



# Evidence Brief: The Comparative Effectiveness of Bariatric Surgery in Super Obesity (BMI > 50 kg/m<sup>2</sup>)

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## PREFACE

The VA Evidence-based Synthesis Program (ESP) was established in 2007 to provide timely and accurate syntheses of targeted healthcare topics of particular importance to clinicians, managers, and policymakers as they work to improve the health and healthcare of Veterans. QUERI provides funding for four ESP Centers, and each Center has an active University affiliation. Center Directors are recognized leaders in the field of evidence synthesis with close ties to the AHRQ Evidence-based Practice Centers. The ESP is governed by a Steering Committee comprised of participants from VHA Policy, Program, and Operations Offices, VISN leadership, field-based investigators, and others as designated appropriate by QUERI/HSR&D.

The ESP Centers generate evidence syntheses on important clinical practice topics. These reports help:

- Develop clinical policies informed by evidence;
- Implement effective services to improve patient outcomes and to support VA clinical practice guidelines and performance measures; and
- Set the direction for future research to address gaps in clinical knowledge.

The ESP disseminates these reports throughout VA and in the published literature; some evidence syntheses have informed the clinical guidelines of large professional organizations.

The ESP Coordinating Center (ESP CC), located in Portland, Oregon, was created in 2009 to expand the capacity of QUERI/HSR&D and is charged with oversight of national ESP program operations, program development and evaluation, and dissemination efforts. The ESP CC establishes standard operating procedures for the production of evidence synthesis reports; facilitates a national topic nomination, prioritization, and selection process; manages the research portfolio of each Center; facilitates editorial review processes; ensures methodological consistency and quality of products; produces “rapid response evidence briefs” at the request of VHA senior leadership; collaborates with HSR&D Center for Information Dissemination and Education Resources (CIDER) to develop a national dissemination strategy for all ESP products; and interfaces with stakeholders to effectively engage the program.

Comments on this evidence report are welcome and can be sent to Nicole Floyd, ESP CC Program Manager, at [Nicole.Floyd@va.gov](mailto:Nicole.Floyd@va.gov).

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## EXECUTIVE SUMMARY

While experts agree there is high-quality evidence that bariatric surgery leads to greater weight loss and more type 2 diabetes remission than nonsurgical treatments among morbidly obese patients in general, questions remain regarding the precise balance of benefits and harms of bariatric surgery in super obese patients (BMI > 50 kg/m<sup>2</sup>). This subgroup has seen the highest growth in prevalence between 1986 and 2010 and is associated with disproportionately higher health care costs.

However, we found the published literature that separates out the super obese insufficient to determine the precise balance of benefits and harms of bariatric surgery compared to nonsurgical treatment (*ie*, lifestyle, dietary changes, pharmacotherapy) in this subpopulation. Compared with usual care, one large retrospective VA study<sup>1</sup> provided limited evidence that bariatric surgery can increase mortality in the first year, but decrease mortality long-term among super obese Veterans (Table 1). However, the care provided to the control group, nonsurgical or no treatment, was not well-defined, information about many key issues was missing (*eg*, smoking, severity of comorbidities), and the study did not evaluate a complete set of key outcomes, including weight loss, obesity-related disease remission, complications, and cost.

Non-VA studies that compared different bariatric surgical approaches (Table 1) suggested some differences in weight loss and complications. Laparoscopic gastric bypass generally resulted in greater short-term proportion of excess weight loss (%EWL) than did other procedures, particularly when banding was used. Duodenal switch, the most technically complex of all bariatric procedures, led to greater long-term weight loss than did gastric bypass, but there were more complications. However, these findings likely have low applicability to Veterans since patients were primarily females in their mid-30s to 40s and information was missing on diabetes, mental illness, and other important comorbidities. We found no studies that evaluated barriers to obtaining bariatric surgery in super obese adults.

Because current evidence that separates out the super obese is very limited, we recommend that the HSR&D State of the Art Conference (SOTA) prioritize studies to confirm subgroup findings from earlier research (Arterburn et al<sup>1</sup>) comparing bariatric surgery with nonsurgical treatment in the super obese. Answering questions about the long-term comparative effectiveness of these weight loss interventions will help to determine the relevance of questions about surgical approach and barriers. The most practical method is to use a larger sample from existing VA Surgical Quality Improvement Program (VASQUIP) data. To best remedy key limitations of current

### Background

HSR&D is sponsoring a State of the Art Conference (SOTA) to review the state of research evidence on and the relevance to the VA population on a broad range of obesity-related questions, including the role of bariatric surgery in super obesity (BMI > 50 kg/m<sup>2</sup>). As no previous evidence review has broadly focused on the super obese subgroup, the SOTA committee requested that the ESP Coordinating Center (ESP CC) conduct a brief review of the evidence on the barriers to obtaining bariatric surgery in super obese adults and on the comparative effectiveness of bariatric surgery versus nonsurgical treatments and of different bariatric surgical procedures.

### Methods

We searched MEDLINE®, the Cochrane Database of Systematic Reviews, and the Cochrane Central Registry of Controlled Trials using terms for appointments, reminders and schedules. We used prespecified criteria for rating internal validity and strength of the evidence for each outcome and comparison. See our PROSPERO protocol for our full methods.

research, a quality improvement study should consider incorporating some of the following features: (1) match to patients with comparable eligibility for surgery and documented participation in a well-characterized intensive lifestyle intervention such as the VA’s national MOVE!® program; (2) evaluate a more complete set of outcomes, including complications, obesity-related disease remission, and cost; (3) evaluate the role of a broader range of patient factors in the variation of outcomes, including smoking, mental illness, duration of diabetes, preoperative weight loss; (4) identify whether there is a specific BMI threshold > 50 kg/m<sup>2</sup> that is most predictive of benefit and; (5) to help inform how much weight loss is enough to provide health benefits, evaluate the correlation between weight loss and comorbidity resolution and survival. Another option for evaluating the comparative effectiveness of bariatric surgery in the super obese is to use the large body of data from existing studies with broader populations of patients with BMI > 35 kg/m<sup>2</sup> to conduct an individual patient data meta-analysis of included patients with BMI > 50 kg/m<sup>2</sup>.

**Table 1. Summary of Findings: Comparative Effectiveness of Bariatric Surgery versus Non-Surgical Treatment and Between Different Bariatric Surgeries in Studies or Subgroup Analyses Exclusively of Super Obese (BMI > 50 kg/m<sup>2</sup>) Patients**

<b>Number and type of studies and sample sizes</b>	<b>Outcomes &lt; 5 years (All low-strength unless otherwise noted)</b>	<b>Outcomes ≥ 5 years (All low-strength unless otherwise noted)</b>
<i>Surgery vs Non-surgery</i>		
1 VA post-hoc subgroup analysis from a retrospective cohort <sup>1</sup> , N=2860	é mortality at 1 year; 4.93% vs 2.77%, aHR 1.57 (95% CI, 1.08-2.76) ê mortality at > 1 year to 5 years; 5.48% vs 11.4%, aHR 0.46 (95% CI, 0.33-0.64)	ê mortality at > 5 years to 14 years; 9.5% vs 17.5%, aHR 0.45 (95 %CI, 0.34-0.60)
<i>Duodenal Switch (DS) vs Laparoscopic Roux-en-Y Gastric Bypass (LRYGB)</i>		
Short-term: 6 non-VA, retrospective cohorts <sup>3,4,47,49-51</sup> N=27,645 Long-term: 1 non-VA RCT <sup>2</sup> , N=55	Insufficient evidence	é weight loss for DS; % patients with BMI > 40 kg/m <sup>2</sup> : DS=14% vs GB=55.3%, P=0.001 ê hospital admissions; 59% vs 29%, P=0.02 and surgeries related to the initial procedure for DS; 45% vs 10%, P=0.002 = mortality and diabetes remission
<i>Laparoscopic Roux-en-Y Gastric Bypass (LRYGB) vs Laparoscopic Adjustable Gastric Banding (LAGB)</i>		
1 non-VA, single center, retrospective cohort <sup>3</sup> , N=106	é %EWL for LRYGB at 16 months; 52% vs 31%, p<0.001 = mortality and early complications ê late complications for LRYGB; 28% vs 78%, p<0.05	No evidence
<i>Laparoscopic Roux-en-Y Gastric Bypass (LRYGB) vs Laparoscopic Sleeve Gastrectomy (LSG)</i>		
Super obese: 2 non-VA, single center retrospective cohorts <sup>4,5</sup> N=107 Super-super obese: 1 non-VA single center retrospective cohort, <sup>6</sup> N=135	Super obese: é %EWL for LRYGB at 12 months; 63.9% vs 43.9%, p<0.05 = mortality and complications Super-super obese: Insufficient evidence	No evidence

