CURRENT OPINION

Therapeutic and lifestyle approaches to obesity in older persons

Bryan C. Jiang[a,b] and Dennis T. Villareal[a,b]

Purpose of review
Obesity rates worldwide continue to increase and will disproportionately affect older adults because of population aging. This review highlights recent progress pertaining to therapeutic approaches to obesity in older adults.

Recent findings
Caloric restriction alone improves physical function and quality of life in older adults with obesity but is associated with loss of lean mass and increases fracture risk. Adding progressive resistance training to caloric restriction attenuates loss of muscle and bone mass and increasing protein intake enhances this effect. Adding aerobic endurance training to caloric restriction further improves cardiorespiratory fitness but adding both aerobic endurance training and resistance training to caloric restriction results in the greatest improvement in overall physical function while still preserving lean mass. Future promising therapeutic interventions include testosterone, myostatin inhibitors, and bariatric surgery, but there are few studies specific to obese older adults.

Summary
The optimal approach toward obesity in older persons is lifestyle intervention incorporating caloric restriction and exercise consisting of aerobic endurance training and resistance training. Maintenance of adequate protein intake, calcium, and vitamin D is advisable. There is insufficient evidence specific to obese older adults to recommend testosterone or bariatric surgery at this time. Myostatin inhibitors may become a future treatment, and clinical trials are ongoing.

Keywords
caloric restriction, exercise, obesity, older adults, weight loss

INTRODUCTION

The population of older adults (≥65 years) worldwide currently stands at just under 1 billion and is expected to double within the next 30 years. In Europe today, one in four adults is over the age of 65 years; however, this ratio is anticipated to be one in two by 2050 [1]. Coinciding with the future aging of the population is the ongoing public health epidemic of obesity (BMI $\geq 30\,kg/m^2$), which has already tripled in prevalence globally within the past 40 years [2]. In the United States, which has the highest population of obese individuals today, 41% of older adults are currently obese and trends suggest the rate will continue to increase [3,4].

Obesity is associated with multiple chronic diseases including hypertension, diabetes, heart disease, stroke, and cancer and has been shown to decrease quality of life and life expectancy. For older adults, obesity synergistically exacerbates the age-related decline in muscle mass and physical function (sarcopenia) causing frailty, an increase in institutionalization rates, and greater healthcare costs [5]. Despite the inevitability of this looming public health issue, there remains a concerning dearth of knowledge regarding the best therapeutic approaches for managing obesity in older persons [6■■], especially for sarcopenic obese individuals who suffer the worst of both conditions [7].

The current review summarizes updates from the most recent literature pertaining to both lifestyle and pharmacological interventions for combating obesity in older persons. We also address the

[a]Center for Translational Research on Inflammatory Diseases (CTRID), Michael E. DeBakey VA Medical Center and [b]Department of Medicine – Endocrinology, Diabetes, and Metabolism, Baylor College of Medicine, Houston, Texas, USA

Correspondence to Dennis T. Villareal, MD, Baylor College of Medicine, Michael E. DeBakey VA Medical Center, 2002 Holcombe Blvd., Houston, TX 77030, USA. E-mail: Dennis.Villareal@bcm.edu

Curr Opin Clin Nutr Metab Care 2019, 22:30–36

DOI:10.1097/MCO.0000000000000520

KEY POINTS

- The foundation of obesity management in older adults is lifestyle intervention incorporating caloric restriction-induced weight loss with physical activity consisting of aerobic endurance training and progressive resistance training.
- Adequate vitamin D and calcium supplementation in addition to a daily protein intake of ~1.2 g/kg of body weight is recommended in the setting of lifestyle intervention to maximally preserve muscle mass and bone mineral density during caloric restriction.
- Caloric restriction alone is associated with loss of muscle and bone mass which can exacerbate sarcopenia and increase the risk of fractures in obese older adults.
- Further investigation is required before recommending other therapies for obesity in older adults such as bariatric surgery, testosterone, and myostatin inhibitors.

latest evidence surrounding the safety of intentional weight loss interventions in the elderly obese population.

CALORIC RESTRICTION

Clinically significant weight loss is not only achievable in the obese older adults, but evidence suggests that increasing age is a strong predictor of adherence to lifestyle interventions in both men and women [8,9]. In multiple randomized controlled trials (RCTs), caloric restriction ranging from 500 to 1000 kcal/day deficits with or without concurrent exercise training is effective at inducing weight loss [6▪▪]. Early evidence also suggests that an intervention with a very low calorie diet (intake of as little as 800 kcal/day) was tolerated in older adults and resulted in 11.1% decrease in body weight over 12 weeks [10▪].

Caloric restriction alone improves measurable outcomes of physical function and quality of life; however, it has also consistently been shown to decrease lean body mass and bone mineral density (BMD) at the hip assessed by dual-energy X-ray absorptiometry [6▪▪]. Although caloric restriction is the first therapeutic option for the treatment of obesity in the general population, there are concerns that this approach may be harmful in older adults because of associated loss of muscle and bone mass, which can further exacerbate sarcopenia and increase fracture risk [11]. The most recent iteration of the American Heart Association/American College of Cardiology/ The Obesity Society guidelines for the management of obesity states 'the overall safety of weight loss interventions for patients aged 65 and older remains controversial' and '...there is a need for further research to understand the most appropriate strategies and prescriptions for weight loss for some key populations including older adults' [12].

These concerns were reinforced in recently published data from the Look AHEAD (Action for Health in Diabetes) trial, which is the first RCT to show an increased risk of frailty fractures with caloric restriction in obese older adults [13▪▪]. A significant 39% increase in frailty fractures was noted in the group receiving intensive lifestyle intervention (ILI) compared with the weight-neutral group receiving standard of care after a median follow-up time of 11.3 years. This increase in frailty fractures occurred despite previously documented improvements in physical fitness in the ILI group and highlights the potential risks of weight loss in the older population.

EXERCISE TRAINING

Exercise incorporating aspects of both aerobic endurance training and progressive resistance training does not result in significant weight loss in the absence of caloric restriction, but it does exert positive effects on body composition, improve physical function, increase strength, and positively affect quality of life in aging adults with obesity [6▪▪]. A recent study showed that even older adults with class 2+ obesity (BMI $\geq$ 35 kg/m^2) can safely perform moderate intensity physical activity and benefit in terms of mobility [14▪]. Although caloric restriction and exercise both individually improve physical function and quality of life, caloric restriction with concurrent exercise training yields better results than either modality alone [15]. Furthermore, the addition of exercise to caloric restriction has been shown to attenuate, though not completely alleviate, loss of muscle mass and BMD.

Recent studies have also focused on the effects of specific exercise modalities – resistance training and aerobic endurance training. An 18-month RCT studying the effect of caloric restriction, caloric restriction and resistance training, or caloric restriction and aerobic endurance training on body composition in 249 obese older adults found that addition of either exercise regimen to caloric restriction resulted in greater loss of total body mass; however, caloric restriction and resistance training preserved fat-free mass more than caloric restriction and aerobic endurance training [16▪]. These conclusions are supported by data from two separate 5-month RCTs in overweight and obese older adults comparing the effect of caloric restriction and resistance training or caloric restriction and aerobic endurance training on BMD, suggesting that resistance training attenuates loss of hip BMD during caloric restriction but aerobic endurance training does not [17]. Although these findings suggest that resistance training in particular is crucial in mitigating the negative effects of caloric restriction on fat-free mass, the beneficial effects of aerobic endurance training in the setting of caloric restriction have also been highlighted recently. A 20-week RCT studying cardiorespiratory fitness, fatigue, and disability in 180 obese older men and women undergoing aerobic endurance training alone, with moderate (−250 kcal/day) caloric restriction, or with intensive (−600 kcal/day) caloric restriction found that the addition of moderate or intensive caloric restriction to aerobic endurance training equally improves peak oxygen consumption compared to aerobic endurance training alone [18▪].

We recently reported the results of a 6-month RCT involving 160 obese older men and women with the aim to directly compare the effects of aerobic endurance training, resistance training, or combined training added to matched caloric restriction-induced weight loss (Fig. 1) [19▪]. Physical function assessed by the modified physical performance test improved more in combined training compared to aerobic endurance training or resistance training. Peak oxygen consumption improved equally in aerobic endurance training and combined training, which was greater than the improvement seen in resistance training. Decreases in lean body mass and hip BMD were noted in all intervention groups but was less in resistance training and combined training compared to aerobic endurance training. Muscle strength increased equally in resistance training and combined training, whereas it was only maintained in aerobic endurance training. Dynamic balance assessed by the obstacle course completion time and gait speed improved more in combined training compared to aerobic endurance training or resistance training. These findings indicate additive effects of resistance training and aerobic endurance training on physical function without interference effect from concurrent training in these obese older adults [20,21].

