KQ1. In patients who are obese and who would be eligible for Medicare, what is the comparative effectiveness of interventions that are intended to improve outcomes by reducing obesity?

The outcomes of interest include:
   a. Measures of weight, such as body mass index, weight in kilograms, measures of body composition including skinfold thickness, and waist circumference.
   b. Intermediate outcomes, such as change in intervention adherence, blood pressure, glucose levels, inflammatory markers, and lipid levels.
   c. Obesity-related complications such as; cardiovascular disease, dementia, depression, liver disease, mortality, and musculoskeletal disease.
   d. Patient-reported outcomes such as activities of daily living, pain, physical functioning, health-related quality of life and satisfaction with health care delivery.
   e. Adverse effects of interventions such as; activity-related injury, medication side-effects, nutritional deficiencies (including eating disorders), and procedural complications (including death).

KQ2. In patients who are obese and who would be eligible for Medicare, how well does treatment-induced reduction in BMI predict obesity-related outcomes?

The outcomes of interest include:
   a. Obesity-related complications such as; cardiovascular disease, dementia, depression, liver disease, mortality, and musculoskeletal disease.
Figure 1. Analytic Framework

BMI = Body Mass Index; FDA = United States Food and Drug Administration; Kg = kilograms; KQ = Key Question
Background

Burden of Disease. Obesity is defined as a Body Mass Index (BMI) greater than or equal to 30 kg/m². Obesity prevalence is increasing in the US and worldwide. Increased longevity is also prevalent. By 2030-2035, over 20% of the adult US population will be aged 65 years and older. For older adults (age ≥ 60 years), the prevalence of obesity is about 37% among men and 34% among women based upon recent data from the National Health and Nutrition Examination Survey (NHANES). Morbidity and mortality are increased at a BMI above 30 kg/m² in all age groups, including those over 65 years of age. In older adults above 65, overweight and obesity are associated with new or progressive impairments in activities of daily living (ADLs) and instrumental activities of daily living (IADLs).

Population. The Medicare population includes individuals aged 65 years and older and those with qualifying disabilities of all ages. The disability includes an inability to engage in any substantial gainful activity (SGA) by reason of any medically determinable physical or mental impairment(s) which can be expected to result in death or which has lasted or can be expected to last for a continuous period of not less than 12 months. Our preliminary literature search showed the majority of studies used 60 years of age as cutoff point rather than 65 years. As the physiological and clinical differences between 60 and 65 years of age are minimal, the target populations of the proposed review was set to individuals with BMI greater than 30 kg/m² that are older than 60 years of age or disabled.

Interventions to reduce obesity. The interventions available for obesity include obesity surgery, pharmacologic options, lifestyle interventions, and combination of interventions. Obesity surgery has been approved for those with severe obesity (BMI ≥ 40 kg/m2) or those with BMI at or above 35 with comorbid conditions. More recently, the Food and Drug Administration (FDA) approved the LAPBAND® for those with BMI at or above 30 with a comorbid condition. Obesity surgery is not indicated in those with a reversible cause of obesity, those with serious psychiatric illness, or those who cannot understand the risks and benefits of surgery. We expect to consider several options for obesity surgery, including laparoscopic gastric bypass, gastric banding, vertical sleeve gastrectomy and some new devices (if approved by the FDA) such as intragastric balloons.

The pharmacologic interventions include: orlistat which decreases fat absorption; lorcaserin which is a selective serotonin receptor agonist and potentially associated with valvular heart defects; and phentermine-topiramate combination, benzphetamine, diethylpropion, phentermine, and phenidimetrazine, all appetite suppressants.

The lifestyle interventions are comprised of caloric restriction, physical activity, and behavioral modifications (which could include interventions delivered by application of consumer health informatics). The comprehensive lifestyle approach combines monitoring caloric intake and increasing physical activity with behavior modification. Physical activity also contributes to weight loss, decreases abdominal fat, and improves cardiorespiratory fitness. A recent European guideline recommended that the first steps to obesity reduction are lifestyle interventions. Some of the lifestyle interventions recommended include diets with 500 Kcal energy deficits, adequate intake of protein, vitamin D, and calcium, and multi-component exercise. This type of exercise includes flexibility training, balance training, aerobic exercise, and resistance training. The adherence rate is only 75% among the short-term studies that were evaluated.

Choice of interventions. The choice of specific interventions for the elderly and disabled will depend on the specific context and the benefits and risks of interventions. The interventions we
will evaluate are shown in the PICOTS Table. We will focus on interventions that are primarily designed to reduce weight.

**Need for Evidence Review.** Although numerous guidelines and reviews have been published on the treatment of obesity in general, few consider obesity treatments among individuals older than 65 years of age and individuals with Medicare-qualifying disabilities. A joint position statement from the American Society for Nutrition and the North American Association for the Study of Obesity specifically targets strategies to treat obesity in older persons and states that weight-loss therapy improves physical function, quality of life, and the medical complications associated with obesity in older persons. Weight-loss therapy that minimizes muscle and bone losses is recommended for older persons who are obese and who have functional impairments or medical complications that can benefit from weight loss.

Previous evidence reviews have not explored the full range of medical databases available for identifying clinical studies. They have not provided enough details to evaluate their methodological rigor. They have only examined a limited set of interventions and have not assessed the full range of obesity-related clinical outcomes. None of the previous reviews have evaluated the extent to which reduction in BMI mediates clinical outcomes.

**Relevance to Clinical Decision Making or Policymaking.** It would be beneficial to know which interventions for obesity improve long-term clinical outcomes among the elderly and disabled population. This would allow policy makers to inform relevant guidelines for this population. This topic is of interest to the Centers for Medicare and Medicaid Services (CMS) in making decisions as evidence on various interventions may inform future coverage of interventions for this population. A recent policy decision outlined the specific types of bariatric surgery for which evidence on effectiveness was available that would be covered for the Medicare population.

**Availability of Evidence.** A recent systematic review of interventions on the topic suggested that the medical consequences of obesity in the elderly are alleviated by modest weight loss (5-10 kg) through evidence-based management strategies. The review recommended weight management, modest exercise, and moderate caloric restriction with reduction of polypharmacy, and suggested that the risks of bariatric surgery may outweigh the benefits. However, the review did not address a number of important issues. Several pharmacologic options are available for obesity in the United States including lorcaserin, orlistat and Qysmia (phentermine and topiramate combination). Although they are efficacious among adults, the effectiveness and safety of these options for the people above age 65 are unknown. The effectiveness and safety of obesity surgery, intragastric devices and other applications in the elderly is unknown, because the elderly have largely been excluded from clinical trials. Whether weight loss also exacerbates sarcopenic obesity in the elderly and leads to loss of bone density is unknown.

A recent systematic review reported that behavioral strategies are effective in producing statistically significant weight loss without significant risk to obese older adults. The review identified 10 trials longer than one year for behavioral interventions among the elderly and noted some improvement in clinical outcomes. Only 4 of 10 studies were longer than 2 years. It did not identify any studies of pharmacologic options among the elderly or any trials of bariatric surgery among the elderly. None of the studies was assessed for bias. Only one database was searched to identify relevant evidence. A more comprehensive search may yield more evidence, especially related to surgical and pharmacologic interventions.

**Assessment of Other Ongoing Work.** A search of clinicaltrials.gov yielded 71 studies on the Medicare population (any intervention). A separate search on obesity treatment (any
population) showed 2072 on-going studies. We did not find any studies listed in ClinicalTrials.gov on obesity treatment in the Medicare population.

**Potential Audiences.** This topic is of interest to CMS. It is also of interest to internists, endocrinologists, surgeons, nutritionists, pharmaceutical benefit managers, and other policy makers. A current comprehensive review would be particularly valuable to organizations interested in having clinical practice guidelines on the management of obesity.

**Objectives.** The main aim of this project is to synthesize the evidence on the comparative effectiveness of non-invasive and invasive therapeutic options for obesity in two priority populations covered by Medicare.

**PICOTS (patients, interventions, comparators, outcomes, timing, setting)**

<table>
<thead>
<tr>
<th>P: Population</th>
<th>I: Interventions</th>
<th>C: Comparison(s)</th>
<th>O: Outcomes</th>
</tr>
</thead>
</table>
| • Studies with minimum population age of 60 years or mean/median population age 65 or older will be included | • Surgical procedures including anatomic alteration, FDA-approved device placements, open surgery procedures, as well as laparoscopic and endoscopic procedures | • Comparison to placebo, usual care, or another intervention | • Obesity-related clinical outcomes  
  o Cancer  
  o Cardiovascular disease  
  o Mortality  
  o Dementia  
  o Depression  
  o Diabetes  
  o Liver disease  
  o Musculoskeletal disease  
  o Sleep apnea | • Patient-reported outcomes  
  o Activities of Daily Living  
  o Pain  
  o Physical function measures  
  o Quality of Life  
  o Satisfaction with care |
• **Adverse effects**
  - Activity related injuries, including fracture
  - Adverse events of medications (e.g., diarrhea or leakage)
  - Nutritional deficiencies, including eating disorders
  - Procedural complications including mortality

• **Intermediate outcomes***
  - Adherence
  - Change in blood pressure
  - Glucose levels
  - Inflammatory marker levels
  - Lipid levels

**Timing**
- Only studies published in 1990 or later are eligible
- Studies must report at least one outcome of interest that includes follow-up of participants at least 18 months after the commencement of the intervention.
- Follow-up duration will be considered in the analysis.
  - For obesity-related clinical outcomes, we would like to have at least 18 months of follow-up.
  - For intermediate outcomes, health-related quality of life and adverse effects, additional time points of interest include the first reported time and 3, 6, 12, and 18 months after the commencement of the intervention.

**Settings**
- All settings

* BMI and other measures of weight will also be evaluated

### Preliminary Literature Scan

**Databases Searched.** For this preliminary portion of the literature scan, we searched Medline (PubMed) for articles with titles/abstracts and medical subject (MeSH) headings containing terms relevant to obesity and a variety of treatments. These searches were tailored to identify studies relevant to the Medicare population, including people over age 65 or disabled (See Appendix A for full PubMed search strategy). Future searches will include Embase and The Cochrane Collaboration library.

**Relevant Guidelines.** Based on the above search, we found 53 guidelines and position statements on the over 65 year-old population. Of these, there were 3 relevant guidelines (all by American societies) that addressed weight loss therapy and its impact on physical function, quality of life, co-morbidity, secondary prevention of heart disease, and osteoarthritis.5, 8, 9 None of the guidelines or position statements addressed the disabled population.

**Recent Systematic Reviews and Meta-analyses.** We identified 285 potentially eligible meta-analyses that investigated therapeutic options for obesity in an over 65 year old population (or some other population that included this group). Of these, 11 were potentially applicable and addressed the use of lifestyle interventions or surgical options for treating obesity. An additional 49 meta-analyses were identified that could be applicable to the under 65 age group and medically disabled population. Of these, we did not find any meta-analysis that applied
specifically to this population. We did identify some meta-analyses that included populations that had conditions common amongst the medically disabled. We believe these are not directly applicable.

**Feasibility of New Review.** We did not find any other systematic review or meta-analysis that looked at both domains of the Medicare population (over 65 years old, or under 65 years old and disabled), but we found approximately 640 potentially relevant randomized trials based on the initial search strategy. We reviewed 100 of these potentially relevant randomized trials and found eight that were applicable. We estimate that approximately 50 will be identified that apply to this topic. We anticipate that further searching will also identify a number of non-randomized studies.

**Definition of Terms**

**Medicare population:** The Medicare population includes individuals aged 65 years and older and those with qualifying disabilities of all ages. ¹

**Obesity:** Obesity is defined as a BMI greater than or equal to 30 kg/m². ¹

**Disability:** The law defines disability as the inability to engage in any substantial gainful activity (SGA) by reason of any medically determinable physical or mental impairment(s) which can be expected to result in death or which has lasted or can be expected to last for a continuous period of not less than 12 month. ³

**Lifestyle interventions:** Any intervention that included an exercise component, a dietary component or behavior modification element.¹⁰

**References**


Appendix A. Preliminary Search Strategy (PubMed)

Pubmed Search String for Medicare Population ≥ 65 years old:


Pubmed Search String for Medicare Population < 65 years old and disabled: