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## TREATMENT OF OBESITY IN OLDER PERSONS – A SYSTEMATIC REVIEW

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## Abstract

**Objective:** To systematically review the available evidence regarding weight loss interventions (lifestyle, surgical and pharmacological) for obesity in adults aged over 60 years.

**Methods:** A search of prospective, randomised studies took place in January 2018, on Medline (Web of Science) and PubMed databases. Search terms included the following: elderly, obese, hypocaloric, pharmacotherapy and bariatric surgery. Abstracts were screened for eligibility.

**Results:** 256 publications regarding lifestyle interventions were identified; of these, 69 studies were eligible. As no eligible studies were identified for pharmacotherapy or bariatric surgery, the search was broadened to include non-randomised studies. Four pharmacotherapy and 66 surgery studies were included. Lifestyle intervention had similar weight loss efficacy in older compared to younger people, with positive effects on a number of relevant outcomes, including physical function and cardiovascular parameters. There was little data regarding obesity pharmacotherapy in older persons. The available data for bariatric surgery indicate comparable weight loss and resolution of type 2 diabetes, with similar or slightly higher complication rates in older compared with younger people.

**Conclusions:** Older age alone should not be considered a contraindication to intensive lifestyle or surgical intervention for obesity. There are insufficient data to guide clinical decisions regarding obesity pharmacotherapy in older people.

## INTRODUCTION

The prevalence of obesity has increased rapidly in the last 40 years, particularly among adults aged 60-74 years<sup>1</sup>. The presence of obesity in older adults is associated with disability and worsening of chronic diseases including type 2 diabetes, cardiovascular disease and osteoarthritis<sup>2</sup>. The inflammatory milieu of obesity and the metabolic syndrome also occurs in diseases of ageing such as sarcopenia, frailty and dementia, hence these two sets of conditions potentiate each other<sup>3-6</sup>.

Excess weight gain and adiposity-related complications develop through an interaction of environmental and genetic factors, rather than resulting from a person's lack of willpower<sup>7</sup>. A change in diet and/or physical activity to induce a negative energy balance brings about compensatory changes in adipocyte and gut hormones, energy expenditure, and appetite and brain responses to food, making maintenance of weight loss difficult<sup>8-10</sup>. Recent guidelines for treatment of obesity support consideration of intensive interventions, such as very-low-energy diets (VLEDs), pharmacotherapy and bariatric surgery, as adjuncts to lifestyle and behaviour modification in selected patients, to assist loss of weight and maintenance of weight loss<sup>11, 12</sup>.

Despite the increasing prevalence of obesity in older adults, weight loss interventions in this group have been considered controversial due to concerns about whether they might increase mortality, or accelerate the sarcopenia associated with ageing<sup>13</sup>. Furthermore, older adults are more likely to be affected by polypharmacy and cardiovascular disease, which may increase the risks of appetite-reducing pharmacotherapy and bariatric surgery.

A previous review summarised randomised, controlled weight loss intervention studies in the elderly published as of 2010<sup>14</sup>. Since then, four pharmacological agents/combinations have been approved by the U.S. Food and Drug Administration (FDA) for treatment of obesity, and the profile of bariatric surgery has changed, with sleeve gastrectomy increasingly commonly performed<sup>15</sup>. The aim of this

review is to examine current evidence for the efficacy and safety of medical and surgical treatment of obesity in older ( $\geq 60$  years) adults.

## **METHODS**

The review was performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement<sup>16</sup>.

### **Types of studies and eligibility criteria**

Studies were considered eligible if they examined the efficacy and/or safety of weight loss interventions, comprising behavioural/lifestyle, VLEDs, pharmacotherapy, or bariatric surgery, in people with obesity (body mass index [BMI]  $\geq 30$  kg/m<sup>2</sup>), and either (i) included only older adults ( $\geq 60$  years), (ii) reported study results for adults  $\geq 60$  years separately, or (iii) the mean age of participants was  $\geq 60$  years.

For behavioural/lifestyle and diet interventions, only prospective, randomised, controlled trials (RCTs) were evaluated.

No eligible RCTs were identified for pharmacotherapy or bariatric surgery, therefore in order to assess the available evidence in this population, studies which were not randomised and/or controlled were also screened for possible inclusion if they focused on older adults and reported results for weight outcome and/or adverse events.

### **Search methods**

### *Sources*

Medline (Web of Science) and PubMed were searched on 11 January 2018 for articles published from database inception to the current date, using a combination of search terms related to obesity, older adults, and weight loss interventions. Reference lists of retrieved articles and key systematic reviews were also searched for additional potentially eligible papers. An example of the search strategy is shown in **Table 1**.

### *Study selection*

Identified articles were manually screened for possible eligibility based on title and abstract. Full-text screening of potentially relevant articles was done by both authors to identify studies for inclusion, and disagreements resolved by consensus. Data was extracted into a template, including the following: number and age of participants, details of interventions, outcome measures, and adverse events.

### *Assessment of risk of bias*

The Cochrane tool for assessing risk of bias in RCTs<sup>17</sup>, and the TREND (Transparent Reporting of Evaluations with Non-randomized Designs) checklist<sup>18</sup> for non-randomised studies were used to assess potential risk of bias across domains including selection, performance, attrition, reporting, and other biases.

## **RESULTS**

## Search results

### *Lifestyle/behavioural/VLED interventions*

The initial search identified 254 publications, and 81 met the criteria for the review on the basis of the abstract. A further 2 articles were identified as associated studies (i.e. separate publication from the same study). After full text review, 69 publications were included in the final review (**Figure 1**).

### *Pharmacotherapy*

An initial search for RCTs identified 49 studies, of which after removal of duplicates, 32 abstracts were screened, and 4 were eligible for full text review. None of the four remained eligible for inclusion (outcomes for older adults not reported n=2; no pharmacotherapy n=1, mean age in older group <60 years n=1). The search was then broadened to include non-randomised studies, and 167 studies were identified, of which 76 abstracts were screened after removal of duplicates. 68 studies were not eligible for inclusion, leaving 8 studies of which the full text was reviewed, and 4 which were included (**Figure 2**).

### *Bariatric surgery*

An initial search for RCTs identified 41 studies, of which after removal of duplicates, 24 abstracts were screened, and none were eligible for full text review. When the search was broadened to include non-randomised studies, 729 studies were identified, of which 412 abstracts were screened after removal of duplicates, the full text of 92 studies was reviewed, and 66 studies were included (**Figure 3**).

## Characteristics and risk of bias of included studies

### *Lifestyle/behavioural intervention/VLED*

Since the early 2000s, there have been numerous studies examining the effects of intentional weight loss in older adults, examining domains including physical function, quality of life, body composition, cardiovascular and glycaemic markers, cognition, inflammatory markers and sex hormones. Some have prospectively examined effects on mortality. One has analysed the cost compared with benefits of intervention. The results are shown in supplementary **Table S1**, and outlined below, broken down by endpoint.

Randomised controlled studies of lifestyle intervention were assessed for risk of bias using the method described by the Cochrane Collaboration<sup>17</sup>, categorising the risk across different domains as low, medium, high or unclear (i.e. not clearly documented). Supplementary **Table S4** summarises the risk of bias in lifestyle intervention RCTs. Many of the included publications reported different endpoints of large trials e.g. Comprehensive Lifestyle Intervention Program (CLIP)<sup>19</sup>, Arthritis, Diet and Activity Promotion (ADAPT)<sup>20</sup>, Intensive Diet and Exercise for Arthritis (IDEA)<sup>21</sup>, Physical Activity, Inflammation and Body Composition Trial (PACT)<sup>22</sup> and a trial by Villareal et al<sup>23</sup>, and these larger studies had minimal bias. The risk of bias was generally low with most of the smaller studies also.

### *Pharmacotherapy*

The four pharmacotherapy studies included were from single centres in the U.S., Brazil, Italy and Turkey. One described the pharmacokinetics of a single dose of lorcaserin 10 mg in 12 elderly people (mean age 68 years) compared with a younger control group<sup>24</sup>. The remaining 3 papers did not include a control group. As such, the quality of evidence regarding safety and efficacy of pharmacotherapy is weak. Horie and colleagues reported the experience of 51 patients aged 60-79 years treated in an outpatient obesity clinic in Brazil, with at least 6 months' follow-up<sup>25</sup>. Of the

numerous medications used in the clinic (**Table S2**), only orlistat is widely approved (including in the United States, European Union and Australia) for treatment of obesity. Varli *et al* examined the effect of weight loss over 6 months with a low calorie diet and orlistat on cardiac Doppler parameters in 13 older women<sup>26</sup>, and the remaining study was a prospective case series of 9 patients aged 65-75 years with type 2 diabetes who were treated with liraglutide 3.0 mg for 24 weeks<sup>27</sup>.

### *Bariatric surgery*

Characteristics of the included studies are shown in **Table S3**. The majority were retrospective case series descriptions from single centres, primarily in the U.S, with others from Australia, Brazil, Canada and Europe, which reported on more than 20,000 patients aged between 60 and 83 years who underwent surgery. Laparoscopic adjustable gastric banding (LAGB), sleeve gastrectomy, and Roux-en-Y gastric bypass (RYGB) were the most common operations, and the majority of studies had follow-up durations of at least one year (up to 8 years). Due to the nature of the intervention, no studies involved blinding of participants or investigators. Ten studies evaluated only the safety of bariatric surgery<sup>28-37</sup>, and the remainder evaluated weight loss efficacy as well as safety, although the reported measures of efficacy and safety varied between studies. Thirty-nine of the 66 included studies compared outcomes between older adults and a younger group<sup>28-31, 33-35, 37-68</sup>, and in 12 of these studies<sup>39, 48, 50-52, 54-56, 59, 63, 64, 68</sup>, groups were matched for characteristics such as sex, BMI and surgery type. The remaining studies reported results for older persons without a comparison group.

**Figure S1** summarises the risk of bias in the pharmacotherapy and bariatric surgery studies reviewed.

### **Effects of interventions**

## *Lifestyle/behavioural intervention/VLED*

### Weight loss

Overall weight loss efficacy was dependent on the type of diet (balanced hypocaloric versus partial or full meal replacement), and the duration of the intervention. Participants undergoing full meal replacement with very-low-energy diets (VLEDs), consuming 800-1000 kilocalories (kCal) per day, lost between 12 to 15% of their initial body weight over a period of 12 to 24 weeks<sup>69-71</sup>. Use of partial meal replacements and aiming for an energy deficit of 800-1000 kCal per day yielded lower weight loss over a longer time; approximately 8-10% over 6-18 months<sup>21, 22</sup>. Many other studies utilised a balanced hypocaloric diet with normal foods, obtaining a 500-750 kCal energy deficit per day. This yielded weight losses of between 5-10% over 6-18 months<sup>20, 23, 71-77</sup>. The addition of exercise to a hypocaloric diet did not yield significantly greater weight losses than a hypocaloric diet alone<sup>20, 23, 74, 78</sup>. When energy intakes were equal, increasing the protein content above 0.9 g/kg/day<sup>79, 80</sup> or changing protein source<sup>81</sup> did not result in any differences in weight or lean mass loss, nor did changing the glycaemic index of the carbohydrates<sup>82</sup>. In studies where older and younger participants were compared in terms of weight loss efficacy on the same diet intervention, older participants lost more weight than younger participants<sup>83, 84</sup>. Given the same hypocaloric diet, a higher calorie expenditure exercise regimen led to greater weight losses than lower calorie expenditure exercise<sup>85</sup>.

### Long term weight loss maintenance

Weight regain is an issue of concern following intentional weight loss, and a number of studies have explored this in older people. After a follow up of 18 months, two studies have demonstrated weight regain of 40-65% of initial weight loss, and this regain was made up of body fat<sup>86, 87</sup>. However, one of

these studies<sup>86</sup> also followed up physical function, and found that despite weight regain, physical function improvements were maintained. Ongoing counselling with use of an accelerometer<sup>75</sup> and increased water consumption<sup>88</sup> have both been demonstrated to offset weight regain in older persons.

#### Changes in body composition, bone mineral density, and hormone levels

Many of the larger studies examining weight loss in older persons examined the changes in fat, lean and bone mass, usually using Dual Energy X-ray Absorptiometry (DXA). Weight loss with calorie restriction reduces fat mass and lean mass<sup>23, 74, 77, 78, 89-92</sup>. However, fat mass is lost in greater quantities than lean mass during intentional weight loss, such that the percentage of lean mass after the intervention is increased<sup>71, 81</sup>. In studies where changes in body composition were prospectively correlated with changes in physical function, it was demonstrated that improvements in physical function correlated with decreases in fat mass<sup>89-92</sup>.

Intentional weight loss causes bone mineral density to decrease in proportion with the amount of weight loss<sup>23, 78, 93-95</sup>. With 1kg loss of weight, there is a decrease in bone mineral density of 0.1% at the femoral neck<sup>78</sup>. Multimodality exercise, incorporating strength, balance, endurance and flexibility offsets losses in lean mass and bone mass<sup>23, 93, 94</sup>.

Sex hormones (oestrogen and testosterone) decline with age, and their levels alter with changes in body fat. Levels of the adipokine leptin are proportional to body fat, and adiponectin levels are inversely proportional to body fat. Changes in these hormones during intentional weight loss in older persons have been investigated. In a study examining diet and exercise either alone or combined, versus control, it was demonstrated that men randomised to diet alone, or to diet and exercise combined, had increases in testosterone and decreases in oestradiol. However, improvements in

physical function were seen not only in these groups, but also in men randomised to exercise alone with no weight loss, hence changes in these sex hormone levels were unrelated to physical function<sup>96</sup>. In another study, levels of growth hormone were higher in women (but not men) randomised to a dietary intervention than those who were not, but none of the changes in other hormones measured (cortisol, sex-hormone binding globulin, testosterone, and dehydroepiandrosterone) correlated with changes in physical function<sup>97</sup>. Leptin was decreased after a weight loss intervention compared to before weight loss in women only<sup>98</sup>; another small study revealed no change in adiponectin in a weight loss plus exercise group compared with an exercise alone group<sup>99</sup>.

#### Changes in physical function

Significant overweight in older adults is most problematic because of its association with poorer physical function, disability, and increased risk of residential care admission, hence the importance of examining the effects of weight loss interventions on physical function. Physical function has most commonly been measured utilising gait speed, muscle strength by 1-repetition maximum, and balance. Exercise regimens varied between studies, but incorporated strength, cardiovascular endurance or both. Various combinations of diet alone, diet and exercise, exercise alone and attention controls have been compared. Where diet plus exercise is compared with control, there is a clear and significant improvement in physical function in the treatment group<sup>76, 100</sup>. Studies which compared exercise alone with diet and exercise revealed similar improvements in physical function<sup>77, 101, 102</sup>. Studies comparing diet plus exercise, diet alone and exercise alone revealed improved self-reported<sup>20</sup> or objective<sup>21, 23, 103</sup> physical function in the diet plus exercise groups, followed by exercise, diet then control. A single study comparing weight loss with diet and exercise with differing

protein intakes revealed improved physical function in the higher protein intake (1.2 g/kg/day versus 0.8 g/kg/day) group<sup>73</sup>.

#### Cardiovascular and glycaemic outcomes, markers of inflammation

Obesity is a risk factor for hypertension, dyslipidemia and type 2 diabetes<sup>104</sup>. Weight loss induced by hypocaloric diet and exercise, of the order of 5-10%, led to significantly reduced systolic and diastolic blood pressure<sup>105-107</sup>. More modest weight losses of 3-4% combined with sodium reduction to 1.8 g/day led to a significant reduction (hazard ratio 0.47 [95% CI 0.35-0.64]) in a combined endpoint (requirement for blood pressure medication, hypertension, cardiovascular event) in older hypertensive study participants with obesity, relative to usual care<sup>108</sup>. Effects on lipid measures were more variable; one study revealed a reduced atherogenic total to high-density lipoprotein (HDL) ratio in the intensive exercise (greater weight loss) arm than the less intensive exercise arm<sup>85</sup>. Another study<sup>107</sup> found that improvements in HDL and glucose metabolism were correlated with weight loss, however aerobic exercise improved maximal oxygen uptake ( $VO_{2max}$ ). Weight loss was associated with reduction in triglycerides<sup>105, 107</sup>. Calorie restriction leading to weight loss, exercise, and a combination of both improve insulin sensitivity in older adults with obesity<sup>109, 110</sup>. In older adults with heart failure with preserved ejection fraction and obesity, a diet and exercise intervention led to a 10% weight loss over 20 weeks, with improved  $VO_{2max}$  which correlated with improvement in lean mass<sup>111</sup>. This improvement in  $VO_{2max}$  was superior to either diet or exercise alone. Markers of inflammation such as interleukin 6 (IL-6), Tumour Necrosis Factor alpha (TNF- $\alpha$ ) and C-reactive protein (CRP) were generally (but variably) reduced in proportion to weight loss<sup>112-114</sup>, however one study revealed no absolute change in these biomarkers with weight loss<sup>115</sup>.

### Nutritional parameters

It is important that adequate intake of protein, fatty acids and micronutrients be maintained in the face of caloric restriction, particularly in older adults who have chronic diseases. Where nutritional quality of weight loss diets (including meal replacements) was assessed by food recall diaries, it was found that those randomised to weight loss ate fewer calories and fats (with a higher percentage of carbohydrates) however the adequacy of micronutrient intake was variable<sup>116, 117</sup>. A study comparing VLEDs with hypocaloric balanced diets and healthy eating examined the effects on serum vitamin D, B12, ferritin, albumin and red cell folate, and found that use of a VLED was associated with a significant increase in all of these parameters despite having the greatest caloric deficit<sup>71</sup>.

### Quality of life

Weight loss studies examining quality of life found that improvement in quality of life scores correlated with weight decrease<sup>118, 119</sup> and gains in strength<sup>118</sup>. Another study found that improvement in quality of life score related to weight loss was limited to physical health domains<sup>120</sup>.

### Cognition

In 12-month weight loss studies examining participants with normal cognition<sup>118</sup> and mild cognitive impairment<sup>121</sup>, diet plus exercise and exercise alone was demonstrated to improve scores on global cognitive tests.

### Adverse effects

Other than decrements in lean mass, adverse events were not commonly reported, with the exception of those studies examining the use of VLEDs. VLEDs were associated with constipation, dizziness, cold intolerance (all of which are well documented)<sup>70, 71</sup> and minor increases in urea and

creatinine<sup>69</sup>. Where adverse events were reported, these were related to falls during exercise interventions<sup>20, 23, 122</sup>. Large weight loss studies, which followed up participants for seven<sup>123</sup> and nine<sup>124</sup> years, found no increase in mortality in those randomised to the weight loss arm compared with those who were not.

### Cost-Effectiveness

Only one study has examined the cost-effectiveness of weight loss intervention, and it found that, while the diet plus exercise arm was most expensive, it had the greatest effect on stiffness, pain and joint function, which are the strongest predictors of downstream health utilisation<sup>125</sup>.

### *Pharmacotherapy*

The examination of the pharmacokinetics of a single dose of lorcaserin 10 mg in 12 elderly people (mean age 68 years) compared with a younger control group concluded that there were no clinically relevant differences in pharmacokinetics and tolerability, and therefore no dose adjustment was required in older people with normal renal function, although the findings cannot be extrapolated to the recommended dosing of 10 mg bd<sup>24</sup>. Orlistat was used by 11 attendees of an outpatient clinic for a mean of 8.7 ± 5.0 months, and resulted in a mean weight loss of 3.3 ± 5.9 kg in the report by Horie et al<sup>25</sup>, and by 13 women for 6 months in the study by Varli<sup>26</sup> resulting in a mean weight loss of 8.4 kg (9.4%). All completers (13/18) achieved weight loss of ≥5% at 6 months. In the prospective case series of 9 patients aged 65-75 years with type 2 diabetes treated with liraglutide 3.0 mg for 24 weeks, median losses of weight and fat mass of 2.0 and 1.5 kg, respectively were reported<sup>27</sup>.

### *Bariatric surgery*

## Efficacy

Of the 28 studies in which weight outcomes for older and younger persons were compared, 16 found no significant difference in weight loss between groups<sup>38, 40, 42-46, 48, 54, 59, 61, 64-68</sup>, and 7 studies reported less weight loss in older than younger participants<sup>39, 41, 47, 50, 51, 55, 62</sup>. Greater total weight loss in younger participants but no difference in % excess weight loss (%EWL) between groups was reported in 2 studies<sup>52, 63</sup>. One study reported no difference in %EWL between groups with LRYGB, but greater %EWL in younger patients after LAGB<sup>57</sup>, while another reported no difference in % total weight loss (%TWL) after LAGB, but greater %TWL after RYGB and laparoscopic sleeve gastrectomy (LSG) in younger patients<sup>58</sup>. One study reported no difference in total weight loss or %EWL between groups at 1 year, but greater %EWL in younger patients 5 years post-LAGB<sup>49</sup>. No studies found significantly greater weight loss in the older compared with younger group. Studies in which percentage total weight loss (%TWL) was reported in older people found loss of 17-38% after 1-6 years following gastric bypass and sleeve gastrectomy<sup>38, 40, 44, 47, 50-52, 58, 61, 63-65, 68, 126-131</sup>, and loss of 14-20% after adjustable gastric banding<sup>58, 132, 133</sup>. For studies in which weight outcome was reported as percentage excess weight loss (%EWL), older persons undergoing RYGB or LSG lost 46-77% excess weight at 12-21 months<sup>39, 42-44, 46, 47, 50-52, 55, 60, 65-68, 134, 135</sup>, and 43-72% two to six years post-operatively<sup>47, 55, 63, 135-137</sup>. After LAGB, studies reported %EWL of 14-36% at 1 year, and 35-48% at 5 years' follow-up<sup>49, 57, 138-140</sup>. Studies comparing types of surgery reported that RYGB was associated with greater or equal weight loss compared with sleeve gastrectomy, and both RYGB and sleeve gastrectomy were associated with more weight loss than LAGB<sup>57, 58, 133, 140-144</sup>. Most studies reported rates of resolution of type 2 diabetes, which ranged widely from 22 to 100%, apart from the study by Moon and colleagues which reported remission of diabetes a mean of 24 months post-operatively in only 10% of patients after LAGB, 19% after RYGB and 34% after SG<sup>133</sup>. Studies

generally did not find a significant difference in diabetes resolution rates in the older compared with younger group<sup>39-42, 46, 48, 52, 54, 55, 59, 63, 145</sup>, although a higher rate of diabetes remission was reported in participants under the age of 40, compared with the  $\geq 60$  year old group in one study<sup>51</sup>. No studies reported outcomes of physical or cognitive function.

### Safety

Of 38 studies comparing the safety of bariatric procedures in older vs younger groups, 16 found no difference in early mortality or complication rates between groups<sup>29, 31, 38, 40, 41, 43, 44, 47, 48, 51, 52, 54, 55, 59, 61, 63, 68, 146</sup>. A further four studies found no difference between groups in overall complications, but higher rates of certain events in older participants, such as cardiac complications<sup>66</sup>, intubation for longer than 48 hours, acute kidney injury, sepsis and pulmonary embolus<sup>28</sup> and bleeding<sup>39</sup>. In one study, in which a higher proportion of participants in the older group underwent LAGB, there was no difference in overall complications, but older participants had significantly lower 30-day readmission rates and higher new-onset gastro-oesophageal reflux compared to younger patients<sup>35</sup>. Dunkle-Blatter reported no significant differences after RYGB between older and younger participants in 30-day mortality or complications <30 days or >90 days, but a higher risk of major complications between 31 and 90 days in older compared with younger patients<sup>42</sup>. Higher risks of early mortality and/or complications (particularly early) were reported in older people in 15 studies<sup>29, 30, 33, 34, 37, 46, 50, 53, 58, 60, 64, 65, 67, 146, 147</sup>. One study<sup>29</sup> of Medicare beneficiaries who underwent bariatric surgery from 1997 to 2002 reported higher early mortality in those aged  $\geq 65$  years compared with younger patients (6.9 vs 2.3%), which was attributable in part to a higher proportion of older patients operated on by surgeons in the lowest quartile of bariatric surgery volume. Surgeons in the highest quartile of bariatric procedure volume had similar rates of early mortality across age groups (90-day

mortality 1.8% in older vs 1.1% in patients <65 years;  $p=0.4$ )<sup>29</sup>. One study<sup>49</sup> found total complications and complications requiring re-operation were significantly more common in younger than older patients.

