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# The Obesity Paradox in the Elderly: Potential Mechanisms and Clinical Implications

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#### **KEYWORDS**

- Obesity 
  Body composition 
  Elderly
- Mortality Epidemiology

Obesity is a well-established and independent risk factor for cardiovascular disease and mortality in the general population.<sup>1</sup> Obesity is related to several diseases including diabetes mellitus, hypertension, dyslipidemia, coronary artery disease, and chronic heart failure.<sup>2</sup> An independent association between obesity and all-cause mortality exists in adults.<sup>3</sup> According to the Framingham Heart Study, increased life span can be achieved by reducing the prevalence and severity of obesity.<sup>4</sup> Recent data from the National Health and Nutrition Examination Survey indicate that approximately 32% of adults in the United States are obese.<sup>5</sup> In Canada, 20% of adults are obese.<sup>6</sup> The prevalence of obesity increases up to age 60 to 69 years in men and women, and then declines (**Table 1**).<sup>7</sup> At the same time, the prevalence of obesity is increasing among older age groups in both developed<sup>8</sup> and developing countries.<sup>9</sup> Those over 65 years of age account for approximately 12% to 13% of the population in Canada and the United States,<sup>10</sup> and that proportion is expected to grow to approximately 21%<sup>11</sup> and 18%,<sup>12</sup> respectively, by the year 2025.

The prevalence of overweight and obesity in the elderly has become a growing concern. It is a common presumption that older adults with higher body mass index (BMI) are at risk of shortened survival. Recent evidence, however, indicates that in

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Table 1 Obesity prevalence in older adults (NHANES 1999–2000)						
Age (Years)	% Men	% Women				
40–49	26.3	35.4				
50–59	32.2	41.2				
60–69	38.1	42.5				
70–79	28.9	31.9				
≥80	9.6	19.5				

Data from Flegal KM, Carroll MD, Ogden CL, et al. Prevalence and trends in obesity among US adults, 1999–2000. JAMA 2002;288:1723–7.

the elderly, obesity is paradoxically associated with a lower, not higher, mortality risk. In contrast to younger individuals, numerous studies<sup>13–38</sup> and several systematic<sup>39,40</sup> and critical reviews<sup>41–44</sup> do not support the view that being overweight (ie, BMI in the range of 25–30 kg/m<sup>2</sup>) is a risk factor for all-cause and cardiovascular mortality among elderly men or women. Most studies show this BMI range to be associated with the lowest mortality risk in older adults, and report an inverse or U-shaped association between BMI and all-cause mortality. These seemingly counterintuitive observations have been termed the "obesity paradox"<sup>45</sup> or "reverse epidemiology."<sup>46</sup> Although it is true that obesity in the general adult population is associated with higher mortality, this relationship is unclear for persons of advanced age and has led to great controversy regarding the relationship between obesity and mortality in the elderly, the definition of obesity in the elderly, and the need for its treatment in this population. This article examines the evidence on these controversial issues, explores potential explanations for these findings, discusses the clinical implications, and provides recommendations for further research in this area.

#### METHODS

An extensive electronic search was conducted in MEDLINE (1966–January 2009), EM-BASE (1988–January 2009), the Cochrane Library (1990–January 2009), and Web of Science (1900–January 2009) to retrieve research articles on obesity in older adults. Primary studies, review articles, letters, and commentaries were included. Reference lists of primary studies and review articles were also scanned. Key search terms were used: obesity, body mass, body mass index, body weight, weight, weight change, waist circumference, waist-to-hip ratio, body fat, adiposity, and body composition in combination with elderly, older adults, older people, old age, geriatric, oldest old, older men, older women, octogenarians, nonagenarians, veterans, nursing home residents, and aging. Search strategies were limited to publications in English.

#### DEFINITIONS AND MEASUREMENTS

Several classifications of obesity exist. Some methods for measuring body composition, such as hydrostatic densitometry (underwater weighing), dual-energy x-ray absorptiometry, and near-infrared interactance, although accurate, require technologies and expertise that are not readily available.

BMI, calculated as body weight in kilograms divided by the square of the height in meters, is the most commonly used measure of obesity. Current American College of Cardiology and American Heart Association guidelines<sup>47</sup> suggest using BMI at all ages

to define obesity, and recommend the same cut-off values of BMI in the elderly as in younger adults. A BMI under 18.5 kg/m<sup>2</sup> is almost universally considered underweight and a BMI between 18.5 and 24.9 kg/m<sup>2</sup> is usually, but not always, viewed as normal or ideal weight.<sup>48</sup> Individuals with a BMI in the 25 to 30 kg/m<sup>2</sup> range are considered overweight, and those with a BMI 30 kg/m<sup>2</sup> or greater are considered obese. This index is based on the assumption that most of the variation in weight among individuals of the same height is caused by fat mass. Because BMI calculations do not differentiate between weight because of fat versus lean muscle, age-related body composition changes, such as decreased lean tissue and height and increased fat deposits, make the use of BMI less valid in determining obesity in older adults. There is an age-related decline in height because of thinning of the intervertebral disks and loss of vertebral body height, and the cumulative height loss from age 30 to 80 years averages about 5 cm for men and 8 cm for women.<sup>49</sup> Age-dependent height decreases may induce a false BMI increase of 1.5 to 2.5 kg/m<sup>2</sup> in the elderly despite minimal changes in body weight. Furthermore, beginning in the third decade lean body mass declines at a rate of 0.3 kg per year.<sup>50</sup> At the same time, there is an increase in body fat, which continues up to age 70.<sup>51</sup> As a result, the total body weight tends to peak in the fifth to sixth decade, remains stable until age 65 to 70 years, and then slowly declines. This is in contrast to young adults where an increase in total body mass is also associated with an increase in skeletal muscle acquired to support the extra weight. The combination of increased fat mass and decreased lean body mass in the elderly is termed "sarcopenic obesity" and has been associated with decreased muscular strength and frailty.<sup>52</sup> Elderly persons may seem to have a stable "healthy" BMI despite excess fat and low muscle mass.

Not only do older adults have more body fat than young adults, but the fat is also distributed differently. Aging is associated with a greater proportion of visceral (intra-abdominal) fat.<sup>53</sup> An increase in visceral fat has been associated with increased cardiovascular risk in the general population.<sup>54</sup> In the past few years, waist circumference (WC) has been proposed as a surrogate of abdominal obesity.<sup>55</sup> WC is strongly related to both visceral and total fat as measured by CT.<sup>56</sup> A WC of greater than or equal to 88 cm in women and greater than or equal to 102 cm in men has been suggested as an indicator of obesity and increased health risk.<sup>48</sup> Waist-to-hip ratio (WHR) is another alternative metric: women with ratios greater than or equal to 0.8 and men with ratios greater than or equal to 1 are considered high risk for obesity-related diseases.<sup>57</sup> In 1985, Andres and colleagues<sup>58</sup> published tables of ideal weight standardized by age, suggesting an age-related increase of 5 kg per decade. Clearly, if BMI is to be used as the primary clinical measure of obesity in the elderly, the current definition and target healthy range need to be revised.

#### PATHOPHYSIOLOGY

The results from most studies demonstrate that energy intake does not change, or even declines with age.<sup>59</sup> The age-related increase in fat mass is most likely caused by a decrease in energy expenditure. A decline in the resting metabolic rate and thermal effect of food (the rise in metabolic rate during digestion of food) and reduced physical activity contribute to the decrease in energy expenditure.<sup>60</sup> This, combined with a stable energy intake, results in gradual fat accumulation. Hormonal changes also play a role in the amount of fat and its distribution. These changes include reduced production of growth hormone and testosterone,<sup>61</sup> and decreased responsiveness to thyroid<sup>62</sup> and leptin hormones.<sup>63</sup>

#### ASSOCIATION BETWEEN BMI AND MORTALITY AFTER AGE 65

In younger adults, there is strong evidence that obesity shortens the life span.<sup>64</sup> Data from the American Cancer Society's Cancer Prevention Study<sup>65</sup> have shown, however, that the relative mortality risk decreases with age (**Fig. 1**). This was also demonstrated in a 12-year prospective study of over 1 million Korean men and women (**Fig. 2**).<sup>66</sup> An assessment of 13 observational studies from 1966 to 1999 by Heiat and colleagues,<sup>41</sup> in which nonhospitalized people over 65 years were followed for at least 3 years, found a lower relative mortality risk in obese older persons compared with



**Fig. 1.** The effect of age on the association between BMI and mortality. 62, 116 men and 262, 091 women never smoked followed over 12 years. *Data from* Stevens J, Cai J, Pamuk ER, et al. The effect of age on the association between body-mass index and mortality. N Engl J Med 1998;338:1–7; with permission. Copyright © 2006, Massachusetts Medical Society.



