type72mWtLossPost*	• Code "1" for BMI • Code "2" for Kg • Code "3" for Lbs • Code "4" for %EWL • Code "5" for %TWL • Code "6" for ΔBMI • Code "7" for ΔKg • Code "8" for ΔLbs • Code "9" for %WL • Code "10" for other and write in unit of measurement • If not provided code '-'
68 Sample size 84 months (7 yrs) postop 80mSamplePostop	• Record the number of subjects for which data is reported at 84 months (7 yrs) after undergoing a sleeve gastrectomy • If not included code '-'
69 Weight loss 84 months (7 yrs) postop *84mWtLossPost*	• Weight loss may be reported using different measures across studies and some studies may report more than one measurement • Only record one weight loss measurement • The order of preference is as follows (BMI, Kg, Lbs, %EWL, %TWL, ΔBMI, ΔKg, ΔLbs) • Record postoperative weight loss at 84 months (7 yrs) for all subjects • If not included code '-'
70 Standard deviation 84 months (7 yrs) postop *84mWtLossPostSD*	• Record the standard deviation for 84 months (7 yrs) • If not provided code '-'
71 Unit of measurement used to calculate weight loss Type84mWtLossPost	• Code "1" for BMI • Code "2" for Kg • Code "3" for Lbs • Code "4" for %EWL • Code "5" for %TWL • Code "6" for ΔBMI • Code "7" for ΔKg

	• Code “8” for ΔLbs • Code “9” for %WL • Code “10” for other and write in unit of measurement • If not provided code ‘-‘
72 Sample size 96 months (8 yrs) postop *96mSamplePostop*	• Record the number of subjects for which data is reported at 96 months (8 yrs) after undergoing a sleeve gastrectomy • If not included code ‘-‘
73 Weight loss 96 months (8 yrs) postop *96mWtLossPost*	• Weight loss may be reported using different measures across studies and some studies may report more than one measurement • Only record one weight loss measurement • The order of preference is as follows (BMI, Kg, Lbs, %EWL, %TWL, ΔBMI, ΔKg, ΔLbs) • Record postoperative weight loss at 96 months (8 yrs)for all subjects • If not included code ‘-‘
74 Standard deviation 96 months (8 yrs) postop *96mWtLossPostSD*	• Record the standard deviation for 96 months (8 yrs) postop • If not provided code ‘-‘
75 Unit of measurement used to calculate weight loss *Type96mWtLossPost*	• Code “1” for BMI • Code “2” for Kg • Code “3” for Lbs • Code “4” for %EWL • Code “5” for %TWL • Code “6” for ΔBMI • Code “7” for ΔKg • Code “8” for ΔLbs • Code “9” for %WL • Code “10” for other and write in unit of measurement • If not provided code ‘-‘
76 Sample size 108 months (9 yrs) postop *108mSamplePostop*	• Record the number of subjects for which data is reported at 108 months (9 yrs) after undergoing a sleeve gastrectomy • If not included code ‘-‘
77 Weight loss 108 month (9 yrs) postop *108mWtLossPost*	• Weight loss may be reported using different measures across studies and some studies may report more than one measurement • Only record one weight loss measurement • The order of preference is as follows (BMI, Kg, Lbs, %EWL, %TWL, ΔBMI, ΔKg, ΔLbs) • Record postoperative weight loss at 108 months (9 yrs) for all subjects • If not included code ‘-‘
78 Standard deviation 108 months (9 yrs) postop *108mWtLossPostSD*	• Record the standard deviation for 108 months (9 yrs) • If not provided code ‘-‘

79 Unit of measurement used to calculate weight loss *Type108mWtLossPost*	• Code “1” for BMI • Code “2” for Kg • Code “3” for Lbs • Code “4” for %EWL • Code “5” for %TWL • Code “6” for ΔBMI • Code “7” for ΔKg • Code “8” for ΔLbs • Code “9” for %WL • Code “10” for other and write in unit of measurement • If not provided code ‘-‘
80 Sample size 120 months (10 yrs) postop *120mSamplePostop*	• Record the number of subjects for which data is reported at 120 months (10 yrs) after undergoing a sleeve gastrectomy • If not included code ‘-‘
81 Weight loss 120 months (10 yrs) postop *120mWtLossPost*	• Weight loss may be reported using different measures across studies and some studies may report more than one measurement • Only record one weight loss measurement • The order of preference is as follows (BMI, Kg, Lbs, %EWL, %TWL, ΔBMI, ΔKg, ΔLbs) • Record postoperative weight loss at 120 months (10 yrs) for all subjects • If not included code ‘-‘
82 Standard deviation 120 months (10 yrs) postop *120mWtLossPostSD*	• Record the standard deviation for 120 months (10 yrs) • If not provided code ‘-‘
83 Unit of measurement used to calculate weight loss *Type120mWtLossPost*	• Code “1” for BMI • Code “2” for Kg • Code “3” for Lbs • Code “4” for %EWL • Code “5” for %TWL • Code “6” for ΔBMI • Code “7” for ΔKg • Code “8” for ΔLbs • Code “9” for %WL • Code “10” for other and write in unit of measurement • If not provided code ‘-‘
Outcome Measures-Comorbidities	
84 % of sample with hypertension postoperatively	• Record the % of the sample reported to have hypertension postoperatively • If not provided code ‘-‘

%PostHTN	
85 % of sample with dyslipidemia postoperatively *%PostDysLip*	• Record the % of the sample reported to have dyslipidemia postoperatively • If not provided code '-'
86 % of sample with obstructive sleep apnea postoperatively *%PostOSA*	• Record the % of the sample reported to have obstructive sleep apnea postoperatively • If not provided code '-'

Table 3.2: Statistical Analyses to be conducted for each aim	
Specific Aim 1	Effect size data for 3-6 months and 12-36 months postoperatively • Calculate standardized mean difference: [(difference in mean outcome between groups)/(standard deviation of outcome among participants)] • Hedges' *g*: *J= 1 – [(3)/(4df-1)]* Heterogeneity assessments • Cochran's *Q*: $Q = \sum_{i=1}^{K} Wi(Yi - M)^2$ • I^2: *[(Q-df)/(Q)] X 100* Publication bias • Funnel plot- studies to be evenly distributed around overall estimate if no bias • Egger's test of regression- slope of regression line will be significantly different than 0 ($p < 0.05$) • Orwin's fail safe *N*- value of 0.2 utilized to represent trivial standard difference in means
Specific Aim 2	Effect size data for 12-36 month data point • Calculate standardized mean difference: [(difference in mean outcome between groups)/(standard deviation of outcome among participants)] • Hedges' *g*: *J= 1 – [(3)/(4df-1)]* Dichotomous covariate analysis • Mixed effects analysis- random effect analysis with pooled estimate of T_2 • $T_2 = [(Q-df)/C]$ Heterogeneity assessments • Cochran's *Q*: $Q = \sum_{i=1}^{K} Wi(Yi - M)^2$ • I^2: *[(Q-df)/(Q)] X 100*
Specific Aim 3	Covariates examined: biological sex and baseline BMI (3) separate meta-regressions performed using %female, %male and baseline BMI as covariate • *Z* distribution: $Z=[(B)/(SE_B)]$ Goodness of fit tests • Q_{model}- amount of dispersion seen in the model that is explained by the covariate (p< 0.5= statistical significance) • R^2 analog- assesses proportion of total between study variance explained by model $R^2 = 1 - \left(\frac{T^2_{residual}}{T^2_{total}}\right)$ Heterogeneity assessments • Cochran's *Q*: $Q = \sum_{i=1}^{K} Wi(Yi - M)^2$ • I^2: *[(Q-df)/(Q)] X 100*

Chapter 4: Results

Karasko, D. *A Systematic Review and Meta-analysis Combing Adolescent and Adult Data to Evaluate Weight Loss and the Effect of Age Following the Laparoscopic Sleeve Gastrectomy.* Surgery for obesity and related disease. Manuscript in preparation

Abstract

Obesity is a grave concern within the United States, resulting in lost productivity, increased medical costs comorbidities with lifelong repercussions. The laparoscopic sleeve gastrectomy is a treatment option for obesity. The following meta-analysis sought to combine adolescent and adult literature to determine the overall effect of the sleeve gastrectomy on weight loss, to evaluate the effect of age at the time of surgery on weight loss and to describe and explore variation in weight loss by sample characteristics. Overall weight loss was assessed at proximal and distal points, a dichotomous moderator variable analysis was conducted with subjects < 21 yrs of age and > 21 yrs of age and a meta-regression assessing the % male, % female and baseline BMI was conducted to assess moderator variables. The laparoscopic sleeve gastrectomy was effective at facilitating weight loss with effect sizes varying from 0.916-2.816. Age, biological sex and baseline BMI were not found to have an impact on weight loss. The clinical consequences of prolonged obesity are evident and earlier intervention may be justified to counter the long-term effects caused by obesity related comorbidities. Standardized reporting of comorbidities and the effect of bariatric surgery on comorbid conditions is essential to allow further analysis.