<b>Number and type of studies and sample sizes</b>	<b>Outcomes &lt; 5 years (All low-strength unless otherwise noted)</b>	<b>Outcomes ≥ 5 years (All low-strength unless otherwise noted)</b>
<i>Banded vs Non-Banded Laparoscopic Roux-en-Y Gastric Bypass (LRYGB)</i>		
1 non-VA, single center retrospective cohort <sup>7</sup> , N=189	é %EWL for banded LRYGB at 2 years; 57.5% vs 47.6%, p=0.003	No evidence
<i>Laparoscopic vs Open Gastric Bypass</i>		
1 non-VA, subgroup analysis from a single center retrospective cohort <sup>8</sup> , N=unknown	Insufficient evidence	No evidence
In mega obese (BMI > 70 kg/m <sup>2</sup> ): 1 non-VA, single center retrospective cohort <sup>9</sup> , N=89	é %EWL for laparoscopic at 3 (22.7% vs 17.5, p=0.016) and 6 months (37.6% vs 30.8%, p=0.037), but comparable at 1-2 years ê hernia with laparoscopic surgery = mortality and other complications	No evidence

\*All low-strength evidence; aHR = Adjusted Hazard Ratio, LRYGB = Laparoscopic Roux-en-Y Gastric Bypass, DS = Duodenal Switch, LAGB = Laparoscopic Adjustable Gastric Banding, LSG= Laparoscopic Sleeve Gastrectomy, %EWL = % Excess Weight Loss, T2DM = Type 2 Diabetes Mellitus

## EVIDENCE BRIEF

### INTRODUCTION

#### PURPOSE

Despite substantial investment of resources in the Veteran's Health Administration's (VHA) national MOVE!® weight management program and growing evidence about the effectiveness of bariatric surgery, the prevalence of obese Veterans has continued to rise over the past decade to 41.3% in fiscal year 2014 (FY14)(email communication, October 19, 2015). In response, HSR&D is sponsoring a State of the Art Conference (SOTA) to review the state of research evidence and the relevance to the VA population on a broad range of obesity-related questions, with the goals of (1) defining consensus where evidence is sufficient, (2) defining a research agenda where evidence is conflicting or limited, and (3) making practice or policy recommendations where consensus exists but is at odds with practice. Among the SOTA committee's questions are some regarding the balance of benefits and harms of bariatric surgery in patients with more extreme obesity, such as BMI > 50 kg/m<sup>2</sup>, commonly referred to as super obesity. The importance of resolving questions in the super obese is increasing as this subgroup has seen the highest growth in prevalence between 1986 and 2010 in the United States overall and is associated with disproportionately higher health care costs. The VA FY14 prevalence of super obesity was 0.5% (email communication, October 19, 2015). As no previous evidence review has broadly focused on the super obese subgroup, the SOTA committee requested that the ESP Coordinating Center (ESP CC) conduct a brief review of the evidence on the barriers to obtaining bariatric surgery in super obese adults, and on the comparative effectiveness of bariatric surgery versus nonsurgical treatments and between different bariatric surgical procedures.

#### BACKGROUND

One-third of adults in the United States are obese and it is an important public health issue.<sup>11</sup> Among the various options for treating obesity, including dietary changes, exercise, lifestyle interventions, and medications, consensus has grown in support of bariatric surgery as leading to the greatest improvement in weight loss and weight-associated comorbidities compared with nonsurgical interventions, at least in the short-term.<sup>12-19</sup> Starting as far back as 1991, clinical practice guidelines, supported by data from RCTs and observational studies, have commonly identified bariatric surgery as an appropriate option for adults with body mass index (BMI) ≥ 40 kg/m<sup>2</sup> or BMI ≥ 35 kg/m<sup>2</sup> with obesity-related comorbid conditions and who have not responded to nonsurgical treatment options.<sup>20-23</sup>

Many types of bariatric surgical procedures are available that work in different ways to contribute to weight loss: (1) reducing the amount of calories and nutrients the body absorbs (malabsorptive), (2) physically limiting the amount of food the stomach can hold (restrictive), or (3) a combination of the two.<sup>24</sup> The 4 types of bariatric surgery currently performed are Roux-en-Y gastric bypass (RYGB), sleeve gastrectomy (SG), laparoscopic adjustable gastric banding (LAGB), and duodenal switch with biliopancreatic diversion (DS).<sup>24,25</sup> No guideline has recommended any particular bariatric procedure over another.<sup>12</sup>

Questions remain, however, regarding the balance of benefits and harms of bariatric surgery in patients with the highest levels of obesity. Studies have consistently shown trends toward higher-BMI groups having markedly lower odds of successful weight loss when assessed in relation to ideal body weight (IBW) standards, such as the proportion of excess weight loss (%EWL) measure, which is calculated by dividing the actual postoperative weight loss by the amount of percent excess weight (subtract the IBW from the actual preoperative weight or BMI). This is particularly the case for patients with BMI > 50 kg/m<sup>2</sup>, commonly referred to as super obese, and BMI > 60 kg/m<sup>2</sup>, super-super obese. A 2012 meta-analysis found that super obese patients had a 10% lower EWL after a mean of 30 months (range, 12-72 months) compared to the non-super obese (95% CI, -3.7% to -16.7%; 11 studies; N=3292) after undergoing primarily RYGB.<sup>26</sup> Additionally, a 2015 review found that, compared to patients with BMI ≤ 50 kg/m<sup>2</sup>, odds of achieving EWL ≥ 40% were lower at both 6 months (0.13; 95% CI, 0.06-0.29) and 18 months (0.43; 95% CI, 0.24-0.78) for super obese patients who underwent LAGB and lower at 6 months (0.12; 95% CI, 0.08-0.18) but not at 18 months following RYGB.<sup>19</sup> Secondly, as odds of mood, anxiety, and personality disorders have been shown to increase by 3% for each one BMI unit increase (95% confidence interval range, 1.02 to 1.04), super obese patients are likely to have a higher prevalence of mental health issues which may negatively affect bariatric surgery outcomes.<sup>27</sup> Additionally, compared to the overall population receiving bariatric surgery, super obesity may represent a higher-risk bariatric surgical group, with a reported greater cumulative incidence of mortality at 30 days (1.5% vs 0.28%; mean difference, 1.25%, 95% CI, 0.56-1.94) and from 30 days to 2 years (0.6% vs 0.35%; mean difference, 0.6, 95% CI, 0.00 to 2.42),<sup>25</sup> higher risk of perioperative complications (OR 1.96; 95% CI, 1.29-2.98),<sup>28</sup> and longer hospital stays (8.4 vs 5.9 days; *P*=0.001) compared to the overall population receiving bariatric surgery.<sup>28</sup> Likewise, a recent decision analysis demonstrated that, compared with the increase in life expectancy seen following bariatric surgery for most patients with BMI > 35 kg/m<sup>2</sup> and diabetes, the gain decreases as BMI increases and ultimately results in a net loss at BMI > 62 kg/m<sup>2</sup>.<sup>29</sup>

The mechanisms for the less-than-optimal bariatric surgery outcomes in the super obese are not well-studied, but likely include that they more frequently have obesity-related, life-threatening comorbid health conditions and present greater technical and resource challenges to the surgical team and the health care system in general. For example, in one cohort of 856 Veterans, the super obese group was more likely to have hypertension, congestive heart failure, chronic obstructive pulmonary disease, an open wound or infection, and a higher American Society of Anesthesiologists (ASA) class.<sup>30</sup> In terms of resource challenges, super obese patients may exceed limits on standard equipment, and specialized measuring, lifting, imaging, operating tools, and wheelchairs may be needed.<sup>31</sup> A primary surgical challenge is that, because of the increased intra-abdominal pressure and reduced visualization, greater force is required for manipulating instruments, which can increase operative time and surgeon fatigue.<sup>4</sup> One small study from the Dallas VA Medical Center suggested that substantial preoperative weight loss requirements, such as through a supervised inpatient low-calorie liquid diet program, may improve morbidity and mortality in superobese patients undergoing bariatric surgery.<sup>32</sup>

Clearly, more research is needed to better understand the reasons for higher morbidity and mortality in the super obese and to identify specific clinical predictors that would inform optimization of bariatric surgery in this high-risk population.<sup>30</sup> The importance of resolving questions in the super obese is increasing, as this obesity subgroup has seen the highest growth in prevalence between 1986 and 2010 compared with less-extreme BMI subgroups and is



associated with higher health care costs. Based on data from the Behavioral Risk Factor Surveillance System, since 1986, prevalence increases were 120% for BMI > 50 kg/m<sup>2</sup>, 100% for BMI > 40 kg/m<sup>2</sup>, and 42% for BMI > 30 kg/m<sup>2</sup>.<sup>33,34</sup>