## **DISCUSSION**

The prevalence of obesity is particularly high in older adults<sup>148</sup>. The aim of this review is to examine current evidence for the efficacy and safety of lifestyle, pharmacological and surgical treatment for obesity in older adults. Our main findings are that there is a large pool of randomised, controlled studies demonstrating the benefits of weight loss with hypocaloric diets, including very-low-energy diets, combined with exercise, in older people. Incorporation of multimodality exercise offsets loss of lean mass, and there are gains in physical function driven by exercise and fat loss. Where reported, adverse effects are generally mild and similar in nature to those seen in younger people. In contrast, there are no randomised studies examining outcomes of pharmacotherapy in elderly persons, and insufficient evidence of either benefit or harm to guide clinical decision-making regarding the use of pharmacotherapy in this age group. No randomised trials examining outcomes of bariatric surgery in elderly persons were identified, but nonetheless, a large number of older people have undergone bariatric surgery. Most of the available data are vulnerable to bias, but indicate no significant differences in weight loss and resolution of type 2 diabetes in older compared with younger patients. Around half of studies reported comparable early mortality and overall complication rates in older and younger patients. Studies which compared types of surgery reported less weight loss and higher late complication rates for LAGB, consistent with findings in younger people<sup>149</sup>.

The effect of the increasing prevalence of obesity in the elderly on mortality is unclear; several epidemiological studies have described a phenomenon called the “obesity paradox”, where obesity seems to be associated with a lower mortality in cardiovascular and other diseases. However, when adjustments for early death, cardiovascular fitness and smoking status are made, the nadir of mortality occurs at a BMI within the normal range<sup>150</sup>. Large RCTs have shown no increase in mortality over 7-9 years in older persons with obesity randomised to lifestyle-based weight loss interventions<sup>123, 124</sup>, and a retrospective examination of U.S. Medicare-covered patients who underwent bariatric surgery between 2001 and 2004 found increased survival rates over two years when compared with a nonsurgical group with obesity, which started 11 months post-operatively in patients over the age of 65, compared with 6 months in patients aged less than 65 years<sup>56</sup>. Thus, the available evidence indicates that intentional weight loss in older people with obesity is not associated with increased mortality.

The limitations of this review include the paucity of data of any sort regarding pharmacotherapy in older persons, the lack of prospective, controlled studies for bariatric surgery, and the lack of long-term mortality data after any of these interventions. Even when older adults were studied, the majority of older participants were under the age of 70 years, which limits the generalisability of the findings to people over this age. This review did not evaluate the cost-effectiveness of treatment of obesity in the elderly, which is an important consideration for resource allocation. A recent cohort analysis in the United Kingdom by Gulliford and colleagues<sup>151</sup> examined this issue and found that the health care costs of bariatric surgery were exceeded by health benefits to people with obesity, with similar estimates in people aged 55 to 74 years compared with younger age groups.

## Future directions

The limitations of the current literature demonstrate the need for studies providing high-level evidence regarding the safety and efficacy of pharmacotherapy and bariatric surgery in older persons, and to delineate their place in the treatment of obesity in this age group. The higher prevalence of medical conditions, including diseases of ageing, and polypharmacy, mean that evaluations of benefits, risks and costs in younger study participants cannot be assumed to be applicable to older persons. Future research should also investigate outcomes particularly relevant to the older age group, such as cognition, urinary incontinence and falls risk.

## Conclusions

Lifestyle interventions for weight loss in older people should no longer be considered controversial, as they have clear benefits for obesity-related complications, and functional impairments. The available evidence suggests that bariatric surgery can be performed in older people with comparable weight loss and beneficial effects on obesity-related complications to younger people, and acceptable complication rates in carefully selected patients. There is a need for further studies examining the safety and efficacy of bariatric surgery, and obesity pharmacotherapy in older people, as well as outcomes of particular relevance to the older age group.

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## TABLE AND FIGURE LEGENDS

**Table 1: example of search strategy**

**Figure 1: overview of study search and selection for RCTs of lifestyle interventions**

**Figure 2: overview of search and selection for non-randomised pharmacotherapy studies**

**Figure 3: overview of search and selection for non-randomised bariatric surgery studies**

#4	Search (#1 AND #2 AND #3)
#3	Search (((low calorie diet[Title/Abstract]) OR hypocaloric[Title/Abstract]) OR weight loss intervention[Title/Abstract]) OR behavioural intervention[Title/Abstract]) OR behavioral intervention[Title/Abstract]
#2	Search (randomised[Title/Abstract] OR randomized[Title/Abstract] OR RCT[Title/Abstract] OR randomly[Title/Abstract] OR random[Title/Abstract])
#1	Search ((obesity[Title/Abstract] OR obese[Title/Abstract] OR "weight loss"[Title/Abstract] OR "weight reduction"[Title/Abstract])) AND (elderly[Title/Abstract] OR older[Title/Abstract] OR geriatric[Title/Abstract])

**Table 1: example of search strategy**

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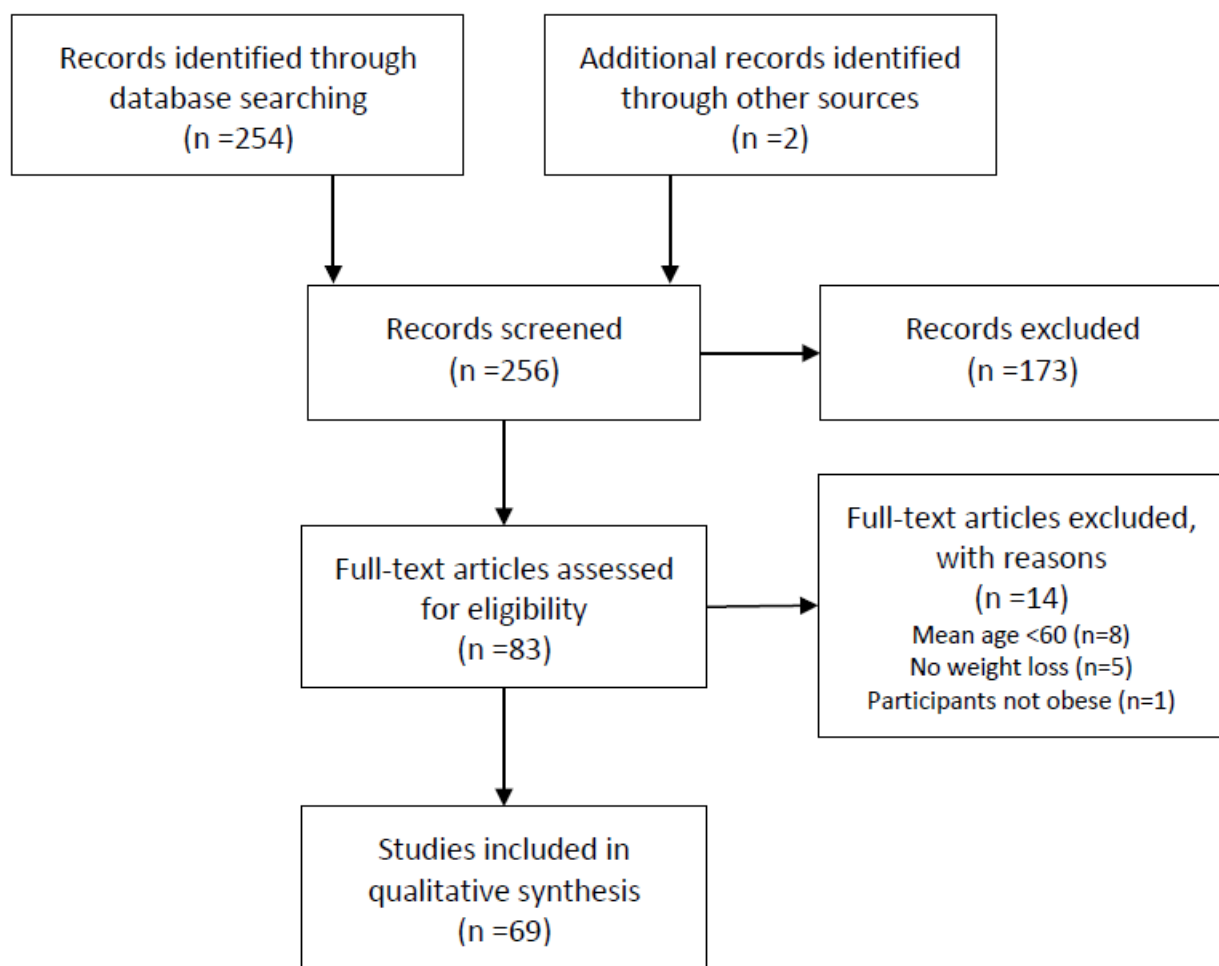
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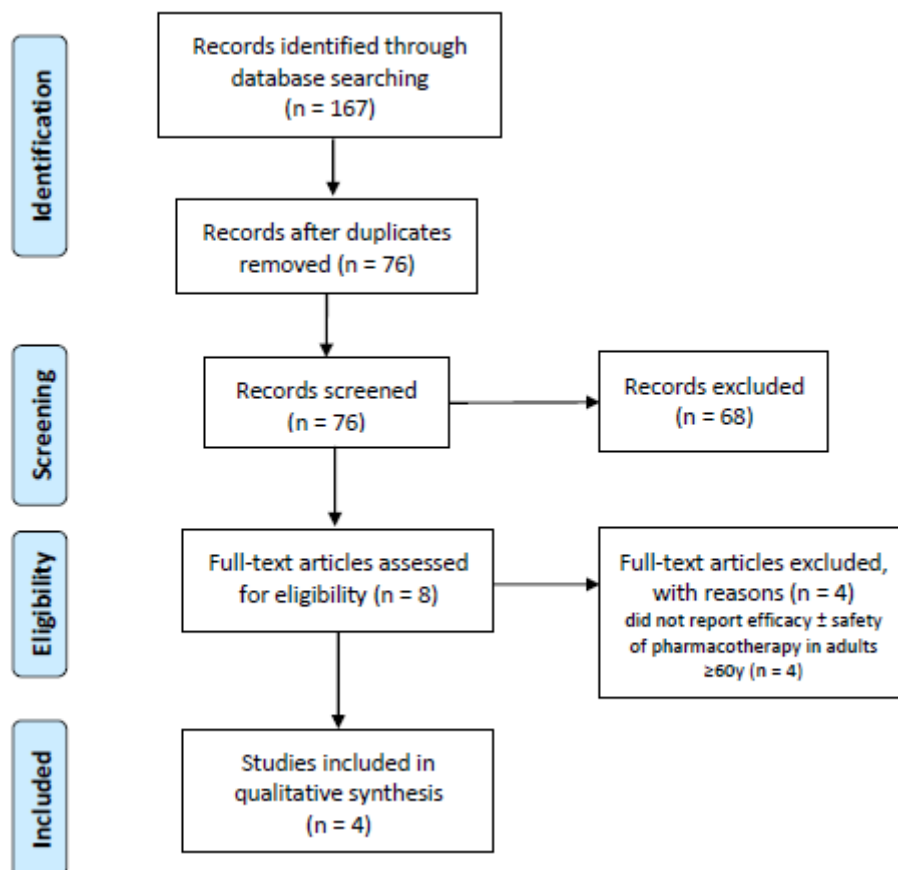
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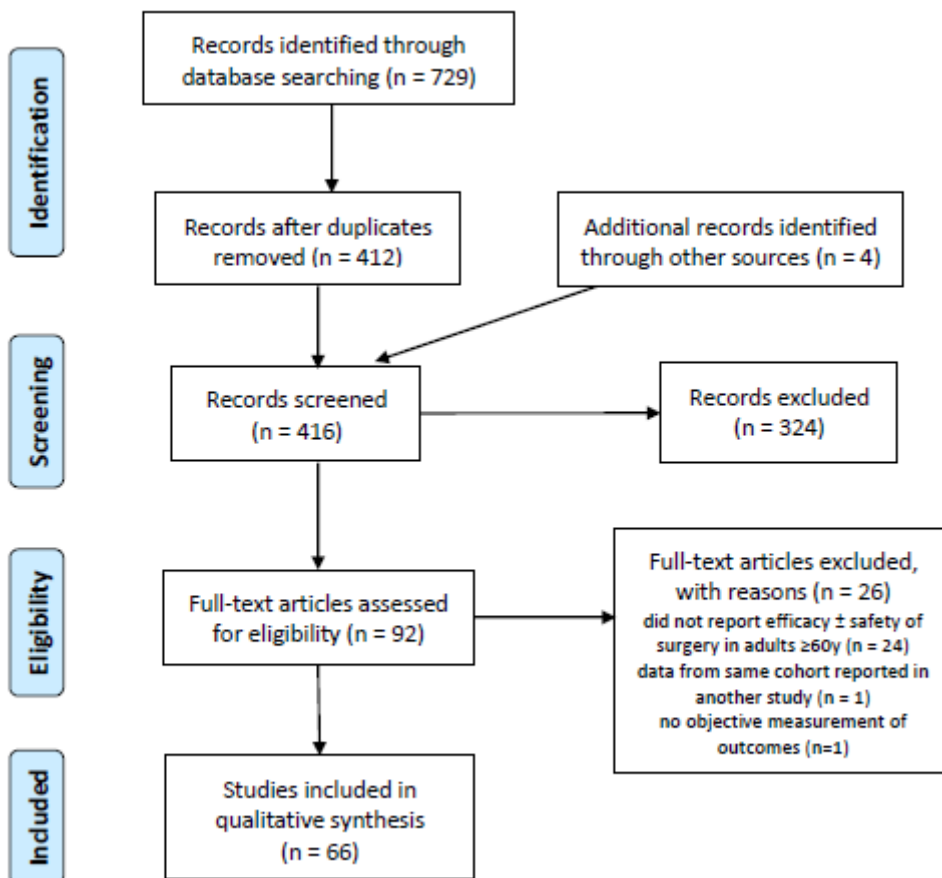
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