Background

Medical care related to obesity and associated comorbidities is estimated to cost $147 billion dollars within the United States while absenteeism from work within the United States due to obesity and associated medical conditions is estimated to cost between $3.38 and $6.38 billion dollars per year ("Overweight and Obesity," 2018). Obesity increases the risk of several disorders that can lead to lifelong complications including diabetes, elevated cholesterol and/or triglyceride levels, musculoskeletal pain or discomfort, obstructive sleep apnea, liver abnormalities such as hepatic steatosis and pseudotumor cerebri (Andrews et al., 2014; Kalra et al., 2005; Kelly et al., 2013; Xanthakos et al., 2015). Obesity is also associated with negative psychosocial effects including depression and eating disorders in the adolescent while adults suffering from depression were more likely to be obese and require the use of antidepressants (Kim et al., 2008; Pratt & Brody, 2014).

Bariatric surgery is a treatment option for obesity with approximately 256,000 bariatric surgeries occurring in 2019, 16.7% of which were revisional procedures ("Estimate of Bariatric Surgery", 2022). Weight regain is one reason that a revision may be required, reflecting the imperfect nature of bariatric surgery as a treatment option for obesity. Historically, three bariatric procedures have been offered including laparoscopic adjustable gastric banding, the roux-en-y gastric bypass procedure and the laparoscopic sleeve gastrectomy (Mattei, 2011). The laparoscopic sleeve gastrectomy, a procedure in which the greater curvature of the stomach is resected, accounts for 59.4% of all bariatric surgeries. Outcomes following bariatric surgery in the adolescent are typically reported separately from bariatric outcomes in the adult. To date, no previous meta-analysis are known to evaluate both adolescent and adult literature together. A previous meta-analysis performed in 2017 evaluated the effect of age in adult patients on weight loss following bariatric surgery and did not find any difference (Golzarand et al., 2017). Combining adult and adolescent literature to examine patient characteristics and their effect on weight loss, with special attention to age, is a novel approach and may result in improved patient counseling regarding expectations and outcomes. The following meta-analysis aims to **1) determine the overall effect of the sleeve gastrectomy on weight loss, 2) evaluate the effect of age at the time of surgery on weight loss and 3) describe and explore variation in weight loss by sample characteristics.**

Method

A systematic literature review and meta-analysis were conducted to evaluate the overall effect size of weight loss following the laparoscopic sleeve gastrectomy. Moderator analyses of sample characteristics including age, biological sex and baseline BMI were conducted to explore their effect on weight loss. PRISMA guidelines were utilized in methodology and reporting (Liberati et al., 2009)

Search Methods

A systematic literature review was performed between the dates of 09/2019-1/20/2020 utilizing PubMed, Scopus, EMBASE, Medline, GoogleScholar, CINAHL and ProQuest Dissertations and Theses for the years 1999 to current. The journal of *Obesity Surgery* was hand searched online from the year 1999 to present to identify potential articles and 3 adolescent bariatric programs were contacted in an attempt to obtain unpublished data. Two separate searches were conducted to identify adolescent and adult literature. Terms searched within articles, abstracts and keywords to identify adult literature were as follows: laparoscopic sleeve gastrectomy or sleeve gastrectomy or

LSG or sleeve AND weight loss or weight outcome or long-term outcome(s). The following terms were used to search for pediatric studies: child or pediatric or paediatric or adolescent or youth or childhood AND sleeve gastrectomy or laparoscopic sleeve gastrectomy or sleeve or LSG. Limits of English language were placed on results. An updated search was carried out on 9/17/2021 to identify any additional articles published proceeding the original search.

Inclusion Criteria

Inclusion criteria was identified a priori and included all published and unpublished works reporting weight as an outcome measure following bariatric surgery that occurred in the year 1999 or later in English. 1999 was chosen as a cutoff year due to the evolution of the sleeve gastrectomy. Previously, the sleeve gastrectomy was part of a staged procedure that has evolved to become a stand-alone weight loss procedure. The laparoscopic sleeve gastrectomy was defined as: a primary surgical procedure in which the greater fundus of the stomach is resected to facilitate weight loss. The minimum age of study participants was 14 yrs of older; there was no upper age limit. Fourteen years was selected as a minimum age because the American Society for Metabolic and Bariatric Surgery (ASMBS) recommends adolescents to be 14 years of age or older to be a candidate for bariatric surgery (Pratt et al., 2018). Studies conducted outside of the United States were excluded. Foreign countries were excluded in an effort to isolate a population of interest and eliminate confounding variables that may affect outcomes, such as societal norms, differences in patient selection and technical aspects as well as selection biases related to language barriers. Studies were required to provide adequate data to calculate an effect size including sample size and outcome statistics such as mean weight loss and standard deviation (SD). Weight was defined as the body's relative mass. Accepted measurements of weight included pounds (lbs.), kilograms (Kg), body mass index (BMI), change in BMI (initial BMI- postoperative BMI), change in Kg (initial weight in Kg-postoperative weight in Kg) and change in lbs. (initial weight in lbs.- postoperative weight in lbs). Due to the nature of a meta-analysis and the process with which data are converted to a standardized measurement, %EWL, defined as: [(preoperative weight- follow up weight)/(preoperative weight- ideal body weight)] X 100 was not able to be accepted as an outcome measurement (Montero et al., 2011). %EWL lacks a standardized approach as the ideal body weight can differ and the measurement lacks a pre intervention value, limiting the ability of the comprehensive meta-analysis software (CMA) to accurately calculate a standardized mean difference (Borenstein et al., 2014; Montero et al., 2011). Studies with less than 5 subjects were excluded to allow for accurate statistical analyses.

Study Selection

Citations were retrieved from reference databases and imported into a reference manager software (Zotero) and then reviewed by the primary author. Most articles were eliminated by review of the abstract and title, those that were unable to be eliminated after reviewing the abstract were accessed in full. Location of the study was the first criterion evaluated to assess for eligibility. If articles took place within the United States, data was evaluated to determine if the article included mean age of the subjects. If the article provided mean age and took place within the United States, a detailed examination followed and the article was attempted to be utilized in the analysis. If the article met inclusion criteria but lacked data required to calculate an effect size, an attempt was made to contact the author utilizing contact information listed on the article.

Assessment of Risk of Bias in Individual Studies

Study components were assessed for biases that may exist by examining each article individually and considering known aspects to influence biases in meta-analyses outlined by Borenstein et al. (2021) such as publication bias, biases related to study design and subject selection. The method of examining and identifying individual components that may affect bias was chosen in lieu of a checklist or scale because checklists and scales utilized in studies of similar methodology and quality can be flawed and problematic (Juni et al., 1999).

Data Extraction

A codebook was created by the author after a systematic review of the literature identified pertinent data for extraction. The codebook was created to be exhaustive of information and was pilot tested on 10 studies. The codebook guided the coder in extracting data and converted information into numerical form to allow entry into statistical software for analyses. Data collected included (but was not limited to) design of the study, number of subjects, years that data was collected, demographic information including mean age, comorbidities, biological sex, ethnicity and outcome measures such as weight and resolution of comorbidities. BMI represented the preferred outcome measure of weight as it is clearly defined and often reported. Weight was recorded at the following points after undergoing a laparoscopic sleeve gastrectomy: 1 month, 3 months, 6 months, 12 months, 18 months and yearly until completion of the study. The time points were selected after a rigorous search within the literature identified the time points to be consistent intervals for reporting outcomes.

Once articles were deemed eligible for inclusion, further investigation occurred to identify overlapping populations. Articles reporting on overlapping populations were deemed “companion articles.” Companion articles were evaluated to identify which article would serve as the “index article,” or the article from which data would be extracted. The following hierarchy was utilized to determine the index article: number of time points the article included, number of subjects, and pertinence of study purpose. For articles that included the same number of time points, the article providing the longest time point was chosen as long term outcomes are of interest to this meta-analysis. If all time points were the same, the number of subjects was identified, if both articles had greater than 10 subjects, the purpose of the each article was examined, and the article with the closest matching purpose was chosen to be included in the analysis. Most companion articles were able to be eliminated following the first or second criterion, with only a handful of articles progressing the third criterion of consideration.

Data from each index article was hand coded onto a code sheet. Subgroups were treated as an individual data set. A second coder familiar with meta-analytic procedures individually reviewed articles and extracted 100% of study effect size data. The second coders’ work was cross-checked to ensure accuracy and reliability. If differences were identified, discussion ensued until a consensus was met. Data from the primary coder’s code sheets were transcribed to an Excel spreadsheet that represented the data to be entered into CMA. Each code sheet was entered and checked at two separate intervals to ensure accuracy.

Data Analysis

Statistical analysis of data was completed using CMA software. Standard meta-analytic procedures were used to derive statistics (Borenstein et al., 2021). Outcome data was converted to Hedges' *g*, a standardized measure defined as the sample estimate of the standardized mean difference. Hedges' *g* was utilized instead of Cohen's *d* due to each cohort consisting of a study with less than 20 subjects. Cohen's *d* has a tendency to overestimate the standardized mean difference in small samples (Borenstein et al., 2021; Higgens et al., 2021). A random-effects model was utilized to calculate all mean effects because of its ability to better account for differences between studies related to technique, implementation and participants, which was anticipated to be present within the included studies (Borenstein et al., 2021; Higgens et al., 2021). The random-effects model better accounts for heterogeneity and studies in a random-effects model are weighted more equally. The articles varied significantly in sample size and utilizing the random-effects model would help prevent skewed results related to sample sizes (Borenstein et al., 2021; Higgens et al., 2021).

Meta-analyses tend to have decreased accuracy with a smaller number of studies; therefore, time points were grouped into proximal and latter time points to incorporate all studies and allow for thorough examination (Borenstein et al., 2021). Two separate analyses were performed, one at 3-6 months and one at 12-36 months. The specific time points were chosen after review of the articles to be inclusive off all articles. A dichotomous moderator variable analysis was utilized after evaluation of the data demonstrated that mean ages centered around the second decade of life and the fourth decade of life, rendering a continuous analysis such as a meta-regression of less benefit.

Studies in the 12-36 month range were categorized into 2 groups: those with a sample mean age less than or equal to 21 years of age (≤ 21 yrs) and those with a mean age greater than 21 years of age (≥ 21 yrs). A mixed effects analysis (random effects analysis with pooled estimate of T^2) was chosen as the two groups were assumed to vary on characteristics and the subgroups in the analysis were not randomly chosen. A pooled estimate consisting of T^2 computed within groups and then pooled across groups was employed as the group of studies in ≤ 21 yrs consisted of 4 studies and variance estimates are not as reliable with 5 or less studies per subgroup (Borenstein et al, 2021). A *p*-value < 0.05 was chosen to indicate significance. Baseline BMI and biological sex were explored to assess variation in weight loss by conducting 3 separate meta-regressions. Covariates in the meta-regressions consisted of the percent of the sample identified as female (%female), the percent of the sample identified as male (%male) and baseline BMI. The slope of the relationship and significance of the slope was evaluated using the Z-distribution. A *p*-value of 0.05 indicated significance. Goodness of fit tests were conducted including Q_{model} and R^2 analog to validate if differences seen are greater than expected by chance and likely related to the covariate. See table 4.1 for statistical analyses.

Heterogeneity statistics Cochran's *Q* along with its *p*-value and *I*-squared (I^2) were calculated to assess for heterogeneity. Cochran's *Q* utilizes a p-value to denote differences and is sensitive to the number of studies while I^2 is not. I^2 is represented as a percentage with 0-24%, 25-49%, 50-74% and 75-100% considered to represent no heterogeneity, mild heterogeneity, moderate heterogeneity and severe heterogeneity respectively (Borenstein et al., 2021). A funnel plot, Egger's regression intercept and

Orwin's fail-safe *N* were calculated to assess for publication bias. The funnel plot is expected to be evenly distributed, Egger's test was defined as significant if the p-value was < 0.05 and to calculate Orwin's fail-safe *N*, a value of 0.2 represented trivial standard difference in means. Orwin's fail-safe *N* calculates how many additional studies with a null effect are required to result in a non-significant effect size.

Results

Study Selection

Articles screened totaled 3,858 while 783 were accessed and reviewed. Seventy-five articles were excluded because they did not report required data such as weight or age of the sample. Forty-nine articles were excluded for lacking data needed to perform a meta-analysis such as mean, standard deviation (SD) or number of subjects. Forty-two articles were excluded because outcome data or demographic data was combined with another bariatric procedure limiting ability to isolate outcomes following the laparoscopic sleeve gastrectomy. Thirty-five articles did not provide original subject data and were excluded, examples include letters to editors, review articles, poster presentations and abstracts. Thirteen articles were eliminated because they reported %EWL as the sole outcome measure. Eleven articles utilized a national database or registry that encompassed different health care systems, making it impossible to identify subject overlap. Eight articles studied individuals in organ failure undergoing a laparoscopic sleeve gastrectomy. Organ failure represents severe disease progression and the effect of a laparoscopic sleeve gastrectomy in individuals with organ failure has the potential to be significantly different than in healthy individuals. The population of interest includes healthy individuals not in organ failure, thus, the 8 articles were excluded for representing a different population. Seven articles reported on individuals undergoing a different or additional procedure such as an endoscopic sleeve gastrectomy, removal of a gastric band or revisional laparoscopic sleeve gastrectomy and were excluded from the analyses. Three articles had less than 5 subjects and were excluded from the analysis. One article was unable to be included in analysis because results were reported at 60 months and there were no other studies reporting outcomes at this time point. Twenty-nine articles were identified as companion articles and were excluded. Management and identification of companion articles is discussed in further detail below. Fifteen individual articles and one unpublished data set were included in the final analysis (Figure 4.1).

Study Characteristics

The number of individuals undergoing laparoscopic sleeve gastrectomy varied significantly from 9-1,303. Subjects reporting postoperative outcomes ranged from 7-974 individuals. Most studies exhibited attrition; however, three studies eliminated individuals with missing data from their analysis (Froylich et al., 2016; Holsen et al., 2018; Smith et al., 2020). In the remaining studies, attrition ranged from 2 subjects to 763 subjects. Studies included in the analysis reported outcomes varying from 3 months to 3 years. The mean age of subjects for the adolescent literature ranged from 17.0 years of age to 20.3 years of age (Inge et al., 2015; Khan et al., 2016; Nadler et al., 2012; Pedroso et al., 2015; Prout, 2021.

Sample Characteristics

The mean age of subjects for the adult literature ranged from 38.2-46.4 years of age (Cottam et al., 2018, Froylich et al., 2016; Holsen et al., 2018; Kindel et al., 2018; McNickle et al., 2017; Saif et al., 2012; Serrano et al., 2016; Snyder et al., 2016; Smith et al., 2020; Tweksbury et al., 2016). The majority of studies reported a higher percentage of female subjects undergoing a laparoscopic sleeve gastrectomy, percentages ranged from 52%-100%, with most reporting around 70-80% female (Cottam et al., 2018; Froylich et al., 2016; Holsen et al., 2018; Khan et al., 2016; Kindel et al., 2018; McNickel et al., 2017; Nadler et al., 2012; Pedroso et al., 2015; Saif et al., 2012; Serrano et al., 2016; Smith et al., 2020; Snyder et al., 2016; Tweksbury et al., 2019). Preoperative BMI ranged from 41.8-68.4 and postoperative BMI ranged from 29.6-53.1 (Cottam et al., 2018; Froylich et al., 2016; Holsen et al., 2018; Kindel et al., 2018; McNickel et al., 2017; Nadler et al., 2012; Pedroso et al., 2015; Saif et al., 2012; Serrano et al., 2016; Smith et al., 2020; Snyder et al., 2016; Tweksbury et al., 2019). See table 4.2 for demographics and effect sizes.

Ethnicity and comorbidities were not consistently reported among studies. Eight of the 15 studies provided data on ethnicity and 10 reported on comorbidities. Only one study reported changes in comorbid conditions following the laparoscopic sleeve gastrectomy. Individuals identifying as Caucasian ranged from 21.7-77.8%. Overall percentages of African Americans undergoing laparoscopic sleeve gastrectomy totaled 11.1-60%. Individuals identified as Hispanic ethnicity ranged from 0-56.8%. A range of 1.5-11.1% identified as “other” (Inge et al., 2015; Khan et al., 2016; Nadler et al., 2012; Pedroso et al., 2015; Serrano et al., 2016; Smith et al., 2020; Tweksbury et al., 2021; Tweksbury et al., 2019). Eight studies reported hypertension with percentages varying from 34.8%-82% of the study participants having a diagnosis of hypertension (Cottam et al., 2018; Froylich et al., 2016; Inge et al., 2015; McNickle et al., 2017; Nadler et al., 2012; Serrano et al., 2016; Smith et al., 2020; Tweksbury et al., 2019). Seven studies reported dyslipidemia with ranges between 19.7%-69% (Froylich et al., 2016; Inge et al., 2015; McNickle et al., 2017; Saif et al., 2012; Serrano et al., 2016; Smith et al., 2020; Tweksbury et al., 2019). Diabetes was reported in 9-60.9% and rates of obstructive sleep apnea ranged from 40.2%-64.3% (Cottam et al., 2018; Froylich et al., 2016; Inge et al., 2015; Kindel et al., 2018; McNickle et al., 2017; Nadler et al., 2012; Saif et al., 2012; Serrano et al., 2016; Smith et al., 2020; Tweksbury et al., 2019). The single study that examined comorbidities postoperatively reported improvements in comorbidities including hypertension, diabetes and dyslipidemia with the percentage of individuals diagnosed with hypertension decreasing to 0% from 35%, those diagnosed with diabetes decreasing to 0% from 9% and individuals with dyslipidemia accounting for 20% of the individuals in the study, decreasing from 69% (Inge et al, 2015). See appendix for comorbidity and ethnicity information.

Risk of Bias

Studies included in the meta-analysis were similar in methodology and quality. Subjects were not randomized to receive the laparoscopic sleeve gastrectomy as an intervention in any study and there was no blinding. Most studies were retrospective in nature. Five studies utilized a prospective design for select evaluation of a specific aspect such as undergoing a functional MRI to assess for changes in taste sensations or assessment of bile acids but not for the intervention of undergoing the laparoscopic sleeve gastrectomy (Holsen et al., 2018; Khan et al., 2016; Kindel et al., 2018; Smith et al., 2020; Snyder et al., 2016). All but one study took place within a single healthcare system. Inge et al., (2015) was the singular study to utilize a prospective, multi-center design which is considered a stronger study design. Attrition was commonly reported and is a source of bias across studies. Selection bias due to the non-randomized approach was consistent across all studies. Heterogeneity and publication bias were detected in studies and is discussed further below.

Synthesis of Results

Weight Loss

Effect size for weight loss was calculated for 3-6 months and 12-36 months. Figure 4.2 depicts the overall effect size for the 3-6 month range was large with an overall value of 1.39, a value correlating with a change in BMI ranging from 6-15.3 (k = 9; n = 1,179, 95% CI = 1.202- 1.676) and individual effect sizes (Hedges' g) ranging from 0.916-2.816. Heterogeneity was moderate (Cochran's Q = 18.175, p = 0.02, I^2 = 55.98%).

Overall effect size was 1.818 for the 12-36 month data, a value correlating to a change in BMI from 11.5-21.5 (k = 13, n = 831; 95% CI = 1.579-2.098) with individual effect sizes ranging from 1.041-2.802. Heterogeneity was moderate (Cochran's Q = 42.14, p-value = 0.00, I^2 = 71.5). A funnel plot demonstrated asymmetry; however, Egger's 2-tailed test was not significant with a value of 0.08, suggesting publication bias was not present. Orwin's fail safe n was 94, indicating that 94 studies with a null effect would need to be added to the analysis to produce a non-significant effect size. See figure 4.3 for 12-36 month effect size.

Age as a Predictor of Weight Loss

Age was explored as a moderator variable following the laparoscopic sleeve gastrectomy. Dichotomous variable subgroup analysis of the ≤ 21 yrs of age group demonstrated a large effect size of 1.626 (95% *CI* = 1.102-2.151, p = 0.000, k = 4). The > 21 yrs group also had a large effect size of 1.929 (95% *CI* 1.603-2.256, p = 0.000, k = 9). Studies with a mean age ≤ 21 yrs of age demonstrated no significant difference in effects from studies with a mean age > 21 yrs of age ($Q_{between}$= 0.050, df = 1, p = 0.823). Of note, no significant heterogeneity was observed in the analysis of the≤21 yrs group (Q = 0.488, p = 0.922, I^2 = 0.000). In contrast, the > 21 yrs group analysis demonstrated significant heterogeneity (Q = 42.139, p = 0.000, I^2 = 80.77). Results indicate that both groups had a large effect size and that outcomes did not vary between the two groups.

Baseline BMI and Biological Sex as Predictors of Weight Loss

Sample characteristics including baseline BMI and biological sex were explored to evaluate the effect on weight loss following the laparoscopic sleeve gastrectomy. Two separate meta-regressions assessing the percent of the sample that was male (% male) and female (% female) were conducted and did not reveal a statistically significant effect on the mean effect size (% male: k = 11, B = -0.0057, 95% *CI* = -0.0288, 0.0173, p = 0.63, Q = 21.92, df = 9; % female: k = 11, B = 0.0057, 95% *CI* = - 0.0173, 0.0288; p = 0.6264, Q = 21.93, df = 9). Baseline BMI also did not have a statistically significant effect on the mean effect size (k = 13, B = -0.0229; 95% *CI* = -0.0687, 0.0230; p = 0.3283).

Discussion

Obesity remains a chief medical concern that results in lost productivity, increased medical costs, morbidity and mortality. Obesity within adolescents is particularly concerning as increased BMI in adolescence is strongly associated with cardiovascular mortality later in life (Twig et al., 2016). The results from the meta-analysis showed significant weight loss following the laparoscopic sleeve gastrectomy with a large effect size demonstrated across studies, a finding supported by other review articles and meta-analyses (Black et al., 2013; Chang et al., 2014; Clapp et al., 2018; Golzarand et al., 2017; Perivoliotis et al., 2018). This meta-analysis is the only analysis known to have combined both adolescent and adult literature to examine possible differences in outcomes based on age. Age was not found to influence weight loss, indicating that the laparoscopic sleeve gastrectomy may be equally effective at producing weight loss regardless of age.

Heterogeneity was moderate, indicating significant differences in effects across studies, a finding similar to other meta-analyses evaluating bariatric surgery (Black et al., 2013; Clapp et al.,2018; Golzarand et al., 2017). The mean age of subjects within adult literature ranged from 38-46 years of age, a small range compared to the span of individuals that are reported to undergo the laparoscopic sleeve gastrectomy with ages ranging from 18 to over 65 years of age. Differences in age could account for the heterogeneity seen within the analysis and is supported by the absence of heterogeneity when adolescent literature was analyzed separately ($I^2 = 0.00$). Other contributing factors could include patient selection, differences in surgical technique, differing patient demographics or differences in clinical environments such as a teaching institution versus a community hospital.

Biological sex and baseline BMI were not found to influence weight loss postoperatively; however, primary literature has suggested that a lower baseline BMI results in a greater possibility of obtaining a normal weight and BMI, a clinically significant aspect (Anderson et al., 2014; Inge et al., 2010). While biological sex did not influence weight loss postoperatively all studies included in the analysis had a majority female population possibly limiting the ability to detect differences in outcomes related to biological sex. Similar reviews reported a majority female population as well (Black et al., 2013; Golzarand et al., 2016; Li et al., 2019). The discrepancy of male to females undergoing bariatric surgery opens an area for further research and exploration. Societal norms and expectations of males versus females could be explored in the context of perceptions of individuals seeking bariatric surgery. Lastly, females do have a slightly higher incidence of severe obesity when compared to males, which could contribute to the difference seen but requires further exploration (Hales et al., 2020).