**Fig. 2.** BMI and mortality in men and women by age groups. 12-year prospective cohort study of 1,213,829 individuals between the ages of 30 and 95 years examining 82,372 deaths. *From* Jee SH, Sull JW, Park J, et al. Body-mass index and mortality in Korean men and women. N Engl J Med 2006;355:779–87; with permission. Copyright © 2006, Massachusetts Medical Society.

young and middle-aged obese persons after adjustment for smoking and baseline health status. There was a positive association between mortality and being overweight or obese (BMI  $\geq$  27 kg/m<sup>2</sup>) only in 3 out of the 13 studies among 65 to 74 year olds, with little or no increase in all-cause or cardiovascular mortality for people with BMI greater than or equal to 30 kg/m<sup>2</sup> compared with those with normal BMI among people over 75 years of age. Results were generally consistent between males and females.

There is evidence that the relationship between BMI and mortality in the elderly may be U-shaped or reverse J-shaped, whereby the risk of mortality begins to rise again with extreme BMI values over 35 to 40 kg/m<sup>2</sup>,<sup>14–18,21–23,25–27,31,37,38,67</sup> however, in most studies the increased risk was not significant.<sup>16,17,67</sup> Similarly, a systematic review and meta-analysis by Janssen and Mark<sup>68</sup> showed that whereas elderly individuals with a BMI in the overweight range were not at higher risk for all-cause mortality, a BMI in the moderately obese range was associated with a 10% increase in mortality risk, independent of gender, disease status, and smoking status.

Where studies examining the relationship between BMI and all-cause mortality in older adults identified an optimum BMI (the BMI associated with the lowest risk of death),<sup>13–18,20–23,25–27,30,31,38</sup> the range was between 24 and 35 kg/m<sup>2</sup>, with most in the range 27 to 30 kg/m<sup>2</sup> (**Table 2**). Older women, however, may have a 2 to 5 kg/m<sup>2</sup> higher optimal range than older men.<sup>16,23,27</sup> Optimal targets for BMI in the elderly have yet to be validated in a large prospective trial.

Zamboni and colleagues<sup>42</sup> reviewed the findings of 20 studies from 1997 to 2004 examining the relationship between BMI and mortality with at least 4.5 years followup. The authors concluded that body composition (abdominal fat and lean body mass) is more important than BMI alone in determining the mortality risk associated with obesity in older adults. A prospective study by Wannamethee and colleagues<sup>69</sup> in 4107 men aged 60 to 79 years and followed for a mean of 6 years found that lean body mass, measured by mid arm muscle circumference, was significantly and inversely associated with mortality. The authors further demonstrated that the combined measure of WC and mid arm muscle circumference provided an effective measure of body composition to assess mortality risk in older men. Janssen and colleagues<sup>70</sup> showed that after controlling for WC, increased BMI was protective against mortality, whereas after controlling for BMI, increased WC was linearly associated with mortality in persons 65 years and older. This suggests that BMI reflects lean body mass for individuals with equivalent WC, whereas WC reflects fat mass for individuals with equal BMI.71 The authors recommend using both measures in the clinical setting. Other studies have shown a similar linear positive relationship between WHR and mortality in older adults.<sup>15,34,37,72</sup> In the clinical setting, however, WC has the advantage of requiring only one measurement, whereas two measurements are required to calculate WHR.

Obesity and cardiovascular mortality in the elderly were examined in a recent systematic review by McTigue and colleagues.<sup>39</sup> There was no consistent relationship between cardiovascular mortality and BMI. In one study<sup>65</sup> that excluded underweight individuals from the normal BMI reference group, a significant positive association was reported in men and women up to age 74. In two studies,<sup>15,73</sup> WC and WHR showed stronger positive associations with cardiovascular mortality than BMI.

Longitudinal studies have examined the impact of midlife BMI on survival in the elderly.<sup>13,36,74–76</sup> These studies have consistently shown that current and midlife BMI have independent effects on mortality in the elderly. Although mortality risk is increased in obese older adults who were already obese at midlife, this is not the case for newly obese older adults. In addition, Janssen and Bacon<sup>36</sup> observed that compared with 70 year olds who were nonobese at both 50 and 70 years of age, mortality risk was increased by 47% in those who were obese at both 50 and 70 years of age, increased by 56% in those who were obese at 50 years of age and nonobese at 70 years of age.

# POTENTIAL EXPLANATIONS FOR AGE DIFFERENCES IN THE RELATIONSHIP BETWEEN BMI AND MORTALITY

Several explanations have been offered for the reverse epidemiology of obesity in the elderly (**Table 3**). Overweight and obese individuals who survive to old age may have characteristics that protect them from the adverse effects of being overweight or obese. This is known as the "survival effect." Individuals who are susceptible to the complications of obesity may have already died, leaving behind those who are more resistant.

Another possible explanation for the obesity paradox is that the higher the age, the shorter is the remaining life span, regardless of the presence of obesity. Because most

#### Table 2

Summary of studies with large sample sizes (>1000 subjects), mean follow-up time of at least 5 years, and mean age of  $\geq$  65 indicating a reverse epidemiology of obesity in older adults

Reference	Sample Size	Mean Age and Range	Follow-up Period (Y)	Findings and Source of Data
Losonczy et al, <sup>13</sup> 1995, USA	2449 men, 3938 women	≥70	5	Inverse BMI-mortality association, lowest mortality at BMI 26.3–28.3 in men and $\geq$ 29.2 in women; data from the Established Populations for Epidemiologic Studies of the Elderly
Allison et al, <sup>23</sup> 1997, USA	2769 men, 4491 women	77 (70–99)	6	U-shaped BMI-mortality association, lowest mortality risk at BMI 27–30 for men and 30–35 for women; data from the Longitudinal study of Aging
Wassertheil-Smoller et al, <sup>27</sup> 2000, USA	3975 men and women	71	5	No relationship between death or stroke and BMI in the placebo group, a U- or J-shaped BMI-mortality association in the treatment group. Lowest risk of death for men at BMI of 26 and for women at BMI of 29.6 in the treatment group; data from the Systolic Hypertension in the Elderly Program trial
Dey et al, <sup>18</sup> 2001, Sweden	1225 men, 1403 women	70	15	U-shaped BMI-mortality association, lowest mortality risk at BMI 27–29 for men and 25–27 for women, weight loss increased mortality; cohort study in Sweden
Grabowski and Ellis, <sup>20</sup> 2001, USA	2860 men, 4667 women	77 (≥70)	8	Inverse association between BMI and mortality, lowest mortality risk in subjects with obesity (BMI >28.5) compared with subjects with normal BMI (19.5–28.4); data from the Longitudinal Study of Aging
Janssen et al, <sup>70</sup> 2005, Canada	2262 men, 2938 women	(65–90+)	9	Inverse relationship between BMI and mortality after adjustment of WC, linear positive relationship between WC and mortality after adjustment of BMI; participants of the Cardiovascular Health Study
Price et al, <sup>34</sup> 2006, UK	7892 men, 13,667 women	80 (≥75)	5.9	Inverse association between BMI and mortality, linear positive association between WHR and mortality; data from 53 family practices in United Kingdom
Corrada et al, <sup>38</sup> 2006, USA	8609 women, 4842 men	73 (44–101)	23	U-shaped BMI-mortality association among persons >80, lowest mortality risk at BMI 25–29.9 in persons >80; data from the Leisure World Cohort Study in California
Dolan et al, <sup>31</sup> 2007, USA	8029 women	72 (65–77)	8	U-shaped BMI-mortality and WC-mortality associations, lowest mortality risk at BMI 23.4–29.8; data from Community-based study in Baltimore, Maryland
Al Snih et al, <sup>26</sup> 2007, USA	4870 men, 3489 women	73	7	U-shaped BMI-mortality association, lowest mortality risk at BMI 25–35; 5 sites of the Established Populations for Epidemiologic Studies of the Elderly
Mazza et al, <sup>32</sup> 2007, Italy	1275 men, 1982 women	74 (65–95)	12	Inverse association between BMI and mortality; participants from the Cardiovascular Study in the Elderly

Abbreviations: BMI, body mass index; WC, waist circumference; WHR, waist-to-hip ratio.

Table 3

Possible mechanisms leading to the observed associations between obesity and improved survival in the elderly						
Potential Biases	Potential Beneficial Effects					
Survival effect	Prevention or delay in cognitive decline					
Time discrepancy of competitive risk factors	Protection from bone mineral density loss and osteoporotic fractures					
Reverse causation	Reduction in oxidative stress and inflammation					
Confounding variables	Energy reserve and prevention of malnutrition					
Cohort effect						

obesity-related consequences take years to develop, those who become obese in old age may die of other conditions before the adverse effects of obesity become manifest. This is known as "time discrepancy of competing risk factors," and could potentially explain the finding by Janssen and Bacon<sup>36</sup> that nonobese older adults who were obese in midlife had an increased mortality risk compared with those who were not obese either at midlife or in old age.

A major challenge in analyzing the obesity-mortality association in epidemiologic studies is the phenomenon of reverse causation. It has been observed repeatedly that weight loss and being underweight are strong predictors of mortality, especially in the elderly.<sup>77</sup> Unintentional weight loss caused by unrecognized systemic illness can affect BMI-mortality analyses if the weight loss occurs before the BMI measurement. This can lead to an overestimation of the mortality risk of the "healthy" weight reference group, thereby making the obese group seem protected.

Obesity requires many years to show its harmful effects on health. Studies with short follow-up times generally do not show associations between obesity and mortality, whereas studies with longer follow-up show significant associations.<sup>42</sup> With longer follow-up, it becomes increasingly important to account for the effects of confounding factors, such as smoking, comorbid conditions, socioeconomic status, health insurance, medication compliance, and especially the effect of voluntary versus involuntary weight loss.

A cohort effect occurs when a study compares different cohorts (or groups) of people that are not actually comparable. BMI-mortality associations are often determined for various age groups using different cohorts who have grown up at different time periods. Cohorts may have been exposed to different lifestyles, environments, and risk factors (eg, infections) that were a much more common cause of death before the introduction of antibiotics.

It is also possible that obesity or a high BMI provide beneficial effects later in life. In contrast with younger adults, obesity has not been found to be associated with depression in older adults.<sup>78</sup> Cognitive function is also a major determinant of disability in the elderly population.<sup>79</sup> In one study, being underweight (BMI <18.5 kg/m<sup>2</sup>) was associated with cognitive decline in elderly adults as measured by the Mini Mental State Examination, whereas obesity (BMI  $\geq$  30 kg/m<sup>2</sup>) was not associated with cognitive decline.<sup>80</sup> In addition, Deschamps and colleagues<sup>81</sup> found that subjects with a BMI less than 23 kg/m<sup>2</sup> had a 3.6-fold higher risk of cognitive decline as assessed by the Mini Mental State Examination at 5 years follow-up. This relationship, however, may be different for males and females. For example, Han and colleagues<sup>82</sup> found that increases in BMI and WC in elderly men were associated with improvement in cognitive function, whereas for elderly women, they were associated with cognitive decline.

Another important benefit of a higher BMI later in life is the protection from osteoporotic fractures. A higher BMI is associated with greater bone mineral density (BMD) in both weight-bearing and non-weight-bearing bones.<sup>83</sup> The increase in BMD and the extra cushioning effect of fat surrounding areas, such as the hip, may provide protection against hip fracture during a fall in older obese persons.<sup>84</sup>

Weight loss and sarcopenia in the elderly may also be associated with reduced skeletal muscle oxidative metabolism, leading to oxidative stress and inflammation.<sup>85</sup> Obesity later in life might improve antioxidant defense.

Another potential benefit of excess adiposity later in life could be to serve as an energy reserve. Malnutrition and the inability to maintain weight and protein status are common problems in elderly nursing home residents.<sup>86</sup> Obesity may protect against this protein-energy malnutrition in the elderly.

The "obesity paradox" is not unique to the elderly population; there is considerable evidence supporting the survival benefit of an increased BMI in chronic wasting diseases, such as AIDS,<sup>87</sup> cancer,<sup>88</sup> heart failure,<sup>89</sup> and in patients on hemodialysis.<sup>90</sup> This "reverse epidemiology" may be partially explained by a larger amount of energy stored as fat and the somewhat larger stores of lean mass, but also by the influence of body fat on fuel selection during negative energy balance.<sup>40</sup> During starvation, the proportion of energy expenditure derived from protein metabolism is lower and lean tissue is better preserved in persons with larger fat stores.<sup>91</sup>

## EFFECT OF OBESITY ON MORBIDITY, FUNCTIONAL STATUS, AND QUALITY OF LIFE IN THE ELDERLY

Both cross-sectional and longitudinal studies have shown that a high BMI and increased abdominal fat are associated with metabolic changes even in older age.<sup>39</sup> These changes include insulin resistance, dyslipidemia, and hypertension, which directly contribute to the development of metabolic syndrome, diabetes mellitus, and cardiovascular disease.<sup>92</sup> In the systematic review by McTigue and colleagues,<sup>39</sup> most studies reported a significantly increased risk of incident cardiovascular morbidity (myocardial infarction or stroke) with increasing BMI. The studies that used WC or WHR as the measure of obesity produced similar results. An elevated BMI was also associated with some cancers, including breast, uterine, colon, and leukemia. Studies examining WC or WHR and cancer incidence yielded similar findings. An increase in lean body mass, however, has not been associated with an increase in cardiovascular disease or diabetes mellitus,<sup>93</sup> and has been associated with a neutral<sup>93</sup> or decreased cancer risk.<sup>94</sup> Obesity measured by BMI or WC has also been associated with increased long-term medication use in elderly individuals.<sup>39</sup> The finding of a relationship between higher BMI values and increased cardiovascular morbidity, but a neutral or inverse relationship between higher BMI and total and cardiovascular mortality, seems contradictory and merits further study.

There is a progressive decrease in physical function and mobility with aging because of the loss of lean body mass, strength, and balance, and an increase in joint dysfunction and arthritis.<sup>95</sup> This decrease in physical function is linked to poorer health-related quality of life in older adults.<sup>52</sup> Several studies have shown an inverse association between BMI and physical function in older adults despite no greater risk in mortality.<sup>26,96,97</sup> It is less clear, however, whether it is the increase in body fat or the age-related decline in lean body mass that plays the major role in causing this functional decline, with studies supporting both hypotheses.<sup>98,99</sup> The optimal BMI for the maintenance of functional capacity may be above the normal range; some authors have found that the BMI range associated with the lowest rate of decline in physical function is between 23 and 30 kg/m<sup>2</sup>.<sup>26,81</sup>

#### RELATIONSHIP BETWEEN PHYSICAL FITNESS, OBESITY, AND MORTALITY IN THE ELDERLY

Physical inactivity and a low level of physical fitness are risk factors for all-cause and cardiovascular mortality.<sup>100</sup> Low levels of physical activity and fitness have also been associated with obesity.<sup>100</sup> A study of 831 male veterans<sup>101</sup> showed a strong inverse relationship between exercise capacity (evaluated on a maximal exercise treadmill test) and mortality, independent of BMI. Another study of 35 middle-aged and elderly men and women<sup>102</sup> showed that perceived physical fitness, but not BMI, was an independent risk factor for all-cause or cardiovascular mortality at 16 years follow-up. In the Yale Health and Aging Study, Dziura and colleagues<sup>103</sup> found that even modest levels of physical activity (measured by a physical activity questionnaire) can attenuate age-related weight loss in older adults with chronic disease, independent of smoking and mobility status.

#### EFFECT OF INTENTIONAL WEIGHT LOSS ON MORTALITY IN THE ELDERLY

Because of the potential benefits associated with being overweight or obese in old age, including prevention or delay in cognitive decline, protection from bone fractures, an increase in antioxidant defense, a reserve of fat and energy stores, and possibly an increase in longevity, there has been hesitation to recommend weight reduction in older adults. A recent systematic review by Bales and Buhr<sup>40</sup> identified 16 studies on the effect of weight loss interventions in subjects 60 years of age or older with baseline BMI of at least 27 kg/m<sup>2</sup>, weight loss greater than or equal to 3% or greater than or equal to 2 kg, and trial duration 6 months or longer. The weight loss interventions led to significant benefits for those with osteoarthritis, coronary heart disease, and type II diabetes mellitus, whereas having slightly negative effects on BMD and lean body mass. Markers of inflammation, including interluekin-6, C-reactive protein, and tumor necrosis factor, were reduced with weight loss, and improvements in WC, blood pressure, serum levels of low-density lipoprotein cholesterol, and fasting glucose were evident. One study<sup>104</sup> found that an average weight loss of 3 kg was associated with a 30% reduction in a composite cardiovascular end point (cardiovascular events, poorly controlled blood pressure, and the need to reinitiate antihypertensive medications) at 2.5 years follow-up. In patients with osteoarthritis, significant improvements were seen in the physical function components of the Short Form 36 Health Survey and the Western Ontario and McMaster Universities Osteoarthritis Index.<sup>105,106</sup> An increase in the 6-minute walk time, decrease in stair climb time, and decrease in knee pain were also noted. Two trials<sup>107,108</sup> evaluated BMD changes in response to weight loss. Although significant effects on total body BMD were observed, there was no effect on regional BMD at common sites of fractures, such as the hip or spine. With regard to the loss of lean body mass associated with weight loss reported in some trials, this is a common finding in weight loss trials of any age group, but it is more of a concern in the elderly population. The best way to avoid loss of lean body mass is to couple the weight reduction intervention with a resistance training exercise program.<sup>108</sup> Resistance exercises are beneficial for preserving bone density and for maintaining lean mass and muscular strength.<sup>40</sup> To date, no clinical trials have evaluated the effect of intentional weight loss on mortality in elderly individuals.

These are conflicting findings: intervention trials show clinically important benefits of weight reduction with regard to osteoarthritis, physical function, and possibly diabetes and coronary heart disease, yet longitudinal studies suggest that maintaining weight is favorable in older persons who become obese after age 60. It is clear that evidence-based recommendations for weight loss in obese elderly persons cannot currently be made, and that decisions about whether or not to advise weight loss must be

individualized, with particular attention to the patient's weight history and coexisting medical conditions.<sup>40</sup> Additionally, a focus on physical fitness, muscular strength, and improvement of physical function may be more productive than weight loss in many cases.

**Table 4** summarizes the associations between measures of body composition (BMI, abdominal fat, lean body mass), intentional weight loss, and morbidity and mortality outcomes in the elderly.

#### **CLINICAL IMPLICATIONS**

A summary of clinical implications follows:

 Obesity, as defined by BMI greater than or equal to 30 kg/m<sup>2</sup>, does not carry the same mortality risk in older adults (>60 years of age) as in younger adults. The association between BMI and mortality in older individuals is neutral or inverse. The current targets for normal BMI derived from epidemiologic studies of younger and middle-aged populations (BMI 18.5–24.9) do not seem to apply to the elderly. BMI should be used in

Associations between BMI, abdominal fat, and intentional weight loss with outcomes in the elderly							
	High BMI	High Abdominal Fat	Increased Lean Muscle	Effect of Intentional Weight Loss			
All cause mortality	↓ or neutral	↑	Ļ	Unknown			
Cardiovascular mortality	↓ or neutral	↑ or neutral	Unknown	Unknown			
Cardiovascular morbidity (myocardial infarction or stroke)	↑	¢	Neutral	ţ			
Cancer incidence	↑	<b>↑</b>	↓ or neutral	Unknown			
Diabetes mellitus/ insulin sensitivity	↑	↑	Neutral	Ļ			
Blood pressure	↑	↑	Unknown	Ļ			
Physical function	↓ but higher than normal	Ļ	1	↑			
Quality of life	↓		1				
Cognitive function	↑ or neutral (may be different for females)	↑ or neutral (may be different for females)	Unknown	Unknown			
Long-term medication use	1	↑	Unknown	Potential ↓ for antihypertensives			
Bone mineral density	↑	↑	↑	Slight ↓			
Dyslipidemia	↑	1	Unknown	$\downarrow$			

 $\downarrow$ : decreased;  $\uparrow$ : increased.

conjunction with indices of lean body mass and fat distribution, such as waist circumference and mid arm muscle circumference, to assess mortality risk.

- 2. The ideal BMI target in the elderly may be closer to 25 to 35 kg/m<sup>2</sup> (lower range for males and upper range for females). This and other indices of body composition, however, should be validated in prospective clinical trials in the population to which they are going to be applied.
- 3. Increased weight or a high BMI in advanced age may provide benefits, such as protection from bone loss and fractures, malnutrition, and cognitive decline.
- 4. Obesity, especially abdominal obesity, in older age may confer adverse health risks, such as metabolic syndrome, diabetes, and cancer risk.
- 5. Physical activity and physical fitness are important determinants of mortality risk in the elderly, independent of obesity, and may attenuate age-related weight loss. Physical fitness and functional independence may be a more productive focus than weight loss in older adults with obesity.
- 6. Being underweight in any age group is associated with substantially increased risk of mortality. In the elderly, underweight status by BMI poses far greater threat than being overweight or obese.
- 7. Unintentional weight loss is never normal and requires clinical investigation for the underlying cause.
- 8. Elderly subjects with obesity in conjunction with decreased lean body mass (sarcopenic obesity) are at increased mortality risk. There is no consensus, however, on the definition of sarcopenic obesity or guidelines for management.

#### SUMMARY

The prevalence of obesity is increasing at all ages, including the elderly. The complexity of measuring body fat and fat distribution in the clinical setting makes it difficult to determine the most valid, practical definition of obesity in the elderly population. In contrast to younger people, an overweight BMI is associated with lower mortality risk in the elderly. Similarly, an obese BMI does not confer increased risk of mortality in the elderly, although it is related to cardiovascular morbidity and physical disability. A greater emphasis should be placed on preventing functional decline and muscle loss in older adults through increased physical activity, including resistance training. More research is needed to determine the optimal BMI and other potential indices of body composition to guide therapeutic decisions.

#### REFERENCES

- 1. Bray GA, Macdiarmid J. The epidemic of obesity. West J Med 2000;172:78-9.
- 2. Must A, Spadano J, Coakley EH, et al. The disease burden associated with overweight and obesity. JAMA 1999;282:1523–9.
- 3. Calle E, Thun MJ, Petrelli JM, et al. Body mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med 1999;341:1097–105.
- Pardo Silva MC, De Laet C, Nusselder WJ, et al. Adult obesity and number of years lived with and without cardiovascular disease. Obesity (Silver Spring) 2006;14:1264–73.
- 5. Ogden CL, Carroll MD, Curtin LR, et al. Prevalence of overweight and obesity in the United States, 1999–2004. JAMA 2006;295:1549–55.
- 6. Sokar-Todd HB, Sharma AM. Obesity research in Canada: literature overview of the last 3 decades. Obes Res 2004;12:1547–53.
- 7. Flegal KM, Carroll MD, Ogden CL, et al. Prevalence and trends in obesity among US adults, 1999–2000. JAMA 2002;288:1723–7.

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- 8. Yusuf S. The global problem of cardiovascular disease. Int J Clin Pract Suppl 1998;94:3–6.
- 9. Haslam DW, James WP. Obesity. Lancet 2005;366:1197-209.
- 10. Organization for Economic Co-operation and Development (OECD) Factbook 2008. Economic, environmental and social statistics. Paris (France): OECD Publishing; 2008.
- 11. Moore E, Rosenberg M. Canada's elderly population: the challenges of diversity. Can Geogr 2001;45:145.
- 12. Projections of the population by selected age groups and sex for the United States: 2010 to 2050. Available at: http://www.census.gov/population/www/ projections/summarytables.html. Accessed April 1, 2009.
- Losonczy K, Harris T, Coroni-Huntley J, et al. Does weight loss from middle age to old age explain the inverse weight mortality relation in old age? Am J Epidemiol 1995;141:312–21.
- 14. Thorpe R, Ferraro K. Aging, obesity and mortality. Res Aging 2004;26:108–29.
- 15. Folsom AR, Kushi LH, Anderson KE, et al. Associations of general and abdominal obesity with multiple health outcomes in older women: the Iowa Women's Health Study. Arch Intern Med 2000;160:2117–28.
- Reuser M, Bonneux L, Willekens F. The burden of mortality of obesity at middle and old age is small: a life table analysis of the US Health and Retirement Survey. Eur J Epidemiol 2008;23:601–7.
- 17. Bender R, Jockel KH, Trautner C, et al. Effect of age on excess mortality in obesity. JAMA 1999;281:1498–504.
- Dey DK, Rothenberg E, Sundh V, et al. Body mass index, weight change and mortality in the elderly: a 15 y longitudinal population study of 70 y olds. Eur J Clin Nutr 2001;55:482–92.
- 19. Diehr P, O'Meara ES, Fitzpatrick A, et al. Weight, mortality, years of healthy life, and active life expectancy in older adults. J Am Geriatr Soc 2008;56:76–83.
- Grabowski D, Ellis J. High body mass index does not predict mortality in older people: an analysis of the Longitudinal Study of Aging. J Am Geriatr Soc 2001;49:968–79.
- 21. Grabowski DC, Campbell CM, Ellis JE. Obesity and mortality in elderly nursing home residents. J Gerontol A Biol Sci Med Sci 2005;60:1184–9.
- 22. Landi F, Onder G, Gambassi G, et al. Body mass index and mortality among hospitalized patients. Arch Intern Med 2000;160:2641–4.
- Allison D, Gallagher D, Heo M, et al. Body mass index and all-cause mortality among people age 70 and over: the Longitudinal Study of Aging. Int J Obes 1997;21:424–31.
- 24. McAuley P, