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Benefit-to-Risk Balance of Weight Loss Interventions in Older Adults with Obesity

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Abstract

Purpose of Review Obesity in the older adult is a burgeoning health epidemic that leads to increased morbidity, disability, and institutionalization. This review presents a brief overview of geriatric-specific consequences of obesity by highlighting the risks and benefits of intentional weight loss.

Recent Findings Intentional weight loss reduces the extent of adiposity-related illnesses, yet the approach in older adults is fraught with challenges. Interventions combining caloric restriction and physical exercise (aerobic and resistance) maximize fat loss and minimize loss of muscle and bone. Interventions are also effective at improving physical function, reducing medication burden, and improving symptomatic osteoarthritis in this population. Approaches can mitigate the risks of isolated caloric restriction on muscle and bone in a safe and effective manner.

Summary Effective weight loss strategies should be considered in older adults. While there are potential risks, practical clinical approaches can minimize the potential harms while maximizing their benefits.

Keywords Obesity · Older adults · Benefits · Risks

Introduction

Healthcare advances have resulted in upturns in life expectancy leading to a higher proportion of older adults living into their eighth decade of life [1, 2]. More than 47 million people in the USA are currently aged ≥ 65 (~ 15% of the population) [3], with estimates predicting a doubling of this demographic within the next 40 years [4]. Integral to healthy aging have been reductions in the rates and magnitudes of early mortality from chronic diseases [5]. The healthcare system has begun emphasizing prevention and management of chronic conditions among older adults, as apparent with recent Centers for Medicare and Medicaid Services (CMS) initiatives such as the Annual Wellness Visit [6], Intensive Behavioral Therapy for obesity [7], and chronic care management [8].

One condition proving particularly vexing for primary care providers, especially among older adults, is obesity. The epidemic extends into older adulthood where 41% are classified as having obesity [9•], with rates steadily increasing over the past four decades [9•, 10, 11]. This review provides a brief overview of body composition changes with aging followed by a specific emphasis on the inherent benefits and risks associated with intentional weight loss in older adults. We highlight evidence-based strategies and posit clinical recommendations

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for attenuating the potential deleterious, multifaceted impact of treating this epidemic.

Body Composition with Aging

Adults experience natural changes in body composition resulting from a cascade of biological and sociological factors as part of the aging process. In the fourth decade, lean mass begins declining and, consequently, body mass is gained as fat in higher proportions [12], stemming in part from declines in serum testosterone [13], leptin resistance [14], and reduced responsiveness to thyroid hormone [15]. Reduced mitochondrial volume and oxidative capacity also contribute to declines in resting metabolic rates [16, 17] that incrementally increase body fat. Older adults are also at risk of developing anabolic resistance due to reduced amino acid availability, muscle perfusion and uptake, and digestive capacity [18]. There is a natural tendency for weight redistribution centrally [19], a concurrent loss of height [20], and increased kyphosis [21] due to age-related changes in bone metabolism and architecture [22]. These changes make body mass index (BMI), a marker of excess adiposity [23, 24], a less accurate surrogate for obesity in older adults [25].

In older adults, obesity is associated with worsening physical function [26], impaired quality of life [27], nursing home placement [28, 29], and reduced life expectancy [30]. It is also associated with cardiometabolic disorders [31], obstructive sleep apnea [32], osteoarthritis [33], cancer [34], and cognitive dysfunction [35]. Yet, its treatment is complex as weight loss may paradoxically exacerbate incident frailty or disability and could be an indication of various underlying medical disorders [36, 37]. An increasingly recognized subset of older adults with obesity have co-existent sarcopenia placing them at a synergistically higher risk of functional decline and adverse events [38, 39••, 40, 41]. Sarcopenic obesity is a multifactorial disorder characterized in older adults by low skeletal muscle mass, strength, or function in addition to excess adiposity [42, 43], whose prevalence increases with age [44]. While the definition of this co-defined entity is debated [43, 45], its pathophysiology and treatment strategies are complex and are reviewed elsewhere [46••].

Unintentional vs. Intentional Weight Loss

Discriminating between unintentional and intentional weight loss is crucial in understanding the safety of weight loss in older adults. Unintentional weight loss is a harbinger of serious illness in older adults [47] and directly correlates with decreased quality of life [48]. Significant unintentional weight loss (> 5% in 6 months [49]) can be identified using screening questionnaires [50] to alert providers of underlying cardiopulmonary disorders or malignancies [49]. Major depression, cognitive decline, and food insecurity are other important considerations in an older adult [51].

The "obesity paradox" is a term coined from a 2002 study that found improved outcomes in overweight or obese individuals with coronary artery disease after percutaneous coronary interventions [52]. This paradox has, in part, been explained by reverse causality where cohorts whose study participants with normal weight had worse health [53], undiagnosed cachexia [54], or illness-related weight loss [55, 56]. Flegal and Ioannidis clearly describe the problem in attributing elements of different observational studies whose foci and outcomes differ, which lead to inappropriate population-level recommendations [57]. Previous epidemiological studies have demonstrated negative relationships between weight loss and mortality, but fail to differentiate between intentional and unintentional weight loss [58–61]. Studies also fail to account for smoking, cardiorespiratory fitness, or other socioeconomic variables [55, 57]. Age-related factors that alter the relationship between weight loss and mortality are described elsewhere [62]. Using large data sets to evaluate such relationships requires considerable data manipulation particularly if persons with serious illnesses or those at-risk of early mortality are included [55]. Statistical errors are introduced leading to biased and false positive associations. Hence, clinical trials provide a unique opportunity to resolve such discrepancies by minimizing the impact of confounders on important outcomes.

The recent Cardiovascular Disease Lifetime Risk Pooling Project collected individual-level data across ten prospective cohorts free of cardiovascular disease, with 3.2 million person-years of follow-up [63••]. Long-term follow-up of the 190,672 in-person examinations noted that, compared with normal weight, incident cardiovascular disease for overweight persons demonstrated a hazard ratio (HR) of 1.21 (95% confidence interval 1.14, 1.28) and 1.32 (1.24, 1.40) in men and women, respectively, and 1.67 (1.55, 1.79) and 1.85 (1.72, 1.99) for obesity. The strongest relationship was for morbid obesity (men: HR 3.14 (2.48, 3.97); women: HR 2.53 (2.20, 2.91)). These trends were also observed in adults aged 60–79 at baseline (men: overweight 1.22 (1.14, 1.30); obesity 1.43 (1.32, 1.55); morbid obesity 1.81 (1.31, 2.50); women: overweight 1.18 (1.12, 1.24); obesity 1.57 (1.48, 1.66); morbid obesity 2.22 (1.98, 2.49)). These data provided evidence to challenge the paradox in older adults suggesting that safe and effective weight loss can be recommended by providers as long the specific risks are understood and strategies are employed to mitigate them.

Benefits of Weight Loss in Older Adults

Older adults with obesity can significantly reduce their risk for long-term chronic medical conditions by engaging in weight loss efforts. However, continued skepticism about the effectiveness of weight loss in an older adult population exists due to limited life expectancy [64], difficulties in engaging in behavioral change [65], and other mobility disabilities [66, 67] that may prevent them from participating in interventions. Two recent reviews support the importance of weight loss treatments in older adults. Batsis et al. [39••] evaluated 5741 citations of which six unique studies with a duration ranging from 6 to 18 months (mean participant age 66.7–77.1 years) demonstrated weight loss of 0.5–10.7 kg (0.1–9.3%). Combined dietary and exercise (aerobic/resistance) programs led to greater improvements in physical performance measures and quality of life than either alone. Separately, Haywood and Sumithran [68] evaluated publications related to lifestyle, surgical, and pharmacologic therapy for obesity in adults aged ≥ 60 years. Their findings confirmed the benefits of hypocaloric, diet-induced weight loss combined with exercise. There was insufficient data to guide clinical decisions regarding pharmacotherapy in older adults.

More recently, Villareal et al. evaluated 160 older adults with obesity, demonstrating improvements in the combined caloric restriction, aerobic and resistance groups in physical performance testing, peak oxygen consumption and body weight over aerobic-only or resistance-only and control groups [69••]. While multicomponent weight loss efforts are effective, there may also be long-term reductions in all-cause mortality of approximately 15% [70•] with sustained improvements in function [71]. In an earlier Villareal et al. trial with obese older adults, those randomized to the combined diet-exercise program demonstrated clinically significant weight loss (− 8.6 ± 3.8 kg) and improved physical function by 21% as measured by the physical performance test, even when compared with the diet or exercise-only groups (12% and 15% respectively; $p = 0.04$) [72]. Participants in the Look AHEAD diet-exercise group (mean age 58.6 ± 0.13 years) had improved physical function through peak metabolic-equivalent capacity over 4 years of follow-up compared with their control group [71]. Rejeski et al. also found benefits of using a combined diet-exercise approach to weight loss on physical function in older adults [73•]. Compared with diet-only, older adults engaging in either aerobic or resistance exercise with dieting exhibited improvements in both knee extensor strength (aerobic 4.6 N/m, $p = 0.13$; resistance 6.6 N/m, $p = 0.027$) and in 400-m walk time (16.9 s; $p < 0.001$). The profound benefits of combined diet-exercise weight loss efforts among obese older adults also improve osteoarthritis symptoms. In a randomized trial of 399 obese older adults with knee osteoarthritis, those allocated to a combined diet-exercise program experienced improved 6-min walk (41.5 m; $p < 0.001$), walking speed (− 0.04 m/s; $p = 0.02$), and short-form-36 physical function score of (− 2.26, $p = 0.03$) [74] . The INFINITE study, a 20-week randomized trial of 180 older adults with obesity, demonstrated VO_2 max increases of 7.7%, 13.8%, and 16% in those with exercise alone, exercise with moderate-, and high-caloric restriction, respectively [75]. In contrast, the CROSSROADS trial failed to demonstrate differential improvement of physical function or quality of life with energy restriction or weight maintenance diets compared with an exercise-only control group [76•]. These studies likely suggest a positive effect of weight loss on obese older adult's physical function with obesity and should be considered a key outcome measure for this population.

Risks of Intentional Weight Loss in Older Adults

While intentional weight loss in older adults portends considerable benefits on physical function [69••, 72, 73•, 74, 75, 76•], chronic disease [77, 78], mortality [70•], and quality of life [79, 80], there are inherent risks to be aware of. Caloric restriction during weight loss induces a catabolic state that not only affects fat but also causes undesirable catabolism of other tissues, including skeletal muscle and bone [81]. Because weight loss is also associated with significant loss of fat-free mass, sarcopenia, bone loss, and musculoskeletal injury are some of the negative consequences, as described below and, in part, in Fig. 1.

Adverse Effects on Muscle

Loss of muscle mass and strength are associated with adverse health outcomes, including reductions in physical function and quality of life [83], frailty [84], and all-cause mortality [39••, 85••]. While sarcopenia is a commonly accepted consequence of aging [12], it may also occur following an acute illness or injury [86] or immobilization [87]. Without engaging in concurrent activities to minimize sarcopenia, weight loss initiatives can effectively accelerate its development. A meta-analysis identified the impact of diet-induced weight loss in overweight or obese adults on muscle strength [88] with seven weight loss intervention studies ranging from 8 to 24 weeks (age range 28–70 years). Overall, knee extensor strength by isokinetic dynamometry ($n = 108$) was lower following diet-induced weight loss (− 9.0 N/m [− 13.8, − 4.1]; $p < 0.001$), representing a 7.5% decrease from baseline. Handgrip strength ($n = 231$) demonstrated non-significant declines (− 1.7 kg [− 3.6, 0.1]; $p = 0.07$). While the results were based on varying methods and a wide age range, this study highlighted the effect of diet-induced weight loss on muscle strength. A review of 52 studies (age > 50 years) established that caloric restriction led to loss of substantial proportion of fat-free mass [89]. Even in adults aged 45–65, caloric restriction leads to approximately 4% reduction in lower-extremity lean mass [90]. The Look AHEAD trial (mean age 58 years) also showed significant reductions in total skeletal muscle mass in the intensive lifestyle group [91]. These trials demonstrate that mechanistically, caloric restriction alone during weight loss interventions can lead to the loss of lean mass.

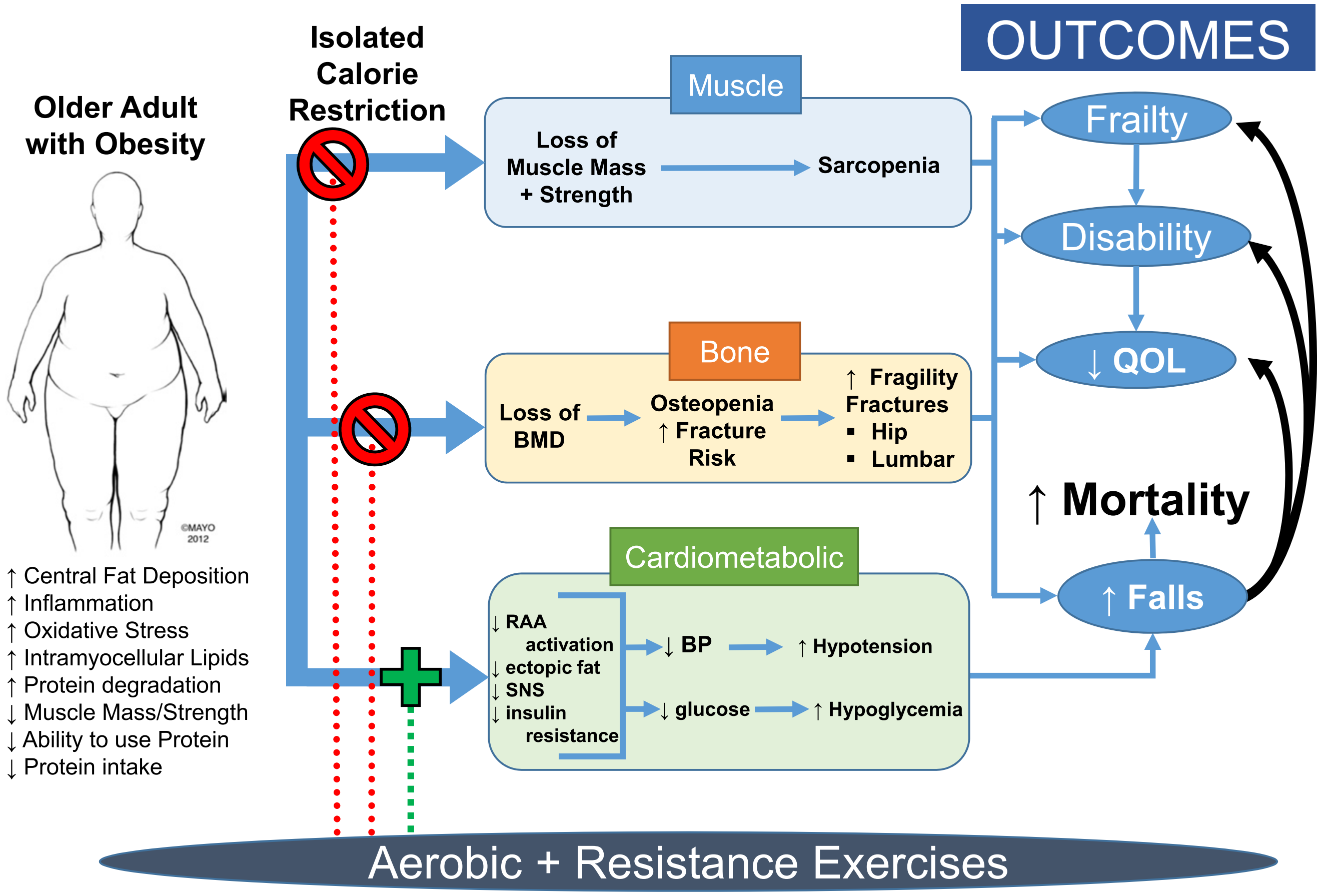

Fig. 1 Risks of diet-induced weight loss in older adults with obesity. This figure represents the major risks associated with isolated calorie restricted, diet-induced weight loss on muscle, bone, and the cardiometabolic system and their impact on key outcomes of frailty, disability, quality of life, falls, and mortality. The inter-relationships between these elements are presented through the *arrows*. Elements of the underlying pathophysiologic processes in aging in the older adult with obesity are presented. Aerobic and resistance exercises coupled with diet-induced weight loss mitigate the loss of muscle mass and strength, and bone mineral density (indicated by *red line and prohibition symbol*). This combination also stimulates enhancement of elements of the cardiometabolic system leading to improvements in glucose homeostasis and blood pressure, requiring providers to be cognizant of relative hypotension and hypoglycemia (indicated by *green line and plus symbol)*. BMD, bone mineral density; BP, blood pressure; RAA, renin, angiotensin, aldosterone; QOL, quality of life; Rx, prescription medications; SNS, sympathetic nervous system. (Figure, in part, reproduced from: Coutinho et al. [82], pp. 553–560, with permission from Elsevier) [82]

In a trial that compared the effects of four interventions (control, diet-only, exercise-only, diet-exercise) among older individuals with obesity, the diet-only group had significant reductions in lean mass at 6 months (− 3.5 ± 2.7 kg) and 1 year (− 3.2 ± 2.0 kg) [72]. Declines in lean mass were mitigated by a combined aerobic, resistance, and stretching program at 6 (− 1.7 ± 1.6 kg) and 12 months (− 1.8 ± 1.7 kg). A 2017 study also demonstrated that a combined diet/exercise group had more extensive weight loss, with less fat-free mass loss (1.8 ± 1.5 kg vs. 3.5 ± 2.1 kg), lower extremity lean mass loss (0.9 ± 0.8 kg vs. 2.0 ± 0.9 kg), and upper extremity lean mass loss (0.1 ± 0.2 kg vs. 0.2 ± 0.2 kg), as compared with the diet-only group ($p < 0.05$) [69••]. Despite loss of lean mass, the diet-exercise group increased upper and lower extremity strength in response to exercise (17–43%), whereas the diet group maintained strength.

Weiss et al. [90] randomly allocated 52 overweight adults (45–65 years) to three groups: (a) caloric restriction-only with maintained physical activity; (b) endurance exercise-only group with maintained calorie consumption; and (c) combined caloric restriction-exercise group. At 12 months, all three groups experienced roughly 7% reduction in body weight and roughly 15% reduction in fat mass [90, 92]. The caloric restriction group experienced a statistically significant 2.1% reduction in whole-body muscle mass, which remained unchanged in the two exercise groups. A distinct study conducted by the same investigators yielded similar results, with only the caloric restriction group demonstrating significantly decreased thigh muscle volume and knee flexion strength [93].

The 1-year CROSSROADS trial [76•] randomized older adults to three groups: exercise, weight maintenance, and a 500-kCal restriction diet. After 1 year, no differences were observed in visceral adipose tissue between groups; however, the exercise group demonstrated a 0.3-kg increase in lean mass while the caloric restriction group experienced a 0.4-kg decrease, though not statistically significant. In a pilot trial of 30 older, frail adults, the diet-only group lost more fat-free mass (3.5 ± 2.1 kg vs. 1.8 ± 1.5 kg, $p = 0.02$), lower extremity lean mass (2.0 ± 0.9 kg vs. 0.9 ± 0.8 kg, $p = 0.001$), and upper extremity lean mass (0.2 ± 0.2 kg vs. 0.1 ± 0.2 kg, $p = 0.03$) than the diet-exercise group over 6 months [94]. In a separate 4-month trial (mean age 67.2 ± 4.2 years), whole-body fat-free mass decreased significantly ($p < 0.05$) in the weight loss alone group (− 4.3 ± 1.2%) but not in the group coupled with exercise (− 1.1 ± 1.0%) [95].

Conflicting findings of the impact of weight loss on muscle strength exist. A 6-month weight loss intervention on muscle strength and quality in older obese adults with knee osteoarthritis noted that the weight loss group exhibited decreases in lean mass ($p < 0.001$) and increases in concentric muscle quality ($p < 0.05$), while concentric extension strength increased non-significantly, suggesting that reductions of lean mass may be overshadowed by maintenance in muscle strength and quality [96]. Rejeski et al. demonstrated that the addition of aerobic training or resistance training to caloric restriction led to greater weight loss and improved mobility among community-based older adults with overweight/obesity [73•]. Finally, a 5-month trial comparing the effects of caloric restriction (CR) and CR plus resistance training among 126 older (65–79 years) individuals with overweight/obesity found no between-group differences in change in knee extensor strength [97].

In summary, isolated caloric restriction could lead to loss of muscle mass and muscle strength. Loss of muscle mass and strength are strongly associated with increased risk of functional decline [98], institutionalization [99], and mortality [39••, 100]. Thus, efforts should guide the need to mitigate the impact of weight loss–induced sarcopenia.

Adverse Effects on Bone

Weight loss from isolated caloric restriction also has negative effects on bone mineral density (BMD) that can exacerbate age-related osteopenia by increasing the risk of fragility fractures [101]. A study of 1342 older men (mean age 73 ± 5.5 years) found that intentional weight loss was associated with an adjusted rate of change in total hip BMD of − 1.4% per year [102]. Similarly, intentional weight loss–induced bone loss exhibited subsequent hip fracture risk was 1.8 [1.43, 2.24] times more likely in women who lost weight compared with those with stable or increased weight, highlighting the increased risk for osteoporotic fractures in older adults losing weight [103]. In fact, significant weight loss (≥ 10%) in older women presents a clinically significant increased risk of fractures among older women (50–64 years, relative risk RR 2.54 [1.10, 5.86]; 65–74 years, 2.04 [1.37, 3.04]) [14, 104]. Consequences of fractures are especially important among older adults and vary from chronic pain and loss of independence to institutionalization and early mortality [105–107]. One year following hip fracture, 47% experience chronic pain [107] and 29% do not reach pre-fracture mobility [107, 108]. Within the first year following hip fracture, older adults have nearly a three-fold risk of death (HR 2.78 [2.12, 3.64]) [108].

A meta-analysis of 38 studies among individuals aged 18 years and older with overweight/obesity found significant reductions by 0.010 to 0.015 g/cm^2 in hip BMD after dietary weight loss interventions for 6 to 24 months [109]. Overall a reduction in hip BMD was observed (− 0.012 g/cm^2; $p = 0.04$). Loss of BMD at the lumbar spine was found in low to very low energy diets (− 0.031 g/cm^2, $p = 0.05$; < 5.0 MJ/day), but not in moderate energy-restricted diets (≥5.0 MJ/day). Further, both premenopausal and postmenopausal women exhibited overall loss of total body BMD, but it was only significant in postmenopausal women ($p = 0.006$).

Soltani analyzed the effect of 32 diet, exercise, or combined diet-exercise weight loss trials on BMD in adults 18 years and older [110]. The authors observed reductions in total body, hip, and lumbar spine BMD among participants in diet-only weight loss interventions, although significance was observed only at the hip and spine (total − 0.003 g/cm^2, $p = 0.14$; hip − 0.017 g/cm^2, $p < 0.001$; spine − 0.020 g/cm^2, $p < 0.001$). BMD at the hip and spine increased for participants in exercise-only weight loss programs (hip 0.005 g/cm^2, $p = 0.005$; spine 0.008 g/cm^2, $p = 0.027$), and increased at total body in the combined diet-exercise group (total 0.004 g/cm^2, $p = 0.009$). Exercise-only programs (− 0.561 kg, $p = 0.006$) did not result in as much overall weight loss as compared with diet-only programs (− 6.883 kg, $p < 0.001$); combined diet-exercise programs offered the greatest prospect of preserving BMD while still achieving meaningful weight loss (− 5.670 kg, $p < 0.001$). In a subanalysis of older adults (≥65 years), only reduction in hip BMD was statistically significant (mean difference − 0.011 (− 0.014, − 0.007); $p < 0.001$).

Bariatric surgery is an effective means in achieving profound weight loss even in older adults [111] and is a model to evaluate the effect of weight loss on BMD. A recent meta-analysis of 10 studies (mean age 33 to 58 years) evaluated BMD after surgery compared with non-surgical groups in adults [112]. While there was no overall differential reduction in BMD at the lumbar spine (− 0.01 g/cm^2 [− 0.07, 0.05]; $p = 0.66$), a reduction in BMD at the femoral neck was observed in the bariatric surgery group (− 0.05 g/cm^2 [− 0.07, − 0.02]; $p = 0.001$). While there are limited studies evaluating the risk of bariatric surgery in older adults on BMD [113], the above reviews provide important overviews of the mechanistic risks inherent to bone loss as a result of bariatric surgery, independent of age. Importantly, the included study results are limited by the heterogeneity of the widely varying methodologies. Below, we highlight salient findings from a number of trials exploring the effect of intentional weight loss on BMD.

A prospective cohort of 6785 older women demonstrated that unintentional and unstructured intentional weight loss led to osteopenia and increased risk of hip fracture [114]. The rate of bone loss in the weight loss group was nearly double that of the weight gain group, and 35% higher than in the weight-maintenance group ($p < 0.001$). The POUNDS LOST trial highlighted the sex-specific effects of diet-only weight loss interventions on BMD among 424 overweight and obese middle-aged and older adults [115]. While both sexes across all four diet-only groups demonstrated both weight loss and significant loss in BMD at the spine, hip, and femoral neck at the end of the 2-year trial, only women ($n = 242$) exhibited a significant, direct correlation between loss of lean mass and loss of BMD at these sites. Men ($n = 182$) exhibited an indirect, paradoxical relationship whereby lean mass decreased and BMD increased. Consequently, middle-aged women may be at a greater risk of bone loss during weight loss interventions than men (mean age 52 years), but sex-specific effects of weight loss interventions on BMD have not been demonstrably explored in older adults (≥ 65 years) [116].

In a 1-year study by Shah et al., 107 obese older adults were randomized to three intervention groups and a control arm [117]. Participants in the diet-only weight loss arm exhibited more loss of BMD at total hip (− 2.6%) compared with the diet-exercise and exercise groups (− 1.1% and + 1.5%; $p < 0.001$). The investigators noted the changes in lean mass predicted changes in BMD at the total hip ($p < 0.05$). In a smaller randomized trial of 48 overweight and obese adults (mean age 57 ± 3 years; mean BMI 27 ± 2 kg/m^2), participants in the exercise-only and diet-only groups showed similar, clinically significant weight loss (10.7 ± 6.3% vs. 8.4 ± 6.3%, respectively; $p = 0.21$). The diet-only group was found to have clinically and statistically significant decreases in BMD at the intertrochanter, total hip, and lumbar spine compared with the exercise-only and control groups, for which BMD remained constant or increased over the 1-year trial at all sites [118].

The Look AHEAD trial randomly allocated 5145 adults with overweight/obesity (mean age 59 years; mean BMI 36 kg/m^2) with type 2 diabetes to either an intensive lifestyle intervention comprising of diet and exercise (ILI) or a diabetes support and education (DSE) [71]. Over a median follow-up of 9.6 years, average weight loss was 6.0% and 3.5% in the ILI and DSE groups. Incident total or hip fracture rates did not differ between the groups, but ILI group had a 39% higher risk of fragility fracture.

Musculoskeletal Injuries

Musculoskeletal injuries are commonly observed during any exercise programs, and the risks of such should be clearly communicated to patients. In a review of adverse events reported by older adults engaging in resistance strength exercises, 68 relevant clinical trials reported on adverse events [119], the most common one being musculoskeletal. The 12-month incidence of exercise-related injuries was studied in 167 older adults (mean age 69 years) [120]. Investigators found that 13.8% reported an exercise-related injury over this period. Even in the LIFE trial [121], the risk ratio was non-significant between the physical activity and the health education group (0.91 [0.56, 1.47]). In the major weight loss trials, the main adverse events were also musculoskeletal [69••, 72, 73•, 75, 76•, 97].

Balancing the Benefits and Risks of Weight Loss with Clinician Monitoring

Focusing on weight loss and improvement in physical function in any multicomponent program through caloric restriction and combination aerobic and resistance exercises are key health promotion objectives for older adults. Our recommendations and guidelines parallel those from the evidence-based LIFE study [121] and are briefly summarized in Table 1.

Muscle strength is emerging as a better predictor than muscle mass for incident disability, physical function [43], and early mortality [100]. The ability to assess strength in clinical practice is a key component and can be conducted easily by clinic support staff to permit monitoring during weight loss efforts. We advise assessing two performance-based measures of upper and lower extremity strength at program onset and quarterly thereafter: handgrip strength and 30-s sit-to-stand. Muscle mass can be assessed using bioelectrical impedance or dual-energy x-ray absorptiometry (DXA). The former can be assessed in place of a regular scale; however, it is contraindicated in older adults with automated implantable defibrillators, fever > 39 °C, or abnormal hydration status. DXA provides additional diagnostic accuracy, is more affordable, and has much less radiation than computer tomography or magnetic resonance imaging. While many DXA scanners have embedded software to permit body composition assessment, reimbursement is possible only if performed for another Medicare-covered indication [122]. Promising markers including D3-creatine may permit ascertainment of muscle mass [123]. Further, the International Classification of Diseases Code for sarcopenia may potentially circumvent such issues in the future [123]. To our knowledge, there are no systematic data to suggest a frequency or timing of muscle mass or strength testing, nor are there thresholds at which practitioners should halt weight loss efforts due to loss of muscle mass.

DXA scans can be considered in the initial evaluation of older adults engaging in a weight loss program. CMS covers BMD testing in post-menopausal females aged 65 years and older every 24 months; in males, the indications are limited to prednisone usage, hyperparathyroidism, or x-ray evidence of osteoporosis, osteopenia, and vertebral fractures. In concert

Table 1 Management approach to weight loss–induced complications in older adults

System affected	Monitoring tools	Treatment options
Muscle	Body composition • DXA • BIA Performance measures • Grip strength • Sit-to-Stand Vitamin D levels	150 min of aerobic exercise activity Resistance exercise—2-3 days of weight-bearing exercises Protein supplementation 1.0–1.2 g/kg/day 1000 IU vitamin D or high-dose supplementation (if necessary)
Bone	Calcium supplementation Vitamin D levels Bone mineral density • DXA	800–1200 mg of calcium—preferably from diet 1000 IU vitamin D or high-dose supplementation (if necessary) Resistance exercise—2-3 days of weight-bearing exercises Osteoporosis therapies
Cardiovascular	Blood pressure	Medication adjustments
Blood glucose	Fasting or POC glucose	Medication adjustments
Musculoskeletal	Clinical, symptoms-based	Guided, incremental exercises, physical therapy referral

BIA, body impedance analysis; *DXA*, dual-energy x-ray absorptiometry

with other variables, DXA permits calculation of the FRAX score [124] which assists in risk-stratification. Clinicians can then promote supplementation with sufficient dosing of calcium or vitamin D or prescribe treatment if fracture risk is elevated (i.e., FRAX > 3% for hip, > 20% any fragility fracture) [125] at the onset of weight loss treatments.

As older adults have a disproportionate number of chronic medical conditions necessitating medications and other therapeutics, including hypertension, diabetes, and dyslipidemia, periodic medication monitoring during weight loss efforts may be indicated. Specifically, primary care providers should monitor antihypertensive and antidiabetic medications (specifically insulin) and encourage patients to communicate closely if downward trends in blood pressure or sugars are observed. Further, complications with antihypertensive medications could lead to greater reductions in blood pressure, impairing cerebral auto-regulatory mechanisms leading to hypotension, falls, and fractures [126]. For instance, in the TONE study, older adults (mean age 66.5 years) randomized to caloric-reduction required a reduction in their use of antihypertensive medications [127]. Patients with diabetes on glucose-lowering agents (including insulin derivatives) are at risk for hypoglycemic episodes. In the Look AHEAD trial, participants with type 2 diabetes on insulin or other antidiabetic medications in the diet-exercise intervention (mean age 59 years) were 8.02 [3.58, 17.95] times more likely to experience a severe hypoglycemic event compared with participants controlling diabetes with diet only [128]; age was not significant in the multivariable analysis. The diet-exercise intervention group was more likely to report severe hypoglycemia than controls in the first year (RR 3.7; $p = 0.023$), but was not different in ensuing years ($p = 0.41$). While older adults with diabetes generally accounted for only 17% of participants, in other geriatric weight loss studies, the rate of hypoglycemia is also low [73•, 75, 76•, 97, 129].

Providers should adhere to core geriatric principles, including "start low, go slow" for engaging in an exercise program. While the American College of Sports Medicine does not routinely recommend cardiovascular stress testing for older adults [130], symptomatic patients should be stratified accordingly by providers in advance of medical clearance. In those with pre-existing musculoskeletal impairments, we suggest referral to a physical therapist and/or an exercise physiologist at the local institution.

Research Gaps and Future Directions

The adverse implications of unintentional weight loss among older adults are well-established in terms of both poor health- and utilization-related outcomes [49], and the phenomenon appropriately alerts providers to the increased risk of serious underlying medical conditions. However, the long-term effects of intentional weight loss among older adults are not as definitive, especially in terms of cognition, quality of life, early institutionalization, and utilization. The lack of consensus regarding optimal body size and composition for older adults in various health circumstances begets a degree of clinical uncertainty regarding recommendations for intentional weight loss. Similarly, the specific nature, duration, and intensity of exercise programs (both aerobic and resistance) for mitigating adverse outcomes from intentional weight loss in older adults need consensus. Whether altering specific components of dietary composition could mitigate risks of muscle and bone changes is currently being investigated.

Future trials with larger sample sizes that include outcomes relevant to older adults within community-based and low-resource (e.g., rural) settings are needed. Such outcomes could focus not only on the efficacy of multicomponent weight-loss interventions on cognition, urinary incontinence, and falls but also on whether there are risks on these elements. Further, interventions evaluating structured, intentional weight loss in older adults have largely been underpowered to detect small yet clinically significant changes in bone or muscle health. Long-term interventional studies powered on changes in muscle mass, strength, and bone loss are critically needed to better understand weight loss–induced risks. Accurate proximal measures of bone and muscle health are also not well-established and would be valuable in clinical settings. Other treatment modalities, including pharmacotherapy and bariatric surgery, are not currently standard of care; however, as they are increasingly offered to older adults, studies should be designed to understand their safety and efficacy in this population.

Conclusion

Weight loss achieved with a comprehensive therapeutic intervention that combines caloric restriction, and aerobic and resistance exercise, can improve physical function and overall health in older adults. In older adults, the negative impact of weight loss achieved with caloric restriction only on muscle and bone physiology and subsequent physical function could be mitigated to some extent by the addition of resistance exercise. Future studies should not only focus on the impact of weight loss on important geriatric outcomes but also evaluate the risk of pragmatic interventions and natural experiments in usual clinical care that are often unstructured as compared with research-based studies. Future initiatives should develop guidelines for clinicians and researchers alike to maximize the health of older adults seeking weight loss efforts.

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Compliance with Ethical Standards

Conflict of Interest Peter R. DiMilia and Alexander Mittman declare that they have no conflict of interest.

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Human and Animal Rights and Informed Consent This article does not contain any procedures with human or animal subjects performed by any of the authors.

Abbreviations BMD, Bone mineral density; BMI, Body mass index; CMS, Center for Medicare and Medicaid; HR, Hazard ratio

References

Papers of particular interest, published recently, have been highlighted as:
• Of importance
•• Of major importance

1. Flegal KM, Graubard BI, Williamson DF, Gail MH. Excess deaths associated with underweight, overweight, and obesity. JAMA. 2005;293:1861–7.
2. Lubitz J, Cai L, Kramarow E, Lentzner H. Health, life expectancy, and health care spending among the elderly. N Engl J Med. 2003;349:1048–55.
3. West L, Cole S, Goodkind D, He W. US Census Bureau: 65+ in the United States: 2010. Washington, DC: US Department of Health and Human Services: National Institutes of Health; 2014.
4. Facts for Features: Older Americans Month: May 2017. In: Bureau USC (ed.). Census Bureau: Washington, DC 2019.
5. Ford ES, Ajani UA, Croft JB, Critchley JA, Labarthe DR, Kottke TE, et al. Explaining the decrease in U.S. deaths from coronary disease, 1980-2000. N Engl J Med. 2007;356:2388–98.
6. Ganguli I, Souza J, McWilliams JM, Mehrotra A. Trends in use of the US Medicare annual wellness visit, 2011-2014. JAMA. 2017;317:2233–5.
7. Batsis JA, Bynum JP. Uptake of the centers for Medicare and Medicaid obesity benefit: 2012-2013. Obesity (Silver Spring). 2016;24:1983–8.
8. Basu S, Phillips RS, Bitton A, Song Z, Landon BE. Medicare chronic care management payments and financial returns to primary care practices: a modeling study. Ann Intern Med. 2015;163: 580–8.
9.• Hales CM, Fryar CD, Carroll MD, Freedman DS, Ogden CL. Trends in obesity and severe obesity prevalence in US youth and adults by sex and age, 2007–2008 to 2015–2016. JAMA. 2018;319:1723–5 **Most recent prevalence rates of obesity within the USA demonstrating rising trends.**
10. Flegal KM, Carroll MD, Ogden CL, Curtin LR. Prevalence and trends in obesity among US adults, 1999-2008. JAMA. 2010;303: 235–41.
11. Ogden CL, Carroll MD, Curtin LR, McDowell MA, Tabak CJ, Flegal KM. Prevalence of overweight and obesity in the United States, 1999-2004. JAMA. 2006;295:1549–55.
12. Sayer AA, Syddall H, Martin H, Patel H, Baylis D, Cooper C. The developmental origins of sarcopenia. J Nutr Health Aging. 2008;12:427–32.
13. Yeap BB. Are declining testosterone levels a major risk factor for ill-health in aging men? Int J Impot Res. 2009;21:24–36.
14. Meyer HE, Tverdal A, Selmer R. Weight variability, weight change and the incidence of hip fracture: a prospective study of 39,000 middle-aged Norwegians. Osteoporos Int. 1998;8:373–8.
15. Fontenelle LC, Feitosa MM, Severo JS, Freitas TE, Morais JB, Torres-Leal FL, et al. Thyroid function in human obesity: underlying mechanisms. Horm Metab Res. 2016;48:787–94.
16. Conley KE, Esselman PC, Jubrias SA, Cress ME, Inglin B, Mogadam C, et al. Ageing, muscle properties and maximal O(2) uptake rate in humans. J Physiol. 2000;526(Pt 1):211–7.
17. Conley KE, Jubrias SA, Esselman PC. Oxidative capacity and ageing in human muscle. J Physiol. 2000;526(Pt 1):203–10.

18. Bauer J, Biolo G, Cederholm T, Cesari M, Cruz-Jentoft AJ, Morley JE, et al. Evidence-based recommendations for optimal dietary protein intake in older people: a position paper from the PROT-AGE Study Group. J Am Med Dir Assoc. 2013;14:542–59.
19. Kuk JL, Saunders TJ, Davidson LE, Ross R. Age-related changes in total and regional fat distribution. Ageing Res Rev. 2009;8:339–48.
20. Noppa H, Andersson M, Bengtsson C, Bruce A, Isaksson B. Longitudinal studies of anthropometric data and body composition. The population study of women in Gotenberg, Sweden. Am J Clin Nutr. 1980;33:155–62.
21. Katzman W, Cawthon P, Hicks GE, Vittinghoff E, Shepherd J, Cauley JA, et al. Association of spinal muscle composition and prevalence of hyperkyphosis in healthy community-dwelling older men and women. J Gerontol A Biol Sci Med Sci. 2012;67:191–5.
22. Demontiero O, Vidal C, Duque G. Aging and bone loss: new insights for the clinician. Ther Adv Musculoskelet Dis. 2012;4:61–76.
23. Cheng FW, Gao X, Mitchell DC, Wood C, Still CD, Rolston D, et al. Body mass index and all-cause mortality among older adults. Obesity (Silver Spring). 2016;24:2232–9.
24. Padwal R, Leslie WD, Lix LM, Majumdar SR. Relationship among body fat percentage, body mass index, and all-cause mortality: a cohort study. Ann Intern Med. 2016;164:532–41.
25. Batsis JA, Mackenzie TA, Bartels SJ, Sahakyan KR, Somers VK, Lopez-Jimenez F. Diagnostic accuracy of body mass index to identify obesity in older adults: NHANES 1999-2004. Int J Obes. 2016;40:761–7.
26. Alley DE, Chang VW. The changing relationship of obesity and disability, 1988-2004. JAMA. 2007;298:2020–7.
27. Rosemann T, Grol R, Herman K, Wensing M, Szecsenyi J. Association between obesity, quality of life, physical activity and health service utilization in primary care patients with osteoarthritis. Int J Behav Nutr Phys Act. 2008;5:4.
28. Elkins JS, Whitmer RA, Sidney S, Sorel M, Yaffe K, Johnston SC. Midlife obesity and long-term risk of nursing home admission. Obesity (Silver Spring). 2006;14:1472–8.
29. Zizza CA, Herring A, Stevens J, Popkin BM. Obesity affects nursing-care facility admission among whites but not blacks. Obes Res. 2002;10:816–23.
30. Stenholm S, Head J, Aalto V, Kivimaki M, Kawachi I, Zins M, et al. Body mass index as a predictor of healthy and disease-free life expectancy between ages 50 and 75: a multicohort study. Int J Obes. 2017;41:769–75.
31. Gregg EW, Cheng YJ, Cadwell BL, Imperatore G, Williams DE, Flegal KM, et al. Secular trends in cardiovascular disease risk factors according to body mass index in US adults. JAMA. 2005;293:1868–74.
32. Jehan S, Zizi F, Pandi-Perumal SR, Wall S, Auguste E, Myers AK, et al. Obstructive Sleep Apnea and Obesity: Implications for Public Health. Sleep Med Disord. 2017;1(4). pii: 00019.
33. Felson DT, Anderson JJ, Naimark A, Walker AM, Meenan RF. Obesity and knee osteoarthritis. The Framingham Study. Ann Intern Med. 1988;109:18–24.
34. Basen-Engquist K, Chang M. Obesity and cancer risk: recent review and evidence. Curr Oncol Rep. 2011;13:71–6.
35. Deckers. Obesity and cognitive decline in adults. J Nutr Health Aging. 2016.
36. Knudtson MD, Klein BE, Klein R, Shankar A. Associations with weight loss and subsequent mortality risk. Ann Epidemiol. 2005;15:483–91.
37. Blaum CS, Xue QL, Michelon E, Semba RD, Fried LP. The association between obesity and the frailty syndrome in older women: the Women's Health and Aging Studies. J Am Geriatr Soc. 2005;53:927–34.
38. Batsis JA, Mackenzie TA, Lopez-Jimenez F, Bartels SJ. Sarcopenia, sarcopenic obesity, and functional impairments in older adults: National Health and Nutrition Examination Surveys 1999-2004. Nutr Res. 2015;35:1031–9.
39.•• Batsis JA, Gill LE, Masutani RK, Adachi-Mejia AM, Blunt HB, Bagley PJ, et al. Weight loss interventions in older adults with obesity: a systematic review of randomized controlled trials since 2005. J Am Geriatr Soc. 2017;65:257–68 **A systematic review of randomized trials in older adults with obesity that demonstrates the importance of improved physical function after diet and exercise**.
40. Mei KL, Batsis JA, Mills JB, Holubar SD. Sarcopenia and sarcopenic obesity: do they predict inferior oncologic outcomes after gastrointestinal cancer surgery? Perioper Med (Lond). 2016;5:30.
41. Baumgartner RN, Wayne SJ, Waters DL, Janssen I, Gallagher D, Morley JE. Sarcopenic obesity predicts instrumental activities of daily living disability in the elderly. Obes Res. 2004;12:1995–2004.
42. Studenski SA, Peters KW, Alley DE, Cawthon PM, McLean RR, Harris TB, et al. The FNIH sarcopenia project: rationale, study description, conference recommendations, and final estimates. J Gerontol A Biol Sci Med Sci. 2014;69:547–58.
43. Cawthon PM, Travison TG, Manini TM, Patel S, Pencina KM, Fielding RA, et al. Establishing the link between lean mass and grip strength cut-points with mobility disability and other health outcomes: proceedings of the sarcopenia definition and outcomes consortium conference. J Gerontol A Biol Sci Med Sci. 2019. https://doi.org/10.1093/gerona/glz081.
44. Batsis JA, Barre LK, Mackenzie TA, Pratt SI, Lopez-Jimenez F, Bartels SJ. Variation in the prevalence of sarcopenia and sarcopenic obesity in older adults associated with different research definitions: dual-energy X-ray absorptiometry data from the National Health and Nutrition Examination Survey 1999-2004. J Am Geriatr Soc. 2013;61:974–80.
45. Cruz-Jentoft AJ, Bahat G, Bauer J, Boirie Y, Bruyère O, Cederholm T, et al. Sarcopenia: revised European consensus on definition and diagnosis. Age Ageing. 2019;48(1):16–31. https://doi.org/10.1093/ageing/afy169.
46.•• Batsis JA, Villareal DT. Sarcopenic obesity in older adults: aetiology, epidemiology and treatment strategies. Nat Rev Endocrinol. 2018;14:513–37 **A recent review article outlining the underlying pathophysiology and treatment strategies in older adults with sarcopenic obesity.**
47. Bosch X, Monclús E, Escoda O, Guerra-García M, Moreno P, Guasch N, et al. Unintentional weight loss: clinical characteristics and outcomes in a prospective cohort of 2677 patients. PLoS One. 2017;12:e0175125.
48. Kim M, Kim J, Won CW. Association between involuntary weight loss with low muscle mass and health-related quality of life in community-dwelling older adults: nationwide surveys (KNHANES 2008–2011). Exp Gerontol. 2018;106:39–45.
49. Gaddey HL, Holder K. Unintentional weight loss in older adults. Am Fam Physician. 2014;89:718–22.
50. Vellas B, Guigoz Y, Garry PJ, Nourhashemi F, Bennahum D, Lauque S, et al. The mini nutritional assessment (MNA) and its use in grading the nutritional state of elderly patients. Nutrition. 1999;15:116–22.
51. Huffman GB. Evaluating and treating unintentional weight loss in the elderly. Am Fam Physician. 2002;65:640–50.
52. Gruberg L, Weissman NJ, Waksman R, Fuchs S, Deible R, Pinnow EE, et al. The impact of obesity on the short-term and long-term outcomes after percutaneous coronary intervention: the obesity paradox? J Am Coll Cardiol. 2002;39:578–84.

53. Banack HR, Kaufman JS. Does selection bias explain the obesity paradox among individuals with cardiovascular disease? Ann Epidemiol. 2015;25:342–9.
54. Brida M, Dimopoulos K, Kempny A, Liodakis E, Alonso-Gonzalez R, Swan L, et al. Body mass index in adult congenital heart disease. Heart. 2017;103:1250–7.
55. Flegal KM, Graubard BI, Williamson DF, Cooper RS. Reverse causation and illness-related weight loss in observational studies of body weight and mortality. Am J Epidemiol. 2011;173:1–9.
56. Pocock SJ, McMurray JJ, Dobson J, Yusuf S, Granger CB, Michelson EL, et al. Weight loss and mortality risk in patients with chronic heart failure in the candesartan in heart failure: assessment of reduction in mortality and morbidity (CHARM) programme. Eur Heart J. 2008;29:2641–50.
57. Flegal KM, Ioannidis JPA. The obesity paradox: a misleading term that should be abandoned. Obesity (Silver Spring). 2018;26:629–30.
58. Park SY, Wilkens LR, Maskarinec G, Haiman CA, Kolonel LN, Marchand LL. Weight change in older adults and mortality: the multiethnic cohort study. Int J Obes. 2018;42:205–12.
59. Darmon P. Intentional weight loss in older adults: useful or wasting disease generating strategy? Curr Opin Clin Nutr Metab Care. 2013;16:284–9.
60. Wannamethee SG, Shaper AG, Lennon L. Reasons for intentional weight loss, unintentional weight loss, and mortality in older men. Arch Intern Med. 2005;165:1035–40.
61. Wannamethee SG, Shaper AG, Whincup PH, Walker M. Characteristics of older men who lose weight intentionally or unintentionally. Am J Epidemiol. 2000;151:667–75.
62. Wang S, Ren J. Obesity paradox in aging: from prevalence to pathophysiology. Prog Cardiovasc Dis. 2018;61:182–9.
63.•• Khan SS, Ning H, Wilkins JT, Allen N, Carnethon M, Berry JD, et al. Association of body mass index with lifetime risk of cardiovascular disease and compression of morbidity. JAMA Cardiol. 2018;3:280–7 **This report aggregates ten cardiovascular studies providing data that disproves the obesity paradox.**
64. Felix HC, West DS. Effectiveness of weight loss interventions for obese older adults. Am J Health Promot. 2013;27:191–9.
65. Schutzer KA, Graves BS. Barriers and motivations to exercise in older adults. Prev Med. 2004;39:1056–61.
66. Guralnik JM, LaCroix AZ, Branch LG, Kasl SV, Wallace RB. Morbidity and disability in older persons in the years prior to death. Am J Public Health. 1991;81:443–7.
67. Jette AM, Branch LG. Impairment and disability in the aged. J Chronic Dis. 1985;38:59–65.
68. Haywood C, Sumithran P. Treatment of obesity in older persons—a systematic review. Obes Rev. 2019;20:588–98.
69.•• Villareal DT, Aguirre L, Gurney AB, Waters DL, Sinacore DR, Colombo E, et al. Aerobic or resistance exercise, or both in dieting obese older adults. N Engl J Med. 2017;376:1943–55 **A 1-year multicomponent caloric restriction and exercise trial of frail older adults with obesity demonstrating the synergistic improvements in physical function after weight loss and exercise.**
70.• Kritchevsky SB, Beavers KM, Miller ME, Shea MK, Houston DK, Kitzman DW, et al. Intentional weight loss and all-cause mortality: a meta-analysis of randomized clinical trials. PLoS One. 2015;10:e0121993 **A meta-analysis evaluating randomized trials of weight loss interventions in older adults on risk of future death.**
71. Johnson KC, Bray GA, Cheskin LJ, Clark JM, Egan CM, Foreyt JP, et al. The effect of intentional weight loss on fracture risk in persons with diabetes: results from the Look AHEAD randomized clinical trial. J Bone Miner Res. 2017;32:2278–87.
72. Villareal DT, Chode S, Parimi N, Sinacore DR, Hilton T, Armamento-Villareal R, et al. Weight loss, exercise, or both and physical function in obese older adults. N Engl J Med. 2011;364:1218–29.
73.• Rejeski WJ, Ambrosius WT, Burdette JH, Walkup MP, Marsh AP. Community weight loss to combat obesity and disability in at-risk older adults. J Gerontol A Biol Sci Med Sci. 2017;72:1547–53 **An 18-month, community-based, randomized trial of older adults at a YMCA that demonstrated weight loss and enhanced improvements in mobility when dietary weight-loss is coupled with resistance or aerobic training.**
74. Messier SP, Mihalko SL, Legault C, Miller GD, Nicklas BJ, DeVita P, et al. Effects of intensive diet and exercise on knee joint loads, inflammation, and clinical outcomes among overweight and obese adults with knee osteoarthritis: the IDEA randomized clinical trial. JAMA. 2013;310:1263–73.
75. Nicklas BJ, Brinkley TE, Houston DK, Lyles MF, Hugenschmidt CE, Beavers KM, et al. Effects of caloric restriction on cardiorespiratory fitness, fatigue, and disability responses to aerobic exercise in older adults with obesity: a randomized controlled trial. J Gerontol A Biol Sci Med Sci. 2019;74:1084–1090.
76.• Ard JD, Gower B, Hunter G, Ritchie CS, Roth DL, Goss A, et al. Effects of calorie restriction in obese older adults: the CROSSROADS randomized controlled trial. J Gerontol A Biol Sci Med Sci. 2017;73(1):73–80. https://doi.org/10.1093/gerona/glw237 **A 52-week randomized trial of older adults with obesity that demonstated reductions in overall fat and cardiovascular risk factors without significantly more adverse events.**
77. Look ARG. Eight-year weight losses with an intensive lifestyle intervention: the look AHEAD study. Obesity (Silver Spring). 2014;22:5–13.
78. Knowler WC, Barrett-Connor E, Fowler SE, Hamman RF, Lachin JM, Walker EA, et al. Reduction in the incidence of type 2 diabetes with lifestyle intervention or metformin. N Engl J Med. 2002;346:393–403.
79. So ES. The impacts of weight change and weight change intention on health-related quality of life in the Korean elderly. J Aging Health. 2018. https://doi.org/10.1177/0898264318761908.
80. Napoli N, Shah K, Waters DL, Sinacore DR, Qualls C, Villareal DT. Effect of weight loss, exercise, or both on cognition and quality of life in obese older adults. Am J Clin Nutr. 2014;100:189–98.
81. Bosy-Westphal A, Kossel E, Goele K, Later W, Hitze B, Settler U, et al. Contribution of individual organ mass loss to weight loss-associated decline in resting energy expenditure. Am J Clin Nutr. 2009;90:993–1001.
82. Coutinho T, Goel K, Correa de Sa D, Carter RE, Hodge DO, Kragelund C, et al. Combining body mass index with measures of central obesity in the assessment of mortality in subjects with coronary disease: role of "normal weight central obesity". J Am Coll Cardiol. 2013;61:553–60.
83. Groessl EJ, Kaplan RM, Rejeski WJ, Katula JA, King AC, Frierson G, et al. Health-related quality of life in older adults at risk for disability. Am J Prev Med. 2007;33:214–8.
84. Sao Romao Preto L, Dias Conceicao MDC, Figueiredo TM, Pereira Mata MA, Barreira Preto PM, Mateo Aguilar E. Frailty, body composition and nutritional status in non-institutionalised elderly. Enferm Clin. 2017;27:339–45.
85.•• Li R, Xia J, Zhang XI, Gathirua-Mwangi WG, Guo J, Li Y, et al. Associations of muscle mass and strength with all-cause mortality among US older adults. Med Sci Sports Exerc. 2018;50:458–67 **Using epidemiologic data, these authors applied the recent cutoffs for sarcopenia and found that strength was more predictive of mortality than muscle mass.**
86. Welch C, Hassan-Smith ZK, Greig CA, Lord JM, Jackson TA. Acute sarcopenia secondary to hospitalisation - an emerging condition affecting older adults. Aging Dis. 2018;9:151–64.

87. English KL, Paddon-Jones D. Protecting muscle mass and function in older adults during bed rest. Curr Opin Clin Nutr Metab Care. 2010;13:34–9.
88. Zibellini J, Seimon RV, Lee CM, Gibson AA, Hsu MS, Sainsbury A. Effect of diet-induced weight loss on muscle strength in adults with overweight or obesity - a systematic review and meta-analysis of clinical trials. Obes Rev. 2016;17:647–63.
89. Weinheimer EM, Sands LP, Campbell WW. A systematic review of the separate and combined effects of energy restriction and exercise on fat-free mass in middle-aged and older adults: implications for sarcopenic obesity. Nutr Rev. 2010;68:375–88.
90. Weiss EP, Jordan RC, Frese EM, Albert SG, Villareal DT. Effects of weight loss on lean mass, strength, bone, and aerobic capacity. Med Sci Sports Exerc. 2017;49:206–17.
91. Gallagher D, Kelley DE, Thornton J, Boxt L, Pi-Sunyer X, Lipkin E, et al. Changes in skeletal muscle and organ size after a weight-loss intervention in overweight and obese type 2 diabetic patients. Am J Clin Nutr. 2017;105:78–84.
92. Weiss EP, Albert SG, Reeds DN, Kress KS, Ezekiel UR, McDaniel JL, et al. Calorie restriction and matched weight loss from exercise: independent and additive effects on glucoregulation and the incretin system in overweight women and men. Diabetes Care. 2015;38:1253–62.
93. Weiss EP, Racette SB, Villareal DT, Fontana L, Steger-May K, Schechtman KB, et al. Lower extremity muscle size and strength and aerobic capacity decrease with caloric restriction but not with exercise-induced weight loss. J Appl Physiol (1985). 2007;102: 634–40.
94. Frimel TN, Sinacore DR, Villareal DT. Exercise attenuates the weight-loss-induced reduction in muscle mass in frail obese older adults. Med Sci Sports Exerc. 2008;40:1213–9.
95. Chomentowski P, Dube JJ, Amati F, Stefanovic-Racic M, Zhu S, Toledo FG, et al. Moderate exercise attenuates the loss of skeletal muscle mass that occurs with intentional caloric restriction-induced weight loss in older, overweight to obese adults. J Gerontol A Biol Sci Med Sci. 2009;64:575–80.
96. Wang X, Miller GD, Messier SP, Nicklas BJ. Knee strength maintained despite loss of lean body mass during weight loss in older obese adults with knee osteoarthritis. J Gerontol A Biol Sci Med Sci. 2007;62:866–71.
97. Nicklas BJ, Chmelo E, Delbono O, Carr JJ, Lyles MF, Marsh AP. Effects of resistance training with and without caloric restriction on physical function and mobility in overweight and obese older adults: a randomized controlled trial. Am J Clin Nutr. 2015;101: 991–9.
98. Schaap LA, Koster A, Visser M. Adiposity, muscle mass, and muscle strength in relation to functional decline in older persons. Epidemiol Rev. 2013;35:51–65.
99. Cooper R, Kuh D, Cooper C, Gale CR, Lawlor DA, Matthews F, et al. Objective measures of physical capability and subsequent health: a systematic review. Age Ageing. 2011;40:14–23.
100. Li R, Xia J, Zhang XI, Gathirua-Mwangi WG, Guo J, Li Y, et al. Associations of muscle mass and strength with all-cause mortality among US older adults. Med Sci Sports Exerc. 2018;50:458–67.
101. Shapses SA, Riedt CS. Bone, body weight, and weight reduction: what are the concerns? J Nutr. 2006;136:1453–6.
102. Ensrud KE, Fullman RL, Barrett-Connor E, Cauley JA, Stefanick ML, Fink HA, et al. Voluntary weight reduction in older men increases hip bone loss: the osteoporotic fractures in men study. J Clin Endocrinol Metab. 2005;90:1998–2004.
103. Ensrud KE, Ewing SK, Stone KL, Cauley JA, Bowman PJ, Cummings SR, et al. Intentional and unintentional weight loss increase bone loss and hip fracture risk in older women. J Am Geriatr Soc. 2003;51:1740–7.
104. Langlois JA, Mussolino ME, Visser M, Looker AC, Harris T, Madans J. Weight loss from maximum body weight among middle-aged and older white women and the risk of hip fracture: the NHANES I epidemiologic follow-up study. Osteoporos Int. 2001;12:763–8.
105. Johnell O, Kanis JA. An estimate of the worldwide prevalence and disability associated with osteoporotic fractures. Osteoporos Int. 2006;17:1726–33.
106. Sanchez-Riera L, Wilson N. Fragility fractures & their impact on older people. Best Pract Res Clin Rheumatol. 2017;31:169–91.
107. Bertram M, Norman R, Kemp L, Vos T. Review of the long-term disability associated with hip fractures. Inj Prev. 2011;17:365–70.
108. Sernbo I, Johnell O. Consequences of a hip fracture: a prospective study over 1 year. Osteoporos Int. 1993;3:148–53.
109. Zibellini J, Seimon RV, Lee CM, Gibson AA, Hsu MS, Shapses SA, et al. Does diet-induced weight loss Lead to bone loss in overweight or obese adults? A systematic review and meta-analysis of clinical trials. J Bone Miner Res. 2015;30:2168–78.
110. Soltani S, Hunter GR, Kazemi A, Shab-Bidar S. The effects of weight loss approaches on bone mineral density in adults: a systematic review and meta-analysis of randomized controlled trials. Osteoporos Int. 2016;27:2655–71.
111. Batsis JA, Miranda WR, Prasad C, Collazo-Clavell ML, Sarr MG, Somers VK, et al. Effect of bariatric surgery on cardiometabolic risk in elderly patients: a population-based study. Geriatr Gerontol Int. 2016;16:618–24.
112. Ko BJ, Myung SK, Cho KH, Park YG, Kim SG, Kim do H, et al. Relationship between bariatric surgery and bone mineral density: a meta-analysis. Obes Surg. 2016;26:1414–21.
113. Gagnon C, Schafer AL. Bone health after bariatric surgery. JBMR plus. 2018;2:121–33.
114. Ensrud KE, Ewing SK, Stone KL, Cauley JA, Bowman PJ, Cummings SR, et al. Intentional and unintentional weight loss increase bone loss and hip fracture risk in older women. J Am Geriatr Soc. 2003;51:1740–7.
115. Tirosh A, de Souza RJ, Sacks F, Bray GA, Smith SR, LeBoff MS. Sex differences in the effects of weight loss diets on bone mineral density and body composition: POUNDS LOST trial. J Clin Endocrinol Metab. 2015;100:2463–71.
116. Weaver AA, Houston DK, Shapses SA, Lyles MF, Henderson RM, Beavers DP, et al. Effect of a hypocaloric, nutritionally complete, higher-protein meal plan on bone density and quality in older adults with obesity: a randomized trial. Am J Clin Nutr. 2019;109:478–86.
117. Shah K, Armamento-Villareal R, Parimi N, Chode S, Sinacore DR, Hilton TN, et al. Exercise training in obese older adults prevents increase in bone turnover and attenuates decrease in hip bone mineral density induced by weight loss despite decline in bone-active hormones. J Bone Miner Res. 2011;26:2851–9.
118. Villareal DT, Fontana L, Weiss EP, Racette SB, Steger-May K, Schechtman KB, et al. Bone mineral density response to caloric restriction-induced weight loss or exercise-induced weight loss: a randomized controlled trial. Arch Intern Med. 2006;166:2502–10.
119. Liu CJ, Latham N. Adverse events reported in progressive resistance strength training trials in older adults: 2 sides of a coin. Arch Phys Med Rehabil. 2010;91:1471–3.
120. Little RM, Paterson DH, Humphreys DA, Stathokostas L. A 12-month incidence of exercise-related injuries in previously sedentary community-dwelling older adults following an exercise intervention. BMJ Open. 2013;3:e002831.
121. Pahor M, Guralnik JM, Ambrosius WT, Blair S, Bonds DE, Church TS, et al. Effect of structured physical activity on prevention of major mobility disability in older adults: the LIFE study randomized clinical trial. JAMA. 2014;311:2387–96.
122. Bone mass measurements. Centers for Medicare and Medicaid Services: 2019.
123. Clark RV, Walker AC, Miller RR, O'Connor-Semmes RL, Ravussin E, Cefalu WT. Creatine (methyl-d3) dilution in urine

for estimation of total body skeletal muscle mass: accuracy and variability vs. MRI and DXA. J Appl Physiol (1985). 2018;124: 1–9.
124. Kanis JA, Johnell O, Oden A, Johansson H, McCloskey E. FRAX and the assessment of fracture probability in men and women from the UK. Osteoporos Int. 2008;19:385–97.
125. Viswanathan M, Reddy S, Berkman N, Cullen K, Middleton JC, Nicholson WK, et al. Screening to prevent osteoporotic fractures: updated evidence report and systematic review for the US preventive services task ForceUSPSTF evidence report: screening to prevent osteoporotic FracturesUSPSTF evidence report: screening to prevent osteoporotic fractures. JAMA. 2018;319:2532–51.
126. Mol A, Bui Hoang PTS, Sharmin S, Reijnierse EM, van Wezel RJA, Meskers CGM, et al. Orthostatic hypotension and falls in older adults: a systematic review and meta-analysis. J Am Med Dir Assoc. 2019;20:589–97.e5.
127. Whelton PK, Appel LJ, Espeland MA, Applegate WB, Ettinger WH Jr, Kostis JB, et al. Sodium reduction and weight loss in the treatment of hypertension in older persons: a randomized controlled trial of nonpharmacologic interventions in the elderly (TONE). TONE Collaborative Research Group. JAMA. 1998;279:839–46.
128. Look AHEAD Research Group, Greenway FL. Severe hypoglycemia in the Look AHEAD trial. J Diabetes Complicat. 2016;30: 935–43.
129. Beavers KM, Beavers DP, Nesbit BA, Ambrosius WT, Marsh AP, Nicklas BJ, et al. Effect of an 18-month physical activity and weight loss intervention on body composition in overweight and obese older adults. Obesity (Silver Spring). 2014;22:325–31.
130. Riebe D, Franklin BA, Thompson PD, Garber CE, Whitfield GP, Magal M, et al. Updating ACSM's recommendations for exercise preparticipation health screening. Med Sci Sports Exerc. 2015;47: 2473–9.