The current evidence suggests that obese older adults undertaking caloric restriction should participate in both aerobic endurance training and resistance training, which is consistent with the most recent physical activity recommendations by the American Heart Association and American College of Sports Medicine for overall health in the general population [22]. Local community weight loss programs incorporating exercise can be very successful in this population and significantly improves mobility [23▪▪]. We anticipate that these interventions will become increasingly easy to adapt to in community fitness centers and sports clubs as many nations are now adopting more policies to promote health-enhancing physical activity in an effort to combat rising obesity rates [24].

CALCIUM AND VITAMIN D SUPPLEMENTATION

The American Geriatrics Society currently recommends 1000 IU of vitamin D/day in addition to calcium supplementation in all noninstitutionalized older adults [25]. We agree with this recommendation and emphasize that in obese older adults actively undergoing caloric restriction, supplementation of calcium, up to 1200 mg daily, and vitamin D_3 is crucial to minimize the associated loss of BMD. The majority of RCTs involving clinically significant weight loss in obese older adults have employed routine supplementation in their study protocols [6▪▪,15,16▪,17,18▪,19▪].

PROTEIN INTAKE

The Institute of Medicine recommended daily allowance (RDA) of protein intake is 0.8 g/kg/day for all adults regardless of age, but many experts and national organizations currently advocate for a daily protein intake of 1.2 g/kg/day or even higher in older adults on the basis of prior evidence suggesting that skeletal muscle in the elderly has a blunted anabolic response to dietary protein [26]. A well designed 6-month RCT in older men with moderate limitations in physical function found no improvement in lean body mass, muscle strength, or physical function when daily protein intake was increased from 0.8 to 1.3 g/kg/day [27▪▪]. A 10-week study found that older adults undertaking caloric restriction for obesity saw no improvement in fat-free mass with higher protein intake or with resistance training; however, the combination of both high protein intake and resistance training did lead to improved fat-free mass [28▪▪]. These recent trials suggest that the RDA for protein intake of 0.8 g/kg/day is adequate for older adults in most situations, and ∼1.2 g/kg/day of protein intake may be beneficial in the setting of caloric restriction and resistance training in obese older adults.

TESTOSTERONE

Both total and free testosterone levels fall with increasing age in men in a pattern that parallels the gradual loss lean mass and increase in adiposity also seen in aging [29]. Comorbidities including obesity are known to accelerate this age-related decline. Based on these observations, testosterone replacement may be a therapeutic option to reverse

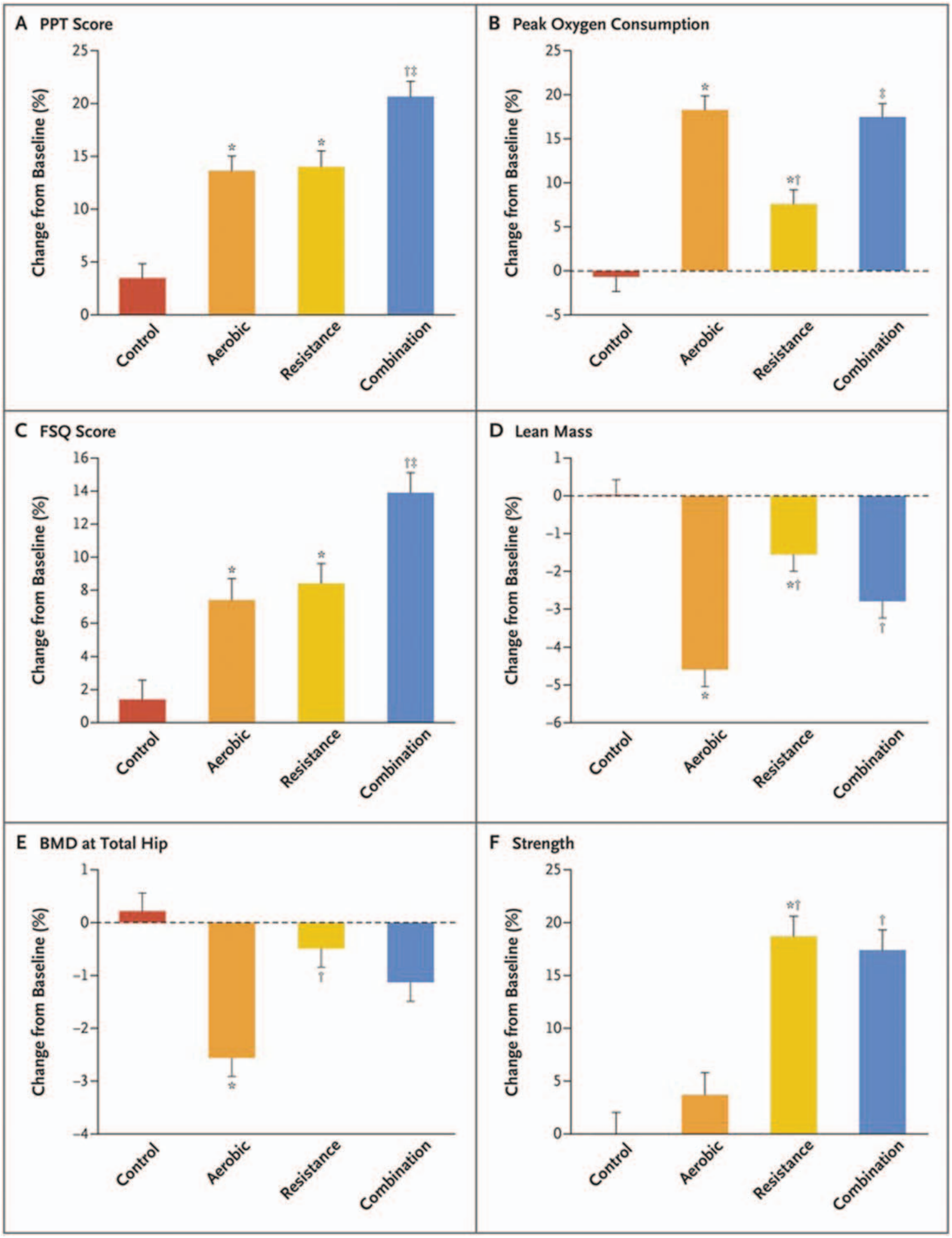

FIGURE 1. Mean percentage changes in physical function, lean mass, and bone mineral density at the total hip during the interventions. Measures of physical function included the Physical Performance Test (PPT; scores range from 0 to 36, with higher scores indicating better functional status), peak oxygen consumption, Functional Status Questionnaire (FSQ; scores range from 0 to 36, with higher scores indicating better functional status), and strength [measured as total one-repetition maximum (i.e., the total of the maximum weight a participant can lift, in one attempt, in the biceps curl, bench press, seated row, knee extension, knee flexion, and leg press)]. Scores on the PPT were used as an objective measure of frailty (primary outcome), and scores on the FSQ were used as a subjective measure of frailty. The asterisk indicates $P < 0.05$ for the comparison with the control group, the dagger $P < 0.05$ for the comparison with the aerobic group, and the double dagger $P < 0.05$ for the comparison with the resistance group. Percentage changes are presented as least-squares–adjusted means; T bars indicate standard errors. Reprinted with permission [19▪].

the negative trends in body composition in aging men [30]. A series of seven coordinated RCTs involving 788 hypogonadal older men (63% with BMI $\geq 30\,kg/m^2$) who received testosterone gel or placebo for a year was completed to clarify the potential benefits [31▪]. The trial authors recently reviewed their conclusions which found that volunteers on testosterone were noted to have small improvements in walking distance and markedly increased volumetric bone density and estimated strength relative to volunteers taking placebo.

Testosterone has recently been shown to protect against loss of lean mass during weight loss in hypogonadal obese middle-aged men (aged 50 years or older) undergoing caloric restriction. A 56-week trial found that testosterone administration during weight loss led to a reduction in loss of lean mass and an increase in fat loss despite similar overall weight loss compared to placebo [32]. Unfortunately, the favorable changes in body composition seen at the conclusion were no longer apparent over a year after discontinuation of testosterone [33▪▪]. Although still a promising future therapy, further research is needed to clarify the benefits and risks of testosterone specifically in obese older adults during weight loss therapy.

BARIATRIC SURGERY

A survey suggests that almost 600 000 bariatric surgery procedures were conducted worldwide in 2014 with sleeve gastrectomy (45.9%) and Roux-en-Y gastric bypass (RYGB) (39.6%) being the most popular procedures [34]. Both sleeve gastrectomy and RYGB are effective in older adults at inducing significant weight loss and reducing obesity-associated comorbidities [35]. RYGB appears to be particularly effective at inducing weight loss in older adults compared with sleeve gastrectomy [36▪]; however, older individuals undergoing RYGB have been noted to have an increased risk of nearly all perioperative complications associated with laparoscopic bariatric surgery and longer hospital stays [37]. Despite these findings, older bariatric patients still have a reduced rate of hospitalization following surgery and no difference in 30-day morality rates [38▪].

Additional concerns regarding bariatric surgery center around the loss of lean body mass and BMD associated with the profound weight loss following the surgery, which would be particularly detrimental in older adults. In middle-aged adults, one study found minimal loss of lean body mass 5 years after bariatric surgery despite significant overall weight loss [39]. On the other hand, patients undergoing RYGB were noted to have ongoing declines in estimated bone strength at the radius and tibia even after weight stabilization [40]. Furthermore, a retrospective analysis found that RYGB was not only associated with an increased risk of falls and fractures that increased with time, but these risks also had no association with weight lost or calcium and vitamin D supplementation [41▪▪]. Given these findings, extreme caution should be exercised before promoting weight loss surgery in older adults until further research can clarify the potential risks and benefits.

MYOSTATIN INHIBITORS

Produced in skeletal muscle and adipose tissue, myostatin (also known as growth and differentiation factor 8) is a part of the transforming growth factor beta superfamily of secreted growth factors which has been shown to act as a negative regulator of muscle growth [42▪▪]. Myostatin levels are known to be elevated in atrophied skeletal muscle in both animals and humans. Significant skeletal muscle hypertrophy and hyperplasia has been shown to occur in loss-of-function mutations in myostatin in cases involving humans and a variety of animals including cattle, mice, and dogs. Similar findings were also shown in mouse skeletal muscle overexpressing the myostatin inhibitor follistatin and in cases involving inactivating mutations in the primary myostatin receptor activin receptor IIB [43]. These findings suggest that myostatin inhibition may be a potent therapeutic option in a range of muscle wasting conditions including sarcopenic obesity and muscle loss associated with weight loss.

Significant progress continues to be made in showing the potency of myostatin inhibition in animal models. Recent reports have found that myostatin inhibition increases lean mass and muscle strength in mouse models of muscular dystrophy [44] and Huntington's disease [45] while preventing muscle atrophy and improving physical function poststroke [46] and after anterior cruciate ligament repair [47]. A number of myostatin inhibitors have already progressed to early phase clinical trials and exert their potential effects by blocking the interaction between mature myostatin and its receptors. This is accomplished through use of antibodies, ligand traps, or by overexpressing the natural myostatin inhibitor follistatin [48].

Thus far, published reports involving intervention studies in humans have been early phase I and II trials in patients with muscular dystrophy [49▪], sarcopenia [50], after elective orthopedic surgery [51], and in healthy individuals [52,53]. In general, these studies have found the pharmacological intervention to be well tolerated; however, results have been mixed. A study involving a monoclonal antibody targeting myostatin led to increases in appendicular lean mass, decreases in fat mass, and improved gait speed in sarcopenic individuals with a recent history of falls [50]. Others have failed to show improvement over placebo [49■,51,52].

CONCLUSION

In the older adult population, the prevalence of obesity is anticipated to grow substantially in the coming years because of an increase in the aging population and in the prevalence of obesity itself. Given the public health implications, an effective treatment strategy is essential. We propose that the primary treatment of obesity in older adults should remain centered around lifestyle interventions incorporating caloric restriction and an exercise regimen consisting of both aerobic endurance training and resistance training. Caloric restriction in the absence of exercise training or other measures to attenuate anticipated loss of lean mass and BMD should be avoided. We agree with recommendations to ensure adequate calcium and vitamin D supplementation as well as high-quality protein intake in the setting of caloric restriction. Although therapies such as testosterone and bariatric surgery are already available today, we do not believe that there is sufficient evidence specific to older adults to recommend these options at this time. There may be a potential future role for myostatin inhibitors in the treatment of sarcopenic obesity and muscle loss associated with weight loss, and clinical trials are ongoing.

Acknowledgements

The content is solely the responsibility of the authors and does not represent the official views of the National Institutes of Health and the Department of Veterans Affairs.

Financial support and sponsorship

The work was supported by grants RO1 AG031176 and DK109950 from the National Institute of Health, 1–14-LLY-38 from the American Diabetes Association, CX000906 from the Veterans Affairs Office of Research and Development, the Alek Foundation, and resources at the Michael E. DeBakey VA Medical Center.

Conflicts of interest

There are no conflicts of interest.

REFERENCES AND RECOMMENDED READING

Papers of particular interest, published within the annual period of review, have been highlighted as:
■ of special interest
■■ of outstanding interest

1. United Nations, Department of Economic and Social Affairs, Population Division. World population prospects: the 2017 revision, key findings and advance tables. Working paper no. ESA/P/WP/248. (United Nations, 2017)
2. 'Obesity and Overweight.' World Health Organization, 2018 Feb 18; www.who.int/news-room/fact-sheets/detail/obesity-and-overweight
3. Hales CM, Caroll MD, Fryar CD, Ogden CL. Prevalence of obesity among adults and youth: United States 2015-2016. NCHS Data Brief 2017; 1–8.
4. Flegal KM, Kruszon-Moran D, Carroll MD, *et al.* Trends in obesity among adults in the United States, 2005 to 2014. JAMA 2016; 315:2284–2291.
5. Agha M, Agha R. The rising prevalence of obesity: part A: impact on public health. Int J Surg Oncol (NY) 2017; 2:e17.
6. ■■ Batsis JA, Gill LE, Masutani RK, *et al.* Weight loss interventions in older adults with obesity: a systematic review of randomized controlled trials since 2005. J Am Geriatr Soc 2017; 65:257–268.

Systemic review of RCTs since 2005 studying the effect of lifestyle interventions on body composition, physical function, and quality of life in obese older adults.

7. Martínez-Amat A, Aibar-Almazán A, Fábrega-Cuadros R, *et al.* Exercise alone or combined with dietary supplements for sarcopenic obesity in community-dwelling older people: a systematic review of randomized controlled trials. Maturitas 2018; 110:92–103.
8. Mitchell NS, Furniss AL, Helmkamp LJ, Van Pelt RE. Clinically significant weight loss by women in a national nonprofit weight loss program. J Womens Health (Larchmt) 2017; 26:911–917.
9. Burgess E, Hassmén P, Pumpa KL. Determinants of adherence to lifestyle intervention in adults with obesity: a systematic review. Clin Obes 2017; 7:123–135.
10. ■ Haywood CJ, Prendergast LA, Purcell K, *et al.* Very low calorie diets for weight loss in obese older adults: a randomized trial. J Gerontol A Biol Sci Med Sci 2017; 73:59–65.

This preliminary study found that a very low calorie diet was well tolerated and effective at inducing weight loss in obese older adults.

11. Locher JL, Goldsby TU, Goss AM, *et al.* Calorie restriction in overweight older adults: do benefits exceed potential risks? Exp Gerontol 2016; 86:4–13.
12. Jensen MD, Ryan DH, Apovian CM, *et al.* 2013 AHA/ACC/TOS guideline for the management of overweight and obesity in adults: a report of the American College of Cardiology/American Heart Association Task Force on Practice Guidelines and The Obesity Society. J Am Coll Cardiol 2014; 63(25 Pt B):3029–3030.
13. ■■ Johnson KC, Bray GA, Cheskin LJ, *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; 32:2278–2287.

First randomized controlled trial showing that intentional weight loss in overweight and obese older adults with diabetes results in a subsequent increase in frailty fractures later in life. Prior study outcomes were limited to decreases in bone mineral density with intentional weight loss.

14. ■ Kritchevsky SB, Lovato L, Handing EP, *et al.* Exercise's effect on mobility disability in older adults with and without obesity: the LIFE study randomized clinical trial. Obesity (Silver Spring) 2017; 25:1199–1205.

This study showed that structured moderate intensity physical activity benefits older adults at risk for major mobility disability regardless of BMI.

15. Villareal DT, Chode S, Parimi N, *et al.* Weight loss, exercise, or both and physical function in obese older adults. N Engl J Med 2011; 364:1218–1229.
16. ■ Beavers KM, Ambrosius WT, Rejeski WJ, *et al.* Effect of exercise type during intentional weight loss on body composition in older adults with obesity. Obesity (Silver Spring) 2017; 25:1823–1829.

This study utilizing data from the Cooperative Lifestyle Intervention Program found that both resistance and aerobic training increase loss of fat mass when added to caloric restriction, but resistance training preserves lean mass more.

17. Beavers KM, Beavers DP, Martin SB, *et al.* Change in bone mineral density during weight loss with resistance versus aerobic exercise training in older adults. J Gerontol A Biol Sci Med Sci 2017; 72:1582–1585.
18. ■ Nicklas BJ, Brinkley TE, Houston DK, *et al.* Effects of caloric restriction on cardio-respiratory fitness, fatigue, and disability responses to aerobic exercise in older adults with obesity: a randomized controlled trial. J Gerontol A Biol Sci Med Sci 2018; doi: 10.1093/gerona/gly 159. [Epub ahead of print]

This study found that the addition of moderate caloric restriction to aerobic exercise leads to greater improvements in cardiorespiratory fitness. Moderate caloric restriction was as effective as intensive caloric restriction.