Regrettably, comorbidities were unable to be analyzed due to a lack of reporting and consistency among studies. Comorbidities were often defined differently among studies and there was a paucity of data regarding changes in comorbidities postoperatively. The lack of standardization in reporting creates difficulty when attempting to synthesize outcomes. Other reviews have encountered similar problems and while the consensus is that improvements in cardiovascular disease, type 2 diabetes, obstructive sleep apnea and nonalcoholic fatty liver disease occur following bariatric surgery, evidence is weakened by the lack of consistency in reporting (Chang et al., 2014; Pratt et al., 2018; Felsenreich et al., 2019). The effect on comorbidities is of utmost interest as comorbidities impact quality of life and mortality. Obesity in children is particularly concerning as children who are obese are more likely to remain obese into adulthood and have a 3-5 times increased risk of mortality associated with cardiovascular disease, a stunning statistic emphasizing the importance of interventions aimed at decreasing obesity and BMI earlier in life (Ogden et al., 2016; Twig et al., 2016). Given the severe consequences of obesity related comorbidities in childhood and adolescence, recommendations for earlier referrals should be considered.

Attrition is an issue in bariatric programs and can contribute to a lack of available data for analysis. Studies have been conducted to examine the cause of attrition; however, evidence has failed to identify consistent factors that predict follow up (Gourash et al., 2016; Moroshko et al., 2012). Assessing attrition certainly has challenges as the individuals that are lost to follow up are often unavailable to provide insight. Attrition is a barrier for assessing long term outcomes following the laparoscopic sleeve gastrectomy.

Limitations

Results for the 3-6 month effect sizes should be interpreted with caution given the number of studies ($k = 9$) as meta-analyses can be less accurate with a small number of studies (Borenstein et al., 2021). A significant limitation included a paucity of available adolescent literature. The limitation of available data were attempted to be mitigated by including raw unpublished data from an adolescent bariatric center; however, the overall number of adolescent data sets remained low ($k = 5$). The low number of articles may have thwarted attempts at identifying differences in outcomes related to age due to the analysis being underpowered. Additionally, data points centered around two points, further contributing to the inability to thoroughly analyze the effect of age on outcomes across the life span.

Attrition presents a limitation due to missing data. There are two sources of attrition in the data sets analyzed: patients lost to follow up, and patients ineligible for inclusion for all reported time points due to individuals undergoing surgery at different points in time. Ideally, data would be complete; however, the robust effect size exhibited consistently across all studies is encouraging that results are reliable. Publication bias is a limitation of all meta-analyses. Publication bias was mitigated by a rigorous literature search including dissertations, theses, and searches for unpublished data sets. Obtaining and including one unpublished data set helped to mitigate publication bias. Moderate heterogeneity was detected and poses a possible threat to validity; however, studies consistently demonstrated a similarly large effect size, helping to validate findings. A limitation of any meta-analyses is that the analyses rely on data reported by primary studies. Weight can be reported in different ways and can vary slightly depending on which measurement is used. %EWL represents such a measurement as it uses an ideal body weight which can vary (Montero et al., 2011). The included measurements of the preceding meta-analysis consisted of BMI and Kg which have standard definitions, helping to mitigate the limitation of ambiguity that can present threats to the validity of a meta-analysis. The inability to assess comorbidities due to lack of reporting and inconsistencies across studies was a limitation. Meta-analyses are observational in nature and subject to the information presented in primary studies. Biases in original articles can introduce biases in the meta-analysis and limit interpretation and analysis of results. Articles were observational, retrospective designs typically taking place within a single bariatric center. These weaker study designs are a limitation of the present study.

Practice implications

Standardization in reporting of outcomes needs to occur within primary studies to allow synthesis of information. Comorbidities should be clearly defined and reported in a standardized fashion to allow accurate and meaningful comparisons across studies as well as statistical analysis. Practitioners and researchers should utilize definitions put forth by the American Society for Metabolic and Bariatric Surgery for comorbidities and weight loss to achieve consistency and allow for greater synthesis of existing literature (Brethauer et al., 2015). Pediatric practitioners should be aware of the severe consequences of obesity in childhood and associated comorbidities. General practitioners should be aware that bariatric surgery is an effective treatment for weight loss for both adolescents and adults, allowing for greater dissemination of available treatment options to individuals that have failed to achieve weight loss with medical management. Current guidelines set forth by the American Society for Metabolic and Bariatric Surgery to identify adolescents potentially eligible for bariatric surgery include those with a BMI > or = to 35 or at the 120% percentile with a clinically significant co-morbid condition or individuals with a BMI of 40 or above or at the140th percentile on the growth chart without a comorbidity (Pratt et al., 2018). Adult bariatric programs should consider partnering with their adolescent counterparts to facilitate continued follow up into adulthood, allowing for long term follow up data.

Conclusion

The effect of obesity related comorbidities in adolescents is striking. While the meta-analysis failed to show that age affected weight loss, it did show that it is equally effective at weight loss in adolescents as in adults. Given the severe consequences of obesity related comorbidities in childhood and adolescence, recommendations for earlier referrals should be considered and explored. Further research including exploring long term changes in comorbidities following the laparoscopic sleeve gastrectomy should be a priority. General practitioners should be aware of the laparoscopic sleeve gastrectomy and indications for referral. Perhaps the laparoscopic sleeve gastrectomy is equally effective at reducing weight across the lifespan; but clinical consequences of prolonged obesity are evident and support earlier referral.

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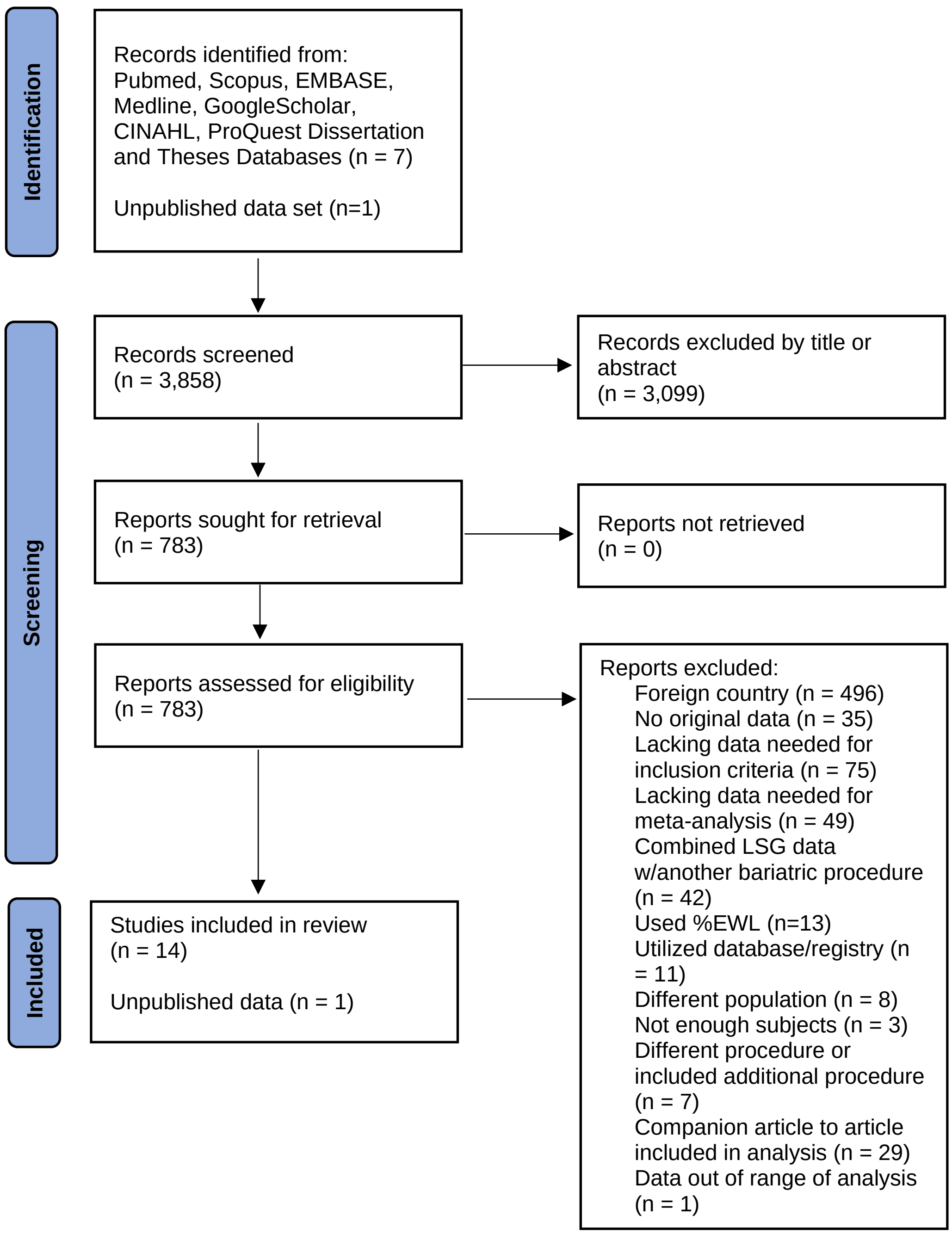
Figure 4.1

PRISMA DIAGRAM



Page et al (2021).

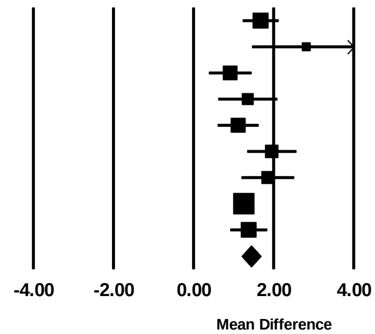
Figure 4.2

Weight Loss at 3-6 Months

Study name	Hedges's g	Standard error	Variance	Lower limit	Upper limit
Cottam et al. (2018)	1.675	0.227	0.052	1.229	2.121
Khan et al. (2016)	2.816	0.689	0.475	1.465	4.166
Kindel et al. (2018)	0.916	0.271	0.073	0.386	1.447
Nadler et al. (2012)	1.355	0.375	0.141	0.620	2.090
Pedroso et al. (2015)	1.115	0.259	0.067	0.607	1.622
Serrano et al. (2016)	1.954	0.312	0.097	1.342	2.566
Smith et al. (2020)	1.856	0.335	0.112	1.200	2.512
Tweksbury et al. (2019)	1.258	0.046	0.002	1.167	1.348
Tweksbury et al. (2021)	1.378	0.234	0.055	0.920	1.837
Total Effect Size	1.439	0.121	0.015	1.202	1.676

Statistics for each study

Hedges's g and 95% CI



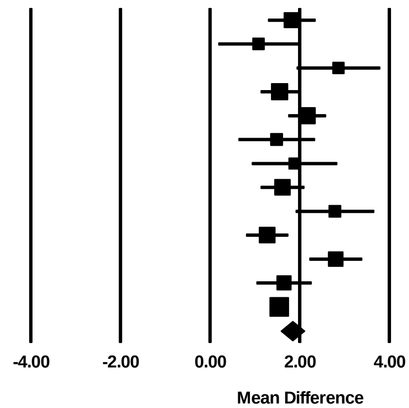
Meta Analysis

Figure 4.3

Weight Loss at 12-36 Months

Study name / Statistics for each study / Std diff in means and 95% CI

Study name	Std diff in means	Standard error	Variance	Lower limit	Upper limit	Z-Value	p-Value
Cottam et al. (2018)	1.824	0.270	0.073	1.295	2.353	6.760	0.000
Froylich et al. (2016)	1.082	0.457	0.208	0.187	1.977	2.370	0.018
Holsen et al. (2018)	2.866	0.475	0.225	1.936	3.796	6.039	0.000
Inge et al. (2015)	1.553	0.215	0.046	1.132	1.975	7.223	0.000
McNickle et al. (2017)	2.167	0.213	0.046	1.748	2.585	10.150	0.000
Nadler et al. (2012)	1.487	0.435	0.189	0.634	2.339	3.419	0.001
Pedroso et al. (2015)	1.885	0.485	0.235	0.935	2.835	3.889	0.000
Saif et al. (2012)	1.617	0.247	0.061	1.132	2.102	6.534	0.000
Serrano et al. (2016)	2.787	0.446	0.199	1.914	3.661	6.256	0.000
Snyder et al. (2016) G1	1.276	0.239	0.057	0.807	1.745	5.332	0.000
Snyder et al. (2016) G2	2.805	0.299	0.089	2.219	3.391	9.380	0.000
Tweksbury et al. (2021)	1.651	0.313	0.098	1.039	2.264	5.281	0.000
Tweksbury et al. (2019)	1.545	0.057	0.003	1.433	1.657	27.035	0.000
Total Effect Size	1.839	0.132	0.018	1.579	2.098	13.891	0.000



Meta Analysis

Figure 4.4

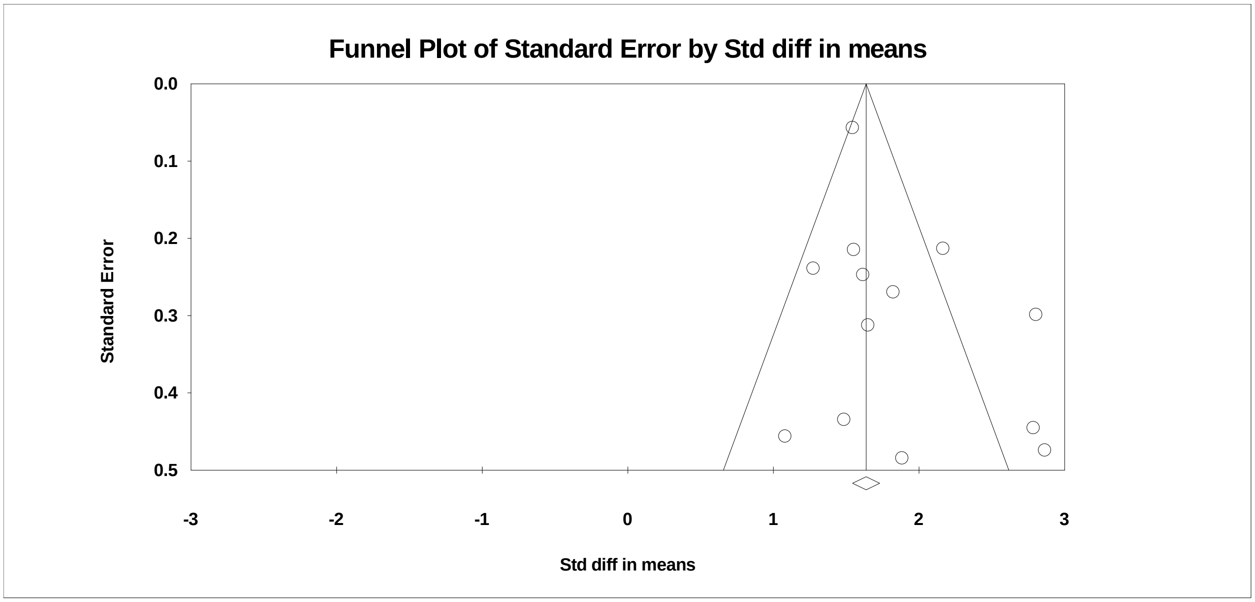

Funnel Plot of Standard Error by Std diff in means
Standard Error
0.0
0.1
0.2
0.3
0.4
0.5
-3
-2
-1
0
1
2
3
Std diff in means

Table 4.1

STATISTICAL ANALYSES TO BE CONDUCTED FOR EACH AIM	
Specific Aim 1	Effect size data for 3-6 months and 12-36 months postoperatively • Calculate standardized mean difference: [(difference in mean outcome between groups)/(standard deviation of outcome among participants)] • Hedges' *g*: *J= 1 – [(3)/(4df-1)]* Heterogeneity assessments • Cochran's *Q*: $Q = \sum_{i=1}^{K} Wi(Yi - M)^2$ • I^2: *[(Q-df)/(Q)] X 100* Publication bias • Funnel plot- studies to be evenly distributed around overall estimate if no bias • Egger's test of regression- slope of regression line will be significantly different than 0 ($p < 0.05$) • Orwin's fail safe *N*- value of 0.2 utilized to represent trivial standard difference in means
Specific Aim 2	Effect size data for 12-36 month data point • Calculate standardized mean difference: [(difference in mean outcome between groups)/(standard deviation of outcome among participants)] • Hedges' *g*: *J= 1 – [(3)/(4df-1)]* Dichotomous covariate analysis • Mixed effects analysis- random effect analysis with pooled estimate of T_2 • T_2 = *[(Q-df)/C]* Heterogeneity assessments • Cochran's *Q*: $Q = \sum_{i=1}^{K} Wi(Yi - M)^2$ • I^2: *[(Q-df)/(Q)] X 100*
Specific Aim 3	Covariates examined: biological sex and baseline BMI (3) separate meta-regressions performed using %female, %male and baseline BMI as covariate • *Z* distribution: $Z=[(B)/(SE_B)]$ Goodness of fit tests • Q_{model}- amount of dispersion seen in the model that is explained by the covariate ($p< 0.5$= statistical significance) • R^2 analog- assesses proportion of total between study variance explained by model $R^2 = 1 - \left(\frac{T^2_{residual}}{T^2_{total}}\right)$ Heterogeneity assessments • Cochran's *Q*: $Q = \sum_{i=1}^{K} Wi(Yi - M)^2$ • I^2: *[(Q-df)/(Q)] X 100*

TABLE 4.2

STUDIES INCLUDED IN ANALYSIS: DEMOGRAPHICS AND EFFECT SIZE

Study name	Sample size pre/post	Mean age	%Sex (M/F)	Preop BMI	Postop BMI	Change in BMI	Time point used in analysis	Effect size (Hedges' *g*)
• 3-6 MONTH ANALYSIS								
Khan et al. (2016)	9/7	17.4(1.5)	22.2/77.8	144.2(6.2)*	123.7(7.7)*	20.5*	3 mo	2.816
Kindel et al. (2018)	31/28	45.4(12.9)	18.0/82.0	45.0(6.8)	38.9(6.3)	6.1	3 mo	0.916
Tweksbury et al. (2021)	68/32	20.3(2.9)	14.5/85.3	51.2(8.9)	39.16(8.1)	12.04	6 mo	1.378
Cottam et al. (2018)	57/47	43.9(10.9)	17.5/82.5	43.5(6.4)	33.0(6.0)	10.5	6 mo	1.675
Nadler et al. (2012)	23/13	17.3(1.5)	21.7/78.3	52.0(9.0)	40.0(8.0)	12.0	6 mo	1.355
Pedroso et al. (2015)	37/31	17.3(1.8)	27.0/73.0	50.1(9.4)	39.5(9.4)	10.6	6 mo	1.115
Serrano et al. (2016)	42/22	38.2(11.3)	48.0/52.0	68.4(7.9)	53.1(7.4)	15.3	6 mo	1.954
Smith et al. (2020)	25/25	38.9(7.6)	0/100	43.4(5.0)	34.3(4.7)	9.1	6 mo	1.856
Tweksbury et al. (2019)	1303/974	44.4(11.9)	24.8/75.2	48.0(8.6)	37.6(7.8)	10.4	6 mo	1.258
• 12-36 MONTH ANALYSIS								
Tweksbury et al. (2021)	68/15	20.3(2.9)	14.5/85.3	51.2(8.9)	36.8(7.8)	14.4	12 mo	1.636
Holsen et al. (2018)	18/18	38.4(10.1)	11.1/88.8	41.8(4.5)	29.6(4.0)	12.2	12 mo	2.802
McNickle et al. (2017)	127/42	40.3(9.0)	6.3/93.7	46.5(5.1)	35.0(5.9)	11.5	12 mo	2.157
Nadler et al. (2012)	23/9	17.3(1.5)	21.7/78.3	52.0(9.0)	39.0(8.0)	13.0	12 mo	1.449
Serrano et al. (2016)	42/10	38.2(11.3)	48.0/52.0	68.4(7.9)	46.9(6.8)	21.5	12 mo	2.745
Snyder et al. (2016) group 1	50/36	44.0(11.0)	-/-	44.0(12.0)	31.0(6.9)	13.0	12 mo	1.264
Snyder et al. (2016) group 2	48/41	44.0(11.0)	-/-	44.0(5.7)	30.0(4.0)	14.0	12 mo	2.781
Froylich et al. (2016)	11/11	46.3(11.7)	27.0/73.0	72.7(21.1)	53.9(12.6)	18.8	14 mo+	1.041
Cottam et al. (2018)	57/28	43.9(10.9)	17.5/82.5	43.5(6.4)	32.0(6.1)	11.5	24 mo	1.808
Pedroso et al. (2015)	37/6	17.3(1.8)	27.0/73.0	50.1(9.4)	33.0(6.2)	17.1	24 mo	1.851
Tweksbury et al. (2019)	1,303/540	44.4(11.9)	24.8/75.2	48.0(8.6)	34.8(8.4)	13.2	24 mo	1.545
Inge et al. (2015)	67/48	17.0(1.7)	33/67	50.0(8.2)	37.0(8.6)	13.0	36 mo	1.543
Saif et al. (2012)	82/27	46.4(13.9)	33.0/67.0	55.7(13.7)	35.5(7.6)	20.2	36 mo	1.605

*Value in Kg

APPENDIX 4.1: ETHNICITY AND COMORBIDITIES

Study Name	Caucasian	African American	Hispanic	Other	Hypertension	Dyslipidemia	Diabetes	Obstructive sleep apnea	Hypertension postop	Dyslipidemia postop	Diabetes postop
Cottam (2018)	-	-	-	-	46	-	30	44	-	-	-
Froylich (2016)	-	-	-	-	82	36	45	-	-	-	-
Inge (2015)	67	22	1	10	35	69	9	-	0	20	0
Khan (2016)	77.8	11.1	0	11.1	-	-	-	-	-	-	-
Kindel (2018)	-	-	-	-	-	-	21	-	-	-	-
McNickle (2017)	-	-	-	-	52.8	19.7	27.6	40.2	-	-	-
Nadler (2012)	21.7	56.5	21.7	-	34.8	-	60.9	52.2	-	-	-
Pedroso (2015)	29.7	5.4	56.8	8.1	-	-	-	-	-	-	-
Saif (2012)	-	-	-	-	-	35.8	27.2	-	-	-	-
Serrano (2016)	14	36	12	38	50	23.8	21.4	64.3	-	-	-
Snyder (2016) Grp 1	-	-	-	-	-	-	-	-	-	-	-
Snyder (2016) Grp 2	-	-	-	-	-	-	-	-	-	-	-
Smith (2020)	36	60	0	4	44	20	20	48	-	-	-

Tweksbury (2021)	42.6	55.8	-	1.5	-	-	-	-	-	-	-
Tweksbury (2019)	49.6	-	-	-	61.4	31.5	34.4	56	-	-	-

Chapter 5: Conclusions

Obesity within the United States is a chief medical concern that results in lost work estimated to cost between $3.38 and $6.38 billion dollars per year. Additionally, medical care related to obesity is estimated to cost $147 billion dollars per year (CDC, 2018). Obesity results in negative outcomes including increased risk of disease and negative psychosocial effects. Obesity within the adolescent is particularly concerning as increased BMI in adolescence is strongly associated with cardiovascular mortality later in life, a significant finding that requires special attention (Twig et al., 2016). Bariatric surgery provides a treatment option for obesity. Improvements in quality of life and disease processes following weight loss surgery are reported (Olbers et al., 2017; Zeller et al., 2017). The laparoscopic sleeve gastrectomy, a procedure in which the greater curvature of the stomach is resected, accounts for 59.4% of all bariatric surgeries. Weight regain has been reported and reoperations represent 16.7% of bariatric surgeries, an indication that bariatric surgery as a weight loss treatment is imperfect (ASMBS, 2022).

There are typically three types of surgery performed including the laparoscopic adjustable gastric band, laparoscopic sleeve gastrectomy and the roux-en-y gastric bypass. The laparoscopic adjustable gastric band appears to be less effective at producing substantial weight loss than the laparoscopic sleeve gastrectomy and roux-en-y gastric bypass (Karasko, 2019). As a result of its ineffectiveness in comparison to the laparoscopic sleeve and roux-en-y, the frequency with which the laparoscopic adjustable gastric band is performed has decreased over the years and currently accounts for only 0.9% of bariatric surgeries (American Society for Metabolic and Bariatric Surgery [ASMBS], 2022). The roux-en-y gastric bypass has longer term data when compared to the laparoscopic sleeve gastrectomy. The majority of individuals undergoing bariatric surgery tend to be female (Karasko, 2019).

Outcomes following bariatric surgery in the adolescent are typically reported separately from adult bariatric outcomes. Bariatric surgery in the adolescent typically occurs between the ages of 14-18, a narrow age range when compared to the overall life span. Given the severe comorbidities and consequences resulting from continued obesity as well as the risk of remaining obese, identifying the optimal age to perform weight loss surgery to achieve the most favorable results is of utmost importance. Combining adult and adolescent literature to examine patient characteristics and their effect on weight loss with special attention to age is a novel approach and may result in improved patient counseling regarding expectations and outcomes. The preceding meta-analysis attempted to **1) determine the overall effect of the sleeve gastrectomy on weight loss, 2) evaluate the effect of age at the time of surgery on weight loss and 3) describe and explore variation in weight loss by sample characteristics.**

Effects of Laparoscopic Sleeve Gastrectomy on Weight Loss

The results from the meta-analysis showed significant weight loss following the laparoscopic sleeve gastrectomy with a large effect size demonstrated across studies (k = 13, n = 831, 95% CI = 1.579-2.098). Age was not found to influence weight loss (Q_{between} = 0.50, df = 1, p = 0.823), though there were several limitations that may have thwarted efforts to identify differences. Limitations included central grouping of mean ages around 2 decades of life and a low number of adolescent studies, possibly resulting in an underpowered analysis. An additional severe limitation of the study was the lack of available information on comorbidities postoperatively with a paucity of data as well as inconsistencies in definitions. Evaluating the effect of comorbidities postoperatively is of greatest importance as obesity related comorbidities are associated with devasting outcomes including increased morbidity and mortality. Despite the limitations, the meta-analysis clearly identified that the laparoscopic sleeve gastrectomy was equally effective at weight loss in adolescents as in adults.

Implications for Research

Findings from this dissertation work highlights future areas of research. For example, access to treatment with special attention to the adolescent should be investigated and explored. A survey among pediatricians identified that nearly half of respondents (48%) would never consider referring an adolescent for bariatric surgery and 46% considered 18 yrs of age to be a minimum age for referral (Woolford et al., 2010). The attitudes of primary care physicians and willingness to refer could affect access for many adolescents who may not be aware that bariatric surgery is an option. Literature has shown bariatric surgery to be safe and effective in the adolescent; however, investigating and exploring the effect of age on outcomes may provide insight and possibly alleviate concerns that affect a pediatrician's willingness to refer an individual (Karasko, 2019). Primary articles need to evaluate age as a moderator variable to assess for any differences in outcomes across the life span. Examining the effect of age at the time of surgery on outcomes may help to provide access to treatment options for individuals. Standardization of reporting of comorbidities should be a priority as obesity itself does not increase mortality, but the comorbid conditions associated with obesity do. Could performing a weight loss surgery earlier in life prevent or lessen the damages of obesity related comorbid conditions? This is a question that requires exploration but must first start with consistent reporting of comorbidities across primary studies. Adult programs should partner with their adolescent counterparts when publishing data to help facilitate a more complete picture regarding long term outcomes and effects following the laparoscopic sleeve gastrectomy. Combining adolescent and adult literature allows for examination of outcomes across the lifespan, providing a more thorough evaluation. Gender should be explored in primary literature to examine why individuals undergoing bariatric surgery are typically female. Exploring differences may provide further insight into motivating factors, access to healthcare or other unexplored variables that may in turn, help to predict differences in outcomes and unearth a contributing factor to successful, sustained weight loss. Primary investigators should evaluate outcome data in a longitudinal fashion with a cohort of adolescent patients as they age into adulthood to better assess long term outcomes. Long term outcomes are lacking in the adolescent who often transition to the adult programs and are lost to follow up. Continuing to follow a cohort of subjects into adulthood would result in a comprehensive and thorough evaluation. Once long term data are obtained from a cohort of patients, investigators could evaluate weight loss in the early postoperative period and compare it to weight loss at later time points to evaluate for trends that may help practitioners predict long term outcomes based on early results. Identifying factors that predict success in the early postoperative period may help practitioners tailor interventions designed to facilitate continued weight loss.

Attrition is an issue and researchers should explore ways to increase long term follow up. Long term follow up would allow for continued evaluation of outcomes and/or unintended consequences of weight loss surgery. Long term follow up is essential when evaluating weight loss surgery to allow for better counseling preoperatively. Additionally, long term follow up may identify certain characteristics that predict better outcomes which in turn may help to guide patient selection, counseling and/or interventions that could be introduced to facilitate better outcomes. Primary researchers should focus on ways to enhance and encourage follow up to allow for more complete reporting on long term outcomes. Primary researchers could investigate partnering with an individual's primary practitioner to facilitate continued reporting of outcomes in postoperative individuals. Utilizing technology such as texts or emails may help to facilitate continued follow up. Investigators could examine whether a text message or email asking for a self-reported outcomes could produce accurate results and serve as another option for follow-up.

Implications for Practice

Improvements seen in obesity related comorbidities and psychosocial effects are presumed to occur as a result of weight loss, not the surgery itself. Weight loss surgery is an intervention profoundly effective at producing weight loss. Weight regain is reported in some individuals and revisional surgery does occur, indicating that the intervention is imperfect. The meta-analysis and literature review in Chapter 2 reveals that weight loss surgery, while imperfect, is effective and safe in the adolescent. Future researchers need to examine and identify causes that increase the likelihood of weight regain and more long term data are required, a task that is difficult in our current healthcare system. Perceptions of primary care providers should be investigated and perhaps mitigated to allow access to an effective treatment for a condition that has profound negative impacts throughout life. The risks of continued obesity are well documented and severe. Weight loss surgery should be considered a viable and acceptable treatment option to prevent the negative outcomes of continued obesity. Earlier referral could be beneficial and result in improvements in comorbidities earlier in life. While baseline BMI was not found to influence weight loss postoperatively in the meta-analysis conducted, a lower baseline BMI increases the likelihood of attaining a normal, or non-obese BMI postoperatively, a clinically important aspect (Anderson et al., 2014; Inge et al., 2010). Attaining a normal weight decreases an individual’s risk of continued obesity related comorbidities. An individual who can attain a “healthy weight” status (as defined by the CDC) has less risks than an individual who is “obese,” preoperatively and “overweight” postoperatively (CDC, 2021).

Provider perceptions potentially limit access to bariatric surgery, but insurance companies are also a barrier to treatment. Insurance companies are notoriously hesitant to approve bariatric surgery in the adolescent patient and providers face many obstacles when attempting to obtain approvals. A review article examining 5 different adolescent bariatric centers found that less than half of bariatric surgeries were approved on initial submission by insurance companies, compared with approximately 80-85% of adults receiving approval (Inge et al., 2014; Thakkar & Michalsky, 2015). Evidence has shown weight loss surgery to be effective. The effects of obesity are extreme and can produce life-long negative consequences, necessitating effective interventions to counter the ill effects of obesity. Mitigating effects of obesity is especially important in the adolescent to facilitate life long health. Weight loss surgery in the adolescent may seem extreme to providers, patients, and insurance companies; however, the effects of prolonged obesity are extreme, influencing life- long health. Clinical consequences of obesity are severe and long-lasting, necessitating an aggressive intervention to mitigate disease. Education of providers regarding indications for treatment as well as the ill effects of obesity may help to increase comfort in referrals. While weight regain is reported, not all individuals experience weight regain. Further research should be implemented to identify factors that facilitate prolonged weight loss, helping to decrease weight regain postoperatively.

Conclusion

The laparoscopic sleeve gastrectomy is an effective intervention that results in weight loss in both adolescents and adults. Long term effects in the adolescent patient and changes in comorbidities require further investigation. Attrition and an inconsistency in defining comorbidities creates challenges in examining long term outcomes. Weight regain has been reported, indicating that the laparoscopic sleeve gastrectomy, while effective, is imperfect. Further research should be conducted to improve rates of attrition. Education among primary practitioners should occur and biases examined to prevent inadequate access to treatment. Risks of continued obesity and the presence of comorbidities should be carefully assessed and discussed amongst providers and patients to determine if the laparoscopic sleeve gastrectomy would benefit a particular individual. Continuing research to identify factors that may predict if an individual is at greater risk of weight gain may help patient counseling

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VITA

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