Although the more extreme BMI categories still account for a smaller proportion of obese adults (0.55% for BMI > 50 kg/m<sup>2</sup>, 3.68% for BMI > 40 kg/m<sup>2</sup>, vs 27.2% for BMI > 30 kg/m<sup>2</sup>), their associated health care costs are disproportionately higher. Data from the Health and Retirement Study estimated that, compared to normal weight, health care costs increased by 21% and 27% for men and women, respectively, for BMI ≤ 30 kg/m<sup>2</sup> to < 35 kg/m<sup>2</sup>, by 58% and 43% for BMI ≤ 35 kg/m<sup>2</sup> to < 40 kg/m<sup>2</sup> and by 105% and 111% for BMI ≥ 40 kg/m<sup>2</sup>.<sup>35</sup> Similarly, an analysis of 16,262 adults from the 2000 Medical Expenditure Panel Survey found that percent of per capita healthcare expenditures were 9.0% for BMI 24-29.9 kg/m<sup>2</sup>, 18.8% for BMI 30-34.9 kg/m<sup>2</sup>, 31.0% for BMI 35-39.9 kg/m<sup>2</sup>, and 44.9% for BMI ≥ 40 kg/m<sup>2</sup>.<sup>36</sup> Additionally, compared to the benefits of bariatric surgery over the best medical management in the global population of BMI > 35 kg/m<sup>2</sup> (1.9 extra QALYs and 13,244€savings), cost-effectiveness analysis has shown lower benefits for super obese patients (1.23 extra QALYs, 10,257€savings).<sup>37</sup> Accordingly, research needs identified by the May 2013 National Institutes of Health Symposium on the long-term outcomes of bariatric surgery included development of a better understanding of the variability in bariatric surgery outcomes due to extent of preoperative obesity.<sup>38,39</sup>

## SCOPE

The objective of this evidence brief is to synthesize the literature on the comparative effectiveness of surgical and nonsurgical treatments for obesity and the barriers to obtaining bariatric surgery among super obese adults. The ESP Coordinating Center investigators and representatives of the SOTA committee worked together to identify the population, comparator, outcome, timing, setting, and study design characteristics of interest. The SOTA committee approved the following key questions and eligibility criteria to guide this review:

## KEY QUESTIONS

Key Question 1: What are the patient, provider, or system-level barriers to obtaining bariatric surgery in super obese adults?

Key Question 2: In super obese adults, what is the comparative effectiveness of bariatric surgery versus nonsurgical treatments (*eg*, dietary changes, lifestyle interventions, medications, usual care)?

Key Question 3: In super obese adults, what is the comparative effectiveness of different bariatric surgery treatments?

## ELIGIBILITY CRITERIA

The ESP included studies that met the following criteria:

- ***P*opulation:** Our primary focus is adult patients with BMI > 50 kg/m<sup>2</sup>. To maximize applicability, we only included studies that exclusively focused on the super obese or that

included a subgroup analysis of super obese. We did not include studies that had mean or median BMI > 50 kg/m<sup>2</sup>, but that encompassed a broader range of patients overall.

- **Intervention:** Bariatric surgery interventions.
- **Comparator:** Nonsurgical weight loss interventions (including lifestyle, dietary changes, medications) and different bariatric surgical procedures, usual care.
- **Outcomes:** Primary outcomes of interest include long-term (defined as ≥5 years, based on recent NIH Funding Opportunity Announcement # PAR-14-262 for long-term outcomes of bariatric surgery using large datasets)<sup>40</sup> weight loss (% excess weight lost, BMI change), mortality, remission/resolution of physical and mental health conditions, complications, and cost. Secondary outcomes include barriers to obtaining bariatric surgery (patient attitudes, provider attitudes, access, etc) and short-term (<5 years) weight loss (% excess weight lost, BMI change), mortality, remission/resolution of physical and mental health conditions, complications, and cost.
- **Timing:** No restrictions.
- **Setting:** Within and outside VA. We will prioritize VA studies, but will look outside of the VA to fill gaps in VA evidence, including international studies.
- **Study design:** Using a Best Evidence approach, we will prioritize evidence from systematic reviews and multisite comparative studies that adequately controlled for potential patient-, provider-, and system-level confounding factors. Inferior study designs (eg, single-site, inadequate control for confounding, noncomparative) will only be accepted to fill gaps in higher-level evidence.

## METHODS

To identify articles relevant to the key questions, our research librarian searched MEDLINE®, the Cochrane Central Registry of Controlled Trials, and PsychINFO, using terms for *bariatric surgery* and *obesity* (see Supplemental Materials for complete search strategies). For searches for studies of barriers to bariatric surgery, we used additional terms for *barriers*. Due to the large volume of well-conducted systematic reviews, we relied on reference lists for studies published through 2012 and conducted new searches for studies published from 2013 onward. Additional citations were identified from hand-searching reference lists and consultation with content experts. We limited the search to published and indexed articles involving human subjects available in the English language. Study selection was based on the eligibility criteria described above. Titles and abstracts were reviewed by one investigator. Full-text articles were reviewed by one investigator and checked by another. All disagreements were resolved by consensus.

We used predefined criteria to rate the internal validity of all longitudinal studies. We used Cochrane's Risk of Bias Tool to rate the internal validity of controlled trials.<sup>41</sup> We rated the internal validity of observational studies based on the AHRQ Methods Guide for Comparative Effectiveness Reviews.<sup>42</sup> We abstracted data from all included studies and results for each included outcome. All data abstraction and internal validity ratings were first completed by one reviewer and then checked by another. All disagreements were resolved by consensus.

We graded the strength of the evidence based on the AHRQ Methods Guide for Comparative Effectiveness Reviews.<sup>43</sup> This approach incorporates 4 key domains: risk of bias (includes study design and aggregate quality), consistency, directness, and precision of the evidence. It also considers other optional domains that may be relevant for some scenarios, such as a dose-response association, plausible confounding that would decrease the observed effect, strength of association (magnitude of effect), and publication bias. Strength of evidence is graded for each key outcome measure and ratings range from high to insufficient, reflecting our confidence that the evidence reflects the true effect.

Among the wide variety of weight loss metrics reported, we preferred percent baseline weight loss per the 2013 analysis by Hatoum and Kaplan, which showed it was least influenced by variation in preoperative BMI.<sup>44</sup> When percent baseline weight was not reported, we evaluated proportion excess body weight loss (%EWL). As Hatoum and Kaplan found that both %EWL and change in BMI were similarly sensitive to preoperative BMI ( $r=-0.52$  and  $r=0.56$ , respectively), we selected %EWL as the secondary weight loss metric as it was most commonly reported and allowed for more comparison across studies. Where studies were appropriately homogenous, we synthesized outcome data quantitatively using StatsDirect statistical software (StatsDirect Ltd. 2013, Altrincham, UK) to conduct random-effects meta-analysis to estimate pooled effects. We assessed heterogeneity using the Q statistic and the  $I^2$  statistic. Where meta-analysis was not suitable due to limited data or heterogeneity, we synthesized the evidence qualitatively by grouping studies by similarity of bariatric surgery comparison.

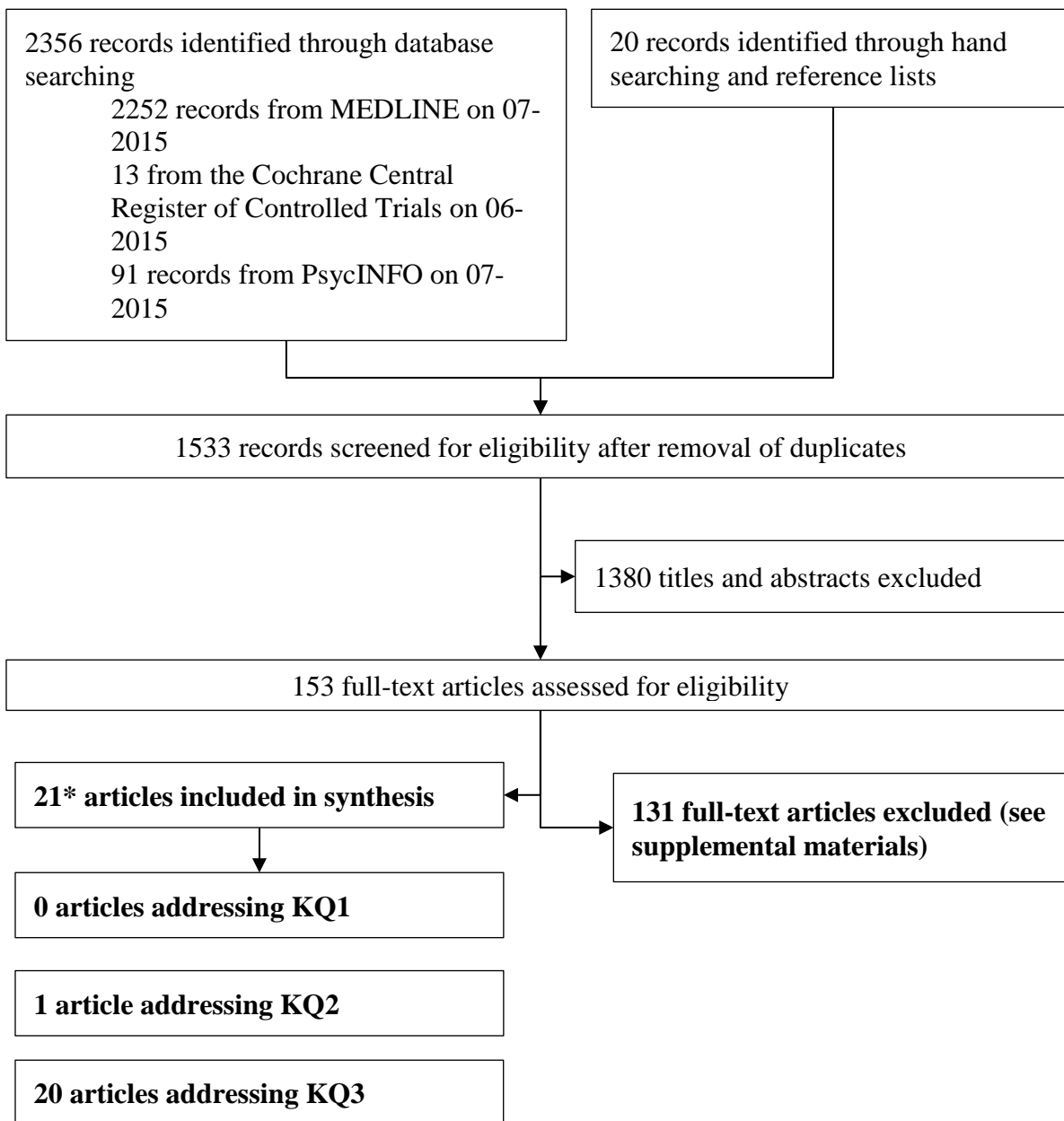
The complete description of our full methods can be found on the PROSPERO international prospective register of systematic reviews (<http://www.crd.york.ac.uk/PROSPERO/>; registration number CRD42015025348).

## RESULTS

### LITERATURE FLOW

We screened 1531 unique records and included 22 articles in this evidence brief (Figure 1): 2 systematic reviews and 20 primary studies. Detailed reasons for study exclusion are provided in the supplemental materials.

**Figure 1: Literature flow chart**



\*1 systematic review included but not synthesized

Among the 2 systematic reviews, one focused on the comparison of duodenal switch and Roux-en-Y gastric bypass<sup>45</sup> and the other was a Cochrane review that broadly focused on surgery for weight loss in adults, with a planned subgroup analysis in the super obese.<sup>14</sup> However, data was too limited for subgroup analyses in the Cochrane review and, therefore, there were no findings to report here. Searches of clinicaltrials.gov and the VA HSR&D website for published, unpublished, and ongoing studies resulted in no additional studies with an explicit focus on the super obese. One potentially relevant clinical trial (NCT01352403) was identified comparing gastric bypass to behavioral intervention, but has a relatively small planned sample size and does not address the outcomes of greatest interest.

For Key Question 1, we did not identify any studies that examined barriers to obtaining bariatric surgery among super obese patients. For Key Question 2, we identified one primary study that compared bariatric surgery to nonsurgical treatment in a VA population and included a subgroup analysis among super obese patients.<sup>1</sup> For Key Question 3, we identified 19 primary studies<sup>2-4,7-9,46-56</sup> and one systematic review<sup>45</sup> which compared various types of bariatric surgery among super obese patients. Table 2 describes the study design and follow-up period for the primary studies included under each surgical comparison.

We rated the systematic review as fair quality.<sup>45</sup> We rated 8 observational studies<sup>5,8,46,48,49,51,52,56</sup> as high risk of bias for not accounting for potential confounders or co-interventions and having high attrition (40-60%). We rated 8 observational studies<sup>1,3,4,6,7,9,47,50</sup> as medium risk of bias. We rated 4 RCTs<sup>2,53-55</sup> from the same trial as low risk of bias. Attrition was low ( $\leq 20\%$ ) for all RCTs<sup>2,53-55</sup> and 5 observational studies<sup>3,8,46,47,50</sup>. Four studies had 20-40% attrition<sup>4,5,7,56</sup> and 4 studies<sup>6,49,51,52</sup> had  $\geq 40\%$  attrition. Two studies<sup>9,48</sup> had no clear data on follow-up. One study<sup>1</sup> had low attrition for short-term outcomes, but moderate attrition for long-term outcomes. The supplemental materials provide complete details on our data abstraction, risk of bias assessments, and strength of evidence ratings.

Overall, this body of evidence likely has low applicability to the Veteran population as the studies included patients who were primarily females in their mid-thirties to forties and rarely reported information about comorbidities. The only exception was the VA study that compared surgery to usual care that we included for Key Question 2.<sup>1</sup>

**Table 2. Studies addressing Key Question 3**

Author Year	Study design	Follow-Up
<b><i>Gastric bypass vs duodenal switch</i></b>		
Risstad 2015 <sup>2</sup>	Randomized controlled trial	5 year
Sovik 2010 <sup>55</sup>	Randomized controlled trial	1 year
Sovik 2011 <sup>53</sup>	Randomized controlled trial	2 year
Sovik 2013 <sup>54</sup>	Randomized controlled trial	2 year
Laurenius 2010 <sup>47</sup>	Observational study	31 months
Nelson, 2012 <sup>49</sup>	Observational study	2 year
O'Rourke 2006 <sup>50</sup>	Observational study	Perioperative
Parikh 2005 <sup>51</sup>	Observational study	1-4 year
Prachand 2006 <sup>52</sup>	Observational study	1-3 year
Topart 2013 <sup>56</sup>	Observational study	3 year

Author Year	Study design	Follow-Up
<b><i>Gastric bypass vs gastric banding</i></b>		
Bowne 2006 <sup>3</sup>	Observational study	1-40 months
Daigle 2015 <sup>5</sup>	Observational study	37 months
Giordano 2015 <sup>46</sup>	Observational study	1 year
Mognol 2005 <sup>48</sup>	Observational study	2 year
Parikh 2005 <sup>51</sup>	Observational study	1-4 year
<b><i>Gastric bypass vs sleeve gastrectomy</i></b>		
Daigle 2015 <sup>5</sup>	Observational study	37 months
Serrano 2015 <sup>6</sup>	Observational study	1 year
Zerrweck 2014 <sup>4</sup>	Observational study	1 year
<b><i>Surgical method comparisons</i></b>		
Heneghan 2014 <sup>7</sup>	Observational study	2 year
Roland 2011 <sup>9</sup>	Observational study	2 year
Sekhar 2007 <sup>8</sup>	Observational study	2 year

## KEY QUESTION 1: What are the barriers to obtaining bariatric surgery in super obese adults?

We found no studies evaluating barriers to obtaining bariatric surgery specifically in super obese adults. A July 2015 systematic review of the general obesity population identified male sex, patient concerns about surgical complications or death, and concern about the financial burden of bariatric surgery as the most frequent barriers to receipt of bariatric surgery.<sup>57</sup> Other less-frequently identified barriers that appear potentially relevant to the VA super obese population include older age, physically incapable of commuting, concern about financial barrier of commuting to appointments, lack of choice regarding surgeon, type of operation, and/or hospital, prefer to lose weight on their own, nonadherence to preoperative program, and inability to stop substance use to meet preoperative requirements. As most participants in the studies were female and mean BMI was not reported, it is unclear how applicable these findings are to super obese Veterans.

## KEY QUESTION 2: In super obese adults, what is the comparative effectiveness of bariatric surgery versus nonsurgical treatments (eg, dietary changes, lifestyle interventions, medications)?

### Summary

- Compared to usual care, a post-hoc subgroup analysis of super obese Veterans provides low-strength evidence that bariatric surgery increased mortality within the first year (4.93% vs 2.77%; HR 1.57; 95% CI, 1.08-2.76; N=2860), then reduced mortality from 1 to 5 years (5.48% vs 11.4%; HR 0.46; 95% CI, 0.33-0.64; N=2723) and from 5 to 14 years (9.5% vs 17.5%; HR 0.45; 95% CI, 0.34-0.60; N=2054).

## Detailed Analysis

No studies have evaluated the comparative effectiveness of bariatric surgery versus any specific active nonsurgical treatment in super obese adults. One retrospective study used administrative data to compare long-term survival among a group of Veterans who underwent bariatric surgery between 2000-2011 to a poorly characterized group of Veterans who were matched for sex, diabetes diagnosis, race, VA region, BMI, and age.<sup>1</sup> The control group was described as representing usual care, but there was no information about what care was provided or their eligibility for bariatric surgery. This study conducted post-hoc analyses to determine if the relationship between surgery and mortality may differ in the super obese.<sup>1</sup>

Overall, 74% of the Veterans in this study were men, their mean age was 52 years, 81% were white, 55% had diabetes, 19% had coronary artery disease, 35% had depression, 17% had posttraumatic stress disorder (PTSD), 6% were abusing alcohol, and 4% were abusing other substances. The surgical procedure types were primarily open (53%) or laparoscopic (21%) Roux-en-Y gastric bypass. Rates of diet, exercise, lifestyle interventions, or weight loss medication use were not reported for either group. However, authors reported that participation in the VA's national MOVE!® weight management program was mandatory for bariatric surgery candidates starting in 2006 and it was likely that many control group patients also participated, as it is VA policy to refer all severely obese patients to MOVE!®.<sup>58</sup>

Compared to usual care, in the study population overall (mean BMI =47 kg/m<sup>2</sup>), the study provided moderate-strength evidence of no significant association between bariatric surgery and mortality at one year (HR 1.28; 95% CI, 0.98-1.68), but that surgery reduced mortality after one to 5 years (HR 0.45; 95% CI, 0.36-0.56) and after 5 to 14 years of follow-up (HR 0.47; 95% CI, 0.39-0.58). Although the post-hoc analyses provided low-strength evidence that the relationship between surgery and mortality was not significantly different in the super obese subgroup (Table 3), mortality rates were consistently numerically higher in the super obese groups and the trend toward increased risk of mortality in the first year of follow-up seen overall (HR 1.28; 95% CI, 0.98-1.68) reached statistical significance in the super obese subgroup (HR1.57; 95% CI 1.08-2.76).

Although matching for some known confounders was done well, the 2 main methodological limitations of the study overall were (1) there was no information about the care provided to the controls, and (2) information from administrative data about many key covariates was either unavailable or missing, including severity of comorbid conditions and smoking. We can't rule out the possibility that the greater mortality risk factors characteristic of surgical ineligibility were overrepresented in the nonsurgery group. Additionally, this study does not fully address the balance of benefits and harms of surgery as it did not evaluate other outcomes of great interest, including comorbid disease remission, complications, and quality of life. Finally, this study did not address whether their findings on the differential effectiveness of surgery according to baseline patient risk factors (*ie*, age, diabetes, period of surgery) for the overall study population apply to the super obese subgroup.

**Table 3. Post-hoc analyses of hazard ratios for the comparison of mortality between bariatric surgery and usual care for subgroups of super obese (BMI > 50 kg/m<sup>2</sup>) and non-super obese (BMI ≤ 50 kg/m<sup>2</sup>)**

Follow-up Period	Mortality rate for surgery vs usual care Adjusted <sup>a</sup> Hazard Ratio (95% confidence interval) Sample size	
	Super obese (BMI > 50 kg/m <sup>2</sup> )	Non-super obese (BMI ≤ 50 kg/m <sup>2</sup> )
Baseline to 1 year	4.93% vs 2.77% 1.57 (1.08-2.76) N=2860	1.4% vs 1.3% 1.13 (0.76-1.68) N=7102
> 1 year to 5 years	5.48% vs 11.4% 0.46 (0.33-0.64) N=2723	2.8% vs 6.1% 0.47 (0.35-0.62) N=6982
> 5 years to 14 years	9.5% vs 17.5% 0.45 (0.34-0.60) N=2054	5.7% vs 10.6% 0.54 (0.41-0.69) N=4227

<sup>a</sup> Covariates included in adjusted analysis were age, body mass index (continuous), Diagnostic Cost Group score, marital status, free Veterans Affairs (VA) care due to disability, free VA care due to low income, and baseline comorbidities not included in sequential stratification match (hypertension, dyslipidemia, arthritis, depression, coronary artery disease, gastrointestinal reflux disease, fatty liver disease, asthma, posttraumatic stress disorder, alcohol abuse, substance abuse, schizophrenia).

### KEY QUESTION 3: In super obese adults, what is the comparative effectiveness of different bariatric surgery treatments?

#### Laparoscopic Roux-en-Y Gastric Bypass (LRYGB) versus Duodenal Switch (DS)

##### Summary

- Compared to gastric bypass, there is low-strength evidence that duodenal switch achieves better weight control (% patients with BMI > 40 kg/m<sup>2</sup>: DS=14% vs GB=55.3%,  $P=0.001$ ), has comparable diabetes remission (100% vs 80%;  $P=0.45$ ) and mortality (3% vs 0%;  $P=0.48$ ) after 5 years, but higher risk of hospital admissions (59% vs 29%;  $P=0.02$ ) and surgeries related to the initial procedure (45% vs 10%;  $P=0.002$ ). Short-term evidence was generally insufficient for supporting conclusions about the comparative effectiveness of gastric bypass and duodenal switch.

##### Detailed analysis

The comparison of duodenal switch and Roux-en-Y gastric bypass in adults with BMI > 50 kg/m<sup>2</sup> has been widely studied in 6 retrospective observational studies<sup>47,49-52,56</sup> and one randomized controlled trial (reported in 4 publications).<sup>2,53-55</sup> However, their findings potentially have low applicability to Veterans, as no study was conducted with Veterans and patients were primarily females in their mid-thirties to forties. Also, although rarely reported, relatively few participants had type 2 diabetes (18% to 35%).<sup>47,55,56</sup> No study reported mental health comorbidities.

The randomized trial was small (N=55) and its risk of bias was low.<sup>55</sup> The risk of bias was higher in the retrospective studies because their designs and analyses did not account for important confounding and modifying variables and some had very low follow-up. We identified a previous



systematic review that focused on the comparison of duodenal switch and Roux-en-Y gastric bypass for any BMI.<sup>45</sup> We relied on its data abstraction and findings from its meta-analyses that are applicable to the subset of studies in patients with BMI > 50 kg/m<sup>2</sup>.

*Long-term outcomes (≥ 5 years)*

The only study with long-term outcomes was a Norwegian randomized trial with 5-year follow-up in 55 participants that found greater weight loss with duodenal switch, but that came at a price of more complications (Table 4).<sup>2</sup> Diabetes remission and mortality were comparable for duodenal switch and gastric bypass. Although it had a moderate risk of bias, it provided only low-strength evidence because it was a single, small study.

*Short-term outcomes (< 5 years)*

Evidence from short-term studies was consistent with the long-term trial in finding greater weight loss with duodenal switch and no differences in diabetes remission, but increased risk of complications (Table 4). However, the largest study of 26,510 super obese patients from the Bariatric Outcomes Longitudinal Database (BOLD) found that duodenal switch was associated with a higher risk of mortality, leaks, infection, and pneumonia (Table 4). However, as BOLD did not use any methods to account for important confounding, such as surgeon skill or comorbidities, the poorer outcomes in the duodenal switch group may also be partially due to their worse baseline rates of congestive heart failure (CHF class 1=2.3% vs 1.4%, 2=1.4% vs 0.6%, 3=0.5% vs 0.3% and 4=0 vs 0.1, overall=4.2% vs 2.4%; *P*<0.001), hypertension (63.4% vs 60.2%; *P*=0.01) and obstructive sleep apnea (60.5% vs 47.8%; *P*<0.001) than in the gastric bypass group (Table 4).<sup>49</sup> Other much smaller retrospective studies found greater weight loss with duodenal switch, no differences in diabetes remission or mortality, but increased risk of leaks and small bowel obstruction. But, those small studies provided insufficient evidence to draw conclusions about those outcomes because the studies lacked information about many key covariates and did not use any methods for accounting for important confounding, such as matching or multivariable regression analyses.

**Table 4. Outcomes in studies that compared duodenal switch versus gastric bypass in the super obese**

Outcomes	Long-term study (> 5 years)	Short-term studies (≤ 5 years)	
	Low-strength evidence on 5 years of follow-up from RCT of 55 participants <sup>2</sup>	Largest retrospective study, Bariatric Outcomes Longitudinal Database (BOLD) <sup>49</sup> N=26,510 in super obese subgroup; mean follow-up of 9 months	Various small retrospective studies with ≤ 3 years follow-up
Weight loss	% patients with BMI > 40 kg/m <sup>2</sup> : DS=14% vs GB=55.3%, <i>P</i> =0.001	% of patients that FAILED to lose ≥ 50% of excess weight at 2 years: 6% vs 20%	Difference in BMI loss: pooled weighted mean difference=8.12 (95% CI, 5.89, 10.34) <sup>47,56</sup>
Diabetes remission	100% vs 80%; <i>P</i> =0.45	NR	87% vs 92%; <i>P</i> =0.69; N=28 <sup>56</sup>
Mortality	3% vs 0%; <i>P</i> =0.48	1.8% vs 0.4%; <i>P</i> =0.001	0.7% vs 0%; OR 3.14 (95% CI, 0.32, 30.42);

Outcomes	Long-term study (> 5 years)	Short-term studies (≤ 5 years)	
	Low-strength evidence on 5 years of follow-up from RCT of 55 participants <sup>2</sup>	Largest retrospective study, Bariatric Outcomes Longitudinal Database (BOLD) <sup>49</sup> N=26,510 in super obese subgroup; mean follow-up of 9 months	Various small retrospective studies with ≤ 3 years follow-up N=519 <sup>47,52,56</sup>
Complications	Patients with surgeries related to the initial procedure: 45% vs 10%; <i>P</i> =0.002	Leak: 2.4% vs 0.9%; <i>P</i> <0.001 Infection: 5.2% vs 2.3%; <i>P</i> <0.001	Leak: 7.3% vs 2.2%; OR 3.41 (95% CI, 1.45, 8.02); N=632 <sup>50,56</sup>
	Patients with hospital admissions: 59% vs 29%; <i>P</i> =0.02	Pneumonia: 1.3% vs 0.4%; <i>P</i> =0.003	Small bowel obstruction: 7.7% vs 3.8%; <i>P</i> =0.67; N=39 <sup>47</sup>

## Laparoscopic Roux-en-Y Gastric Bypass (LRYGB) versus Laparoscopic Adjustable Gastric Banding (LAGB)

### Summary

- A retrospective cohort study comparing 106 super obese patients provides low-strength evidence that LRYGB results in greater %EWL (52% vs 31%, *p*<0.001) and fewer long-term (≥30 day) complications (28% vs 78%, *p*<0.05), and no difference in mortality or early (<30 day) complications compared with LAGB.

### Detailed analysis

Among 5 small, single-site studies that compared outcomes of LRYGB and LAGB,<sup>46,48,51,3,5</sup> the strongest evidence comes from a retrospective cohort of a consecutive series of 106 super obese patients who underwent surgery performed by a single surgeon between February 2001 and June 2004 at a 490-bed community teaching hospital in Brooklyn.<sup>3</sup> Surgical approach was determined based on patient and surgeon preference. Patient and clinical information was obtained from a prospectively maintained hospital database, medical record review, surgical reports, and patient interviews. Pre-operatively, patients were similar in age, sex, BMI, and presence of comorbidities, except for dyslipidemia, which was more common among LRYGB patients. The mean pre-operative BMI was 56.7 kg/m<sup>2</sup> for LRYGB patients and 55.4 kg/m<sup>2</sup> for LAGB patients. The median follow-up was 16.2 months (13.0 months LRYGB and 17.7 months LAGB).

This study provides low-strength evidence that LRYGB results in increased %EWL (52% vs 31%, *p*<0.001) at 16 months compared with LAGB among super obese patients. Additionally, there is low-strength evidence that LRYGB results in lower long-term (≥30 day) complications (28% vs 78%, *p*<0.05) with no difference in early (<30 day) complications (17% vs 18%, *p*=0.33) compared with LAGB. No deaths were reported in either surgical group. Although disease remission was not reported, LRYGB patients had a lower prevalence of type 2 diabetes (0% vs 11%, *p*=0.05) and sleep apnea (8% vs 31%, *p*=0.01) at follow-up. The main limitation of

this study is the lack of data on potentially important confounders, including smoking, and co-interventions such as diet and exercise.

Four additional studies compared LRYGB and LAGB among super obese patients.<sup>46,48,51,5</sup> One focused on elderly patients ( $\geq 65$  years).<sup>5</sup> These studies provided even fewer data than the Brooklyn cohort on important confounders, such as lacking data on hypertension and type 2 diabetes. Similar to the Brooklyn cohort,<sup>3</sup> there was higher %EWL and lower long-term complications among LRYGB patients compared with LAGB patients, and no difference in mortality between the surgeries. Unlike the Brooklyn cohort,<sup>3</sup> these studies reported higher early complications among LRYGB patients. However, the greater number of complications for the LRYGB patients may have been due to poorer prognosis at baseline in 2 of the studies, including a higher proportion with comorbidity<sup>46</sup> and more males with higher BMI.<sup>48</sup> Differences in the classification and reporting of complications may also have contributed to the differing results in early complication. Only one of the 4 studies<sup>46</sup> reported the classification method for complications and 2 studies<sup>48,51</sup> reported only major complications. However, the true reason for this variation is unclear.

## **Laparoscopic Roux-en-Y Gastric Bypass (LRYGB) versus Laparoscopic Sleeve Gastrectomy (LSG)**

### *Summary*

- In super obese patients, the best evidence comes from one small retrospective cohort study which provides low-strength evidence that LRYGB results in greater %EWL (63.9% vs 43.9% at 12 months,  $p < 0.05$ ) with no difference in mortality or early (<30 day) complications compared with LSG.
- Two additional studies in the super obese elderly and in the super-super obese, provide insufficient evidence to draw conclusions due to their high risk of bias.

### *Detailed analysis*

Three retrospective cohorts compared outcomes of LRYGB and LSG.<sup>4-6</sup> Risk of bias was moderate in one study<sup>4,6</sup> and high in the other two.<sup>5,56</sup> The best evidence comes from the study with moderate risk of bias, in which 77 consecutive super obese patients (BMI of 50-59.9 kg/m<sup>2</sup>) underwent either LRYGB or LSG between March 2010 and April 2012 at a single institution in Mexico. Patients with a pre-operative BMI  $> 60$  kg/m<sup>2</sup> underwent a different procedure and were not included in this study. The 2 surgical groups were comparable in age, BMI, and presence of comorbidities at baseline. However, the LRYGB group had more females (96% vs 55%,  $p < 0.001$ ) and lower height (1.6m vs 1.66m,  $p = 0.004$ ) and weight (135.9kg vs 150 kg,  $p < 0.001$ ) at baseline. The mean pre-operative BMI was 52.7 kg/m<sup>2</sup> among LRYGB patients and 53.9 kg/m<sup>2</sup> among LSG patients. In this study of super obese, there is low-strength evidence that LRYGB results in greater %EWL at 6 months (51.6% vs 40%,  $p < 0.05$ ), 9 months (56.5% vs 45.1%,  $p < 0.05$ ), and 12 months (63.9% vs 43.9%,  $p < 0.05$ ) compared with LSG. More early (<30 day) complications were reported with LRYGB (9% vs 22%,  $p = 0.217$ ), but this difference did not reach statistical significance, likely due to the small sample size. No deaths were reported in either surgical group. The main limitations of this study are lack of data or control for important potential confounders, including smoking and potential co-interventions such as diet and

exercise. Additionally, minimal information was reported on methods for data collection and outcome assessment.

Among the 2 studies with high risk of bias, one focused on super-super obesity.<sup>56</sup> In this study, 135 patients (BMI > 60 kg/m<sup>2</sup>) underwent either LRYGB or LSG between January 2008 and December 2013 at a single institution in New York. The 2 surgical groups were comparable in age, sex, BMI, ethnicity, and presence of comorbidities at baseline. The mean pre-operative BMI was 66.3 kg/m<sup>2</sup> among LRYGB patients and 68.4 kg/m<sup>2</sup> among LSG patients. This study provides low-strength evidence that there is no difference in the proportion of patients achieving %EWL success (> 30% EWL) with LRYGB or LSG at 3 months (28.95% vs 25%), 6 months (72.22% vs 59.09%), or 12 months (94.59% vs 100%). One death was reported in the LRYGB group. The main limitations of this study were very high levels of missing data, which reached 76% at one year, and lack of data for important potential confounders, including smoking, and potential co-interventions such as diet and exercise.

The second study with high risk of bias evaluated short-term outcomes in a very small cohort of 30 mostly female elderly super obese patients and found that, after a median of 37 months of follow-up, the most %EWL was achieved after LRYGB, followed by LSG, and LAGB (54.1% vs 48.3% vs 26.2%).<sup>5</sup> But this evidence was insufficient to support conclusions because it was a single small retrospective study that had important methodological limitations, including lack of data on baseline characteristics between surgical groups at baseline and high loss to follow of 53.3%.

## **Banded versus Non-banded Laparoscopic Gastric Bypass**

### *Summary*

- A retrospective cohort comparing 268 super and morbidly obese patients who underwent banded or non-banded laparoscopic gastric bypass between 2007 and 2010 provides low-strength evidence that the banded procedure led to greater 2-year %EWL (57.5% vs 47.6%, p=0.003) among super obese patients compared with the standard non-banded procedure.

### *Detailed analysis*

A single retrospective cohort compared banded versus non-banded laparoscopic gastric bypass in a total of 268 who underwent these procedures between January 2007 and July 2010 at a single institution in Ohio.<sup>7</sup> Non-banded patients were matched to banded patients by preoperative BMI, age, and gender. Analyses were performed in a subgroup of 189 super obese patients. At baseline overall, patients were similar in gender, age, preoperative BMI, and the presence of comorbidities, except dyslipidemia, which was more common among patients receiving the banded procedure (63% vs 46%, p=0.003). No information was provided on the characteristics of the super obese subgroup.

This study provides low-strength evidence that among the super obese subgroup, banded laparoscopic gastric bypass results in increased %EWL at 2 years (57.5% vs 47.6%, p=0.003) compared with the non-banded procedure. Morbidity and mortality outcomes were not reported for the super obese subgroup. For the overall study population, there was no difference in mortality (0.7% vs 0.7%) or in early (19.4% vs 19.4%) or late (10.4% vs 13.4%) complications

with banded surgery. The main limitations of this study are the lack of control for potential confounders, including smoking, and the lack of data on potential co-interventions, such as diet and exercise.

## Laparoscopic versus Open Gastric Bypass

### Summary

- One retrospective non-VA cohort provided low-strength evidence that there is no difference in 2 year %EWL, mortality, or many complications between laparoscopic and open gastric bypass mega obese (BMI > 70 kg/m<sup>2</sup>) patients, but the potential for greater hernia incidence in the open surgery group. Another study provided insufficient evidence to draw conclusions about the comparison of laparoscopic and open procedures in the super obese.

### Detailed analysis

Two retrospective cohort studies compared laparoscopic and open gastric bypass.<sup>8,9</sup> Findings from the 2 studies will be discussed separately, as one focused on a super obese subgroup<sup>8</sup> and the other focused exclusively on a mega obese population (BMI > 70 kg/m<sup>2</sup>).<sup>9</sup> The study of a mega obese sample<sup>9</sup> compared 89 patients undergoing open versus laparoscopic gastric bypass from January 2003 to May 2007 at a single center in Ohio. Patients were similar at baseline in age (42 years), BMI, sex (34% male), and presence of hypertension (63%), non-insulin-dependent diabetes (42%), and other comorbidities. Mean BMI was 80 kg/m<sup>2</sup> in the open surgery group and 77 kg/m<sup>2</sup> in the laparoscopic surgery group. Because it was a single small study, it provided only low-strength evidence that, compared to open surgery, %EWL was greater with laparoscopic surgery at 3 months (22.7% vs 17.5, p=0.016) and 6 months (37.6% vs 30.8%, p=0.037) compared to open surgery, and comparable at one and 2 years (48% and 60% in both groups, respectively). One death was reported in the study period, in the open group (2%). Hernia incidence was greater in the open surgery group (19% vs 3%; P=0.02), but rates of other complications were similar between groups.

In the second study of a morbidly obese sample (BMI ≥ 40 kg/m<sup>2</sup>),<sup>8</sup> a total of 967 patients underwent either open or laparoscopic surgery between January 2001 and July 2005 at Vanderbilt University Medical Center. Mean 2-year % EWL was stratified according to preoperative BMI class (40-50, 51-60 and > 61). In the overall study group, laparoscopic surgery resulted in increased %EWL at one year (66.9% vs 57%, p=0.01) and 2 years (71.3% vs 67.3%, p=0.03) compared to the open surgery. However, among super obese patients, there was no difference in %EWL between the 2 surgical groups at 2 years (62% laparoscopic vs 67% open, BMI 51-60 kg/m<sup>2</sup> and 75% laparoscopic vs 65% open, BMI > 61 kg/m<sup>2</sup> [estimated from Figure 1]) However, this study provides insufficient information to draw conclusions because of the lack of information about the sample size or characteristics of the super obese subgroup. The study had a high risk of selection bias overall without adequate adjustment for confounding. Covariates that were reported suggested a more favorable prognosis in the laparoscopic group, with laparoscopic patients having a lower baseline BMI of (49.1 kg/m<sup>2</sup> vs 58.9 kg/m<sup>2</sup>, p=0.001) and more likely to be female (86% vs 76%, p=0.001), while information on many other important covariates was missing.

## SUMMARY AND DISCUSSION

Table 5 below summarizes the main findings from this review. We found no studies that evaluated barriers to obtaining bariatric surgery in super obese adults. A single VA study provides limited evidence that, compared to usual care, bariatric surgery can increase mortality in the first year, but decrease long-term mortality in super obese Veterans. Although a main advantage of this study is that it directly reflects outcomes that would be expected in the VA system, the care provided to the control group was not well-defined and information about many key covariates was missing.

Non-VA studies that compared different bariatric surgical procedures suggested some differences in weight loss and complications. Laparoscopic gastric bypass generally resulted in greater short-term proportion of excess weight loss (%EWL) than its comparators. The exception was that duodenal switch (DS) led to greater long-term weight loss than gastric bypass, but this came at the expense of more complications, potentially due to its greater technical complexity. However, these findings likely have low applicability to Veterans as patients were primarily females in their mid-thirties to forties and information was missing on diabetes, mental illness, and other important comorbidities.

**Table 5. Summary of Findings: Comparative Effectiveness of Bariatric Surgery versus Non-Surgical Treatment and between Different Bariatric Surgeries in Studies or Subgroup Analyses Exclusively of Super Obese (BMI > 50 kg/m<sup>2</sup>) Patients**

Number and type of studies and sample sizes	Outcomes < 5 years (All low-strength unless otherwise noted)	Outcomes ≥ 5 years (All low-strength unless otherwise noted)
<i>Surgery vs Non-surgery</i>		
1 VA post-hoc subgroup analysis from a retrospective cohort <sup>1</sup> , N=2860	<ul style="list-style-type: none"> <li>€ mortality at 1 year; 4.93% vs 2.77%, aHR 1.57 (95% CI, 1.08-2.76)</li> <li>€ mortality at &gt; 1 year to 5 years; 5.48% vs 11.4%, aHR 0.46 (95% CI, 0.33-0.64)</li> </ul>	<ul style="list-style-type: none"> <li>€ mortality at &gt; 5 years to 14 years; 9.5% vs 17.5%, aHR 0.45 (95 %CI, 0.34-0.60)</li> </ul>
<i>Duodenal Switch (DS) vs Laparoscopic Roux-en-Y Gastric Bypass (LRYGB)</i>		
<ul style="list-style-type: none"> <li>Short-term: 6 non-VA, retrospective cohorts<sup>3,4,47,49-51</sup> N=27,645</li> <li>Long-term: 1 non-VA RCT<sup>2</sup>, N=55</li> </ul>	Insufficient evidence	<ul style="list-style-type: none"> <li>€ weight loss for DS; % patients with BMI &gt; 40 kg/m<sup>2</sup>: DS=14% vs GB=55.3%, P=0.001</li> <li>€ hospital admissions; 59% vs 29%, P=0.02 and surgeries related to the initial procedure for DS; 45% vs 10%, P=0.002 = mortality and diabetes remission</li> </ul>
<i>Laparoscopic Roux-en-Y Gastric Bypass (LRYGB) vs Laparoscopic Adjustable Gastric Banding (LAGB)</i>		
1 non-VA, single center, retrospective cohort <sup>3</sup> , N=106	<ul style="list-style-type: none"> <li>€ %EWL for LRYGB at 16 months; 52% vs 31%, p&lt;0.001</li> <li>= mortality and early complications</li> <li>€ late complications for LRYGB; 28% vs 78%, p&lt;0.05</li> </ul>	No evidence
<i>Laparoscopic Roux-en-Y Gastric Bypass (LRYGB) vs Laparoscopic Sleeve Gastrectomy (LSG)</i>		
Super obese: 2 non-VA, single	Super obese: € %EWL for LRYGB	No evidence

Number and type of studies and sample sizes	Outcomes < 5 years (All low-strength unless otherwise noted)	Outcomes ≥ 5 years (All low-strength unless otherwise noted)
center retrospective cohorts <sup>4,5</sup> N=107 Super-super obese: 1 non-VA single center retrospective cohort, <sup>6</sup> N=135	at 12 months; 63.9% vs 43.9%, p<0.05 = mortality and complications Super-super obese: Insufficient evidence	
<i>Banded vs Non-Banded Laparoscopic Roux-en-Y Gastric Bypass (LRYGB)</i>		
1 non-VA, single center retrospective cohort <sup>7</sup> , N=189	é %EWL for banded LRYGB at 2 years; 57.5% vs 47.6%, p=0.003	No evidence
<i>Laparoscopic vs Open Gastric Bypass</i>		
1 non-VA, subgroup analysis from a single center retrospective cohort <sup>8</sup> , N=unknown	Insufficient evidence	No evidence
In mega obese (BMI > 70 kg/m <sup>2</sup> ): 1 non-VA, single center retrospective cohort <sup>9</sup> , N=89	é %EWL for laparoscopic at 3 (22.7% vs 17.5, p=0.016) and 6 months (37.6% vs 30.8%, p=0.037), but comparable at 1-2 years ê hernia with laparoscopic surgery = mortality and other complications	No evidence

\*All low-strength evidence; aHR = Adjusted Hazard Ratio, LRYGB = Laparoscopic Roux-en-Y Gastric Bypass, DS = Duodenal Switch, LAGB = Laparoscopic Adjustable Gastric Banding, LSG= Laparoscopic Sleeve Gastrectomy, %EWL = % Excess Weight Loss, T2DM = Type 2 Diabetes Mellitus

## LIMITATIONS

An evidence brief differs from a full systematic review in that the scope is narrowly defined and the traditional review methods are streamlined in order to synthesize evidence within a shortened timeframe. Brief or rapid review methodology is still developing and there is not yet consensus on what represents best practice. The 2 main methodological limitations of this evidence brief are its scope and our abbreviated search methods. First, regarding scope, although we focused on the SOTA committee's highest-priority outcomes of weight loss, mortality, obesity-related disease remission, complications, and cost, our time frame did not allow for evaluation of other outcomes that also can have important clinical implications (eg, surgical length, conversion from laparoscopic to open procedure, quality of life, functional capacity, adverse effects of surgery such as gastrointestinal changes, depression, substance abuse, etc). Also, given our abbreviated time frame, to obtain the most precise estimates of outcomes in the super obese, we focused on studies that exclusively included super obese patients or that separated out the super obese subgroup. However, given more time, further assessment of the very large body of existing evidence of broader patient populations of BMI > 35 kg/m<sup>2</sup> could provide additional information about patients with BMI > 50. As many studies that enrolled patients with BMI > 35 kg/m<sup>2</sup> included a subgroup of patients with BMI > 50 kg/m<sup>2</sup>, another option for evaluating the comparative effectiveness of bariatric surgery in the super obese is to use the large body of data from these existing studies to conduct an individual patient data meta-analysis of included patients with BMI > 50 kg/m<sup>2</sup>. Regarding our search methods, although we attempted to use an exhaustive list of search terms, the lack of a standard taxonomy for describing the super obese population in the literature made searching for this topic somewhat difficult. Also, for studies published through 2012, we relied on the reference lists of the large volume of previous well-

conducted systematic reviews and only conducted new searches for studies published in 2013 and onward. For these 2 reasons, our search may have missed some relevant studies.

## GAPS AND FUTURE RESEARCH

Several gaps in the evidence base in studies that separated out the super obese subgroup limited our ability to reach strong conclusions about the comparative effectiveness of bariatric surgery in this subgroup. For each key question, Table 6 below summarizes the gaps and future research recommendations, organized in the PICOTS framework (population, intervention, comparator, outcomes, timing, and setting). As the current evidence is very limited in the super obese, in setting their research agenda, we recommend that the HSR&D SOTA committee prioritize confirmation of the subgroup findings from Arterburn et al about the comparison of bariatric surgery to nonsurgical treatment in the super obese.<sup>1</sup> Answering questions about the long-term comparative effectiveness of surgical and nonsurgical weight loss interventions will help to determine the relevance of questions about choice of surgical approach and barriers to uptake of bariatric surgery. The most practical and applicable way to do this is to use a larger sample from existing VA quality improvement program data. Table 6 summarizes our recommendations about how to best remedy key limitations of previous research.

**Table 6. Gaps in the Evidence Base and Recommendations for Future Research**

Category	Evidence Gap	Recommendations for Future Research
<b>Key Question 1. What are the barriers to obtaining bariatric surgery in super obese adults?</b>		
General	No evidence	To maximize the relevance of new studies to identify barriers to bariatric surgery, the VA may consider waiting for better clarification of the balance of benefits and harms of bariatric surgery for more extreme levels of obesity. By waiting, the VA could better focus the research on barriers in patient subgroups identified as most likely to succeed.
<b>Key Question 2: In super obese adults, what is the comparative effectiveness of bariatric surgery versus nonsurgical treatments (eg, dietary changes, lifestyle interventions, medications)?</b>		
Population	Information about many key covariates was missing: smoking exposure, pre-operative care and requirements, mental health status and care in quaternary systems of care, comorbidity severity, and adherence with post-procedure recommendations. Also, no study evaluated whether differences in important covariates could be used to predict response to bariatric surgery.	Match surgical patients to nonsurgical patients with comparable eligibility for surgery and at least add smoking, mental health status, and comorbidity severity to the list of covariates that Arterburn 2015 adjusted for in multivariate regression analyses.  To help identify predictors of favorable outcomes in super obese patients, evaluate the role of a broader range of key covariates such as those listed as missing.
Comparator	No information about nonsurgical care	As suggested by NIDDKD/NHLBI



Category	Evidence Gap	Recommendations for Future Research
	provided to controls	May 2013 workshop participants, <sup>39</sup> one solution may be to match Veterans from the Surgical Quality Improvement Program database to those from other large VA databases, such as the Corporate Data Warehouse and Outpatient Care File, with documented participation in well-characterized nonsurgical treatments, such as the VA's comprehensive lifestyle intervention, MOVE! <sup>®</sup> <sup>59,60</sup> However, we recognize that matching on MOVE! participation may limit sample size as the program started in 2006.
Outcomes	Literature has not evaluated a complete set of key long-term outcomes, including weight loss, mortality, obesity-related disease remission, complications, and cost.	Evaluate a more complete set of outcomes.
Study Design	No randomized controlled trials (RCTs).	Although RCTs are the ideal, they are likely not feasible. A more practical approach to better characterize the role of bariatric surgery in the super obese may be to use a larger sample from existing VA quality improvement databases. However, as such observational studies are inherently subject to greater risks of bias, they must be carefully designed and executed to address as many threats to internal validity as possible.
<b>Key Question 3: In super obese adults, what is the comparative effectiveness of different bariatric surgery treatments?</b>		
Population	Patients were primarily females in their mid-thirties to forties and were missing information on diabetes, mental illness, and other important comorbidities. Also, these studies had the same covariate limitations as in Key Question 2.	Use data from the VA Surgical Quality Improvement Program database to evaluate the comparative effectiveness of different bariatric surgery approaches using the methods suggested above in Key Question 1 for accounting for and exploring variation based on key covariates.
Outcomes	Literature has not evaluated cost.  Although in 2013 Hatoum and Kaplan recommended adoption of percent of baseline weight loss as the preferred weight loss measure because it was the least influenced by preoperative BMI, we found only one study that used this outcome. <sup>44</sup> Instead, studies used a wide variety of methods, including BMI loss,	Evaluate a more complete set of outcomes in larger samples of patients.  The bariatric surgery field in general would benefit from work toward standardization of outcome definitions. <sup>19,61</sup>

Category	Evidence Gap	Recommendations for Future Research
	<p>weight loss, proportion of excess weight loss, proportion of patients with a BMI over a certain threshold, and proportion of patients that failed to lose 50 percent or more of their excess weight loss, and many studies did not report measures of variance. There is also a lack of standardized definitions for surgical complication outcomes. This heterogeneity makes it difficult to combine and compare findings across studies.</p> <p>Studies were generally inadequately powered to assess mortality and disease remission.</p>	
<p>Timing and setting</p>	<p>For studies comparing different bariatric surgery treatments in the super obese, the majority of the evidence comes from outside of the United States. Differences in health care systems and standards of care from these studies may have low applicability to the VA healthcare system (eg, accreditation, level and type of multidisciplinary care, pre-procedure preparation/post-procedure support).</p> <p>Except for a small study of 55 patients that compared 5-year outcomes between duodenal switch to gastric bypass, studies that compare different bariatric surgeries provided only short-term data.</p>	<p>Use data from the VA Surgical Quality Improvement Program database and evaluate at least 5 years of follow-up.</p>
<b>General</b>		
<p>Outcomes</p>	<p>There are no defined goals for the magnitude of weight loss that is required for a meaningful benefit in longevity and resolution of obesity-related comorbidity. Philosophically, it may be ideal to strive to reduce BMI to a level that would eliminate their eligibility for bariatric surgery.<sup>52</sup> But, as this is more difficult to achieve in super obese patients, it could be clinically useful to document what level of weight loss is really necessary to achieve the greater overall goals.</p>	<p>To help inform how much weight loss is enough, evaluate the correlation between weight loss and longevity and comorbidity resolution.</p>

## CONCLUSIONS

The published literature that separates out the super obese is insufficient for determining the balance of benefits and harms of bariatric surgery in super obese Veterans, primarily due to the lack of long-term data on a complete set of key outcomes and limitations in previous research methods. In setting their research agenda, we recommend that SOTA workgroups prioritize confirmation of subgroup findings from Arterburn et al<sup>1</sup> that, compared to usual care, bariatric surgery can increase mortality in the first year, but decrease long-term mortality in super obese Veterans. Likely the most practical and applicable way to do this is to use a larger sample of existing VA quality improvement program data that matches to a better-characterized nonsurgical control group, evaluates a more complete set of outcomes and adds information on identified key covariates. Another option is to use the large body of data from existing studies with broader populations of patients with BMI > 35 kg/m<sup>2</sup> to conduct an individual patient data meta-analysis of included patients with BMI > 50 kg/m<sup>2</sup>.

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