19. ■ Villareal DT, Aguirre L, Gurney AB, *et al.* Aerobic or resistance exercise, or both, in dieting obese older adults. N Engl J Med 2017; 376:1943–1955.

This randomized controlled trial is the first head-to-head comparison of different exercise types added to match caloric restriction-induced weight loss on physical function in obese older adults. The results showed that among the methods tested, weight loss and combined aerobic and resistance exercise were the most effective in improving functional status of obese older adults.

20. Coffey VG, Hawley JA. Concurrent exercise training: do opposites distract? J Physiol 2017; 595:2883–2896.
21. Villareal DT, Waters DL, Qualls C. Exercise type in dieting obese older adults. N Engl J Med 2017; 377:599–600.
22. Nelson ME, Rejeski WJ, Blair SN, *et al.* Physical activity and public health in older adults: recommendation from the American College of Sports Medicine and the American Heart Association. Circulation 2007; 116:1094–1105.
23. ■■ Rejeski WJ, Ambrosius WT, Burdette JH, *et al.* Community weight loss to combat obesity and disability in at-risk older adults. J Gerontol A Biol Sci Med Sci 2017; 72:1547–1553.

This is a randomized controlled trial showing that community-based weight loss programs incorporating both exercise and dieting interventions can be successful.

24. Breda J, Jakovljevic J, Rathmes G, *et al.* Promoting health-enhancing physical activity in Europe: current state of surveillance, policy development and implementation. Health Policy 2018; 122:519–527.

25. Judge J, Birge S, Goth F, *et al.* Recommendations abstracted from the American Geriatrics Society consensus statement on vitamin D for prevention of falls and their consequences. J Am Geriatr Soc 2014; 62:147–152.

26. Traylor DA, Gorissen SH, Phillips SM. Perspective: protein requirements and optimal intakes in aging: are we ready to recommend more than the daily recommended allowance? Adv Nutr 2018; 9:171–182.

27. ■■ Bhasin S, Apovian CM, Travison TG, *et al.* Effect of protein intake on lean body mass in functionally limited older men: a randomized clinical trial. JAMA Intern Med 2018; 178:530–541.

This is a randomized controlled trial showing that protein intake above the current RDA of 0.8 g/kg/day does not result in improvements in lean body mass, muscle strength, or physical function in older men.

28. ■■ Verreijen AM, Engberink MF, Memelink RG, *et al.* Effect of high protein diet and/or resistance exercise on the preservation of fat free mass during weight loss in overweight and obese older adults: a randomized controlled trial. Nutr J 2017; 16:10.

This is a randomized controlled trial demonstrating resistance training and protein intake above 0.8 g/kg/day do not improve lean mass during caloric restriction, but the combination of both interventions does result in improved preservation of lean mass.

29. Blaya R, Blaya P, Rhoden L, Rhoden EL. Low testosterone levels and metabolic syndrome in aging male. Curr Pharm Des 2017; 23:4470–4474.

30. Sansone A, Sansone M, Lenzi A, Romanelli F. Testosterone replacement therapy: the emperor's new clothes. Rejuvenation Res 2017; 20:9–14.

31. ■ Snyder PJ, Bhasin S, Cunningham GR, *et al.* Lessons from the testosterone trials. Endocr Rev 2018; 39:369–386.

This is a review written by the investigators of the testosterone trials that summarizes the findings from their collective studies.

32. Ng Tang Fui M, Prendergast LA, Dupuis P, *et al.* Effects of testosterone treatment on body fat and lean mass in obese men on a hypocaloric diet: a randomized controlled trial. BMC Med 2016; 14:153.

33. ■■ Ng Tang Fui M, Hoermann R, Zajac JD, Grossmann M. The effects of testosterone on body composition in obese men are not sustained after cessation of testosterone treatment. Clin Endocrinol (Oxf) 2017; 87:336–343.

This is an important follow-up study that found the beneficial effects of testosterone on body composition in obese middle-aged men undergoing weight loss were lost after cessation of testosterone.

34. Angrisani L, Santonicola A, Iovino P, *et al.* Bariatric surgery and endoluminal procedures: IFSO Worldwide Survey 2014. Obes Surg 2017; 27:2279–2289.

35. Garofalo F, Denis R, Pescarus R, *et al.* Long-term outcome after laparoscopic sleeve gastrectomy in patients over 65 years old: a retrospective analysis. Surg Obes Relat Dis 2017; 13:1–6.

36. ■ Casillas RA, Kim B, Fischer H, *et al.* Comparative effectiveness of sleeve gastrectomy versus Roux-en-Y gastric bypass for weight loss and safety outcomes in older adults. Surg Obes Relat Dis 2017; 13:1476–1483.

This study found that gastric bypass was particularly effective at inducing weight loss in older adults compared with the gastric sleeve but was associated with higher complication rates.

37. Haskins IN, Ju T, Whitlock AE, *et al.* Older age confers a higher risk of 30-day morbidity and mortality following laparoscopic bariatric surgery: an analysis of the metabolic and bariatric surgery quality improvement program. Obes Surg 2018; 28:2745–2752.

38. ■ Morgan DJ, Ho KM. Incidence and outcomes after bariatric surgery in older patients: a state-wide data-linked cohort study. ANZ J Surg 2017; 87: 471–476.

This study found that even with higher complication rates, bariatric surgery in older adults led to an overall decreased hospitalization rate.

39. Davidson LE, Yu W, Goodpaster BH, *et al.* Fat-free mass and skeletal muscle mass five years after bariatric surgery. Obesity (Silver Spring) 2018; 26:1130–1136.

40. Shanbhogue VV, Støving RK, Frederiksen KH, *et al.* Bone structural changes after gastric bypass surgery evaluated by HR-pQCT: a two-year longitudinal study. Eur J Endocrinol 2017; 176:685–693.

41. ■■ Axelsson KF, Werling M, Eliasson B, *et al.* Fracture risk after gastric bypass surgery: a retrospective cohort study. J Bone Miner Res 2018; doi: 10.1002/jbmr.3443. [Epub ahead of print]

This study notes an increased risk of falls and fractures after gastric bypass that cannot be attributed to weight lost or the degree of calcium and vitamin D supplementation.

42. ■■ Fan X, Gaur U, Sun L, *et al.* The growth differentiation factor 11 (GDF11) and myostatin (MSTN) in tissue specific aging. Mech Ageing Dev 2017; 164:108–112.

This is a recent review focusing on the physiological role of myostatin in aging.

43. Sakuma K, Yamaguchi A. Recent advances in pharmacological, hormonal, and nutritional intervention for sarcopenia. Pflugers Arch 2018; 470: 449–460.

44. Puolakkainen T, Ma H, Kainulainen H, *et al.* Treatment with soluble activin type IIB-receptor improves bone mass and strength in a mouse model of Duchenne muscular dystrophy. BMC Musculoskelet Disord 2017; 18:20.

45. Bondulich MK, Jolinon N, Osborne GF, *et al.* Myostatin inhibition prevents skeletal muscle pathophysiology in Huntington's disease mice. Sci Rep 2017; 7:14275.

46. Desgeorges MM, Devillard X, Toutain J, *et al.* Pharmacological inhibition of myostatin improves skeletal muscle mass and function in a mouse model of stroke. Sci Rep 2017; 7:14000.

47. Wurtzel CN, Gumucio JP, Grekin JA, *et al.* Pharmacological inhibition of myostatin protects against skeletal muscle atrophy and weakness after anterior cruciate ligament tear. J Orthop Res 2017; 35:2499–2505.

48. Pirruccello-Straub M, Jackson J, Wawersik S, *et al.* Blocking extracellular activation of myostatin as a strategy for treating muscle wasting. Sci Rep 2018; 8:2292.

49. ■ Campbell C, McMillan HJ, Mah JK, *et al.* Myostatin inhibitor ACE-031 treatment of ambulatory boys with Duchenne muscular dystrophy: results of a randomized, placebo-controlled clinical trial. Muscle Nerve 2017; 55:458–464.

This is a phase II trial of a myostatin inhibitor in patients with muscular dystrophy.

50. Becker C, Lord SR, Studenski SA, *et al.* Myostatin antibody (LY2495655) in older weak fallers: a proof-of-concept, randomised, phase 2 trial. Lancet Diabetes Endocrinol 2015; 3:948–957.

51. Woodhouse L, Gandhi R, Warden SJ, *et al.* A phase 2 randomized study investigating the efficacy and safety of myostatin antibody LY2495655 versus placebo in patients undergoing elective total hip arthroplasty. J Frailty Aging 2016; 5:62–70.

52. Glasser CE, Gartner MR, Wilson D, *et al.* Locally acting ACE-083 increases muscle volume in healthy volunteers. Muscle Nerve 2018; 57:921–926.

53. Garito T, Zakaria M, Papanicolaou DA, *et al.* Effects of bimagrumab, an activin receptor type II inhibitor, on pituitary neurohormonal axes. Clin Endocrinol (Oxf) 2018; 88:908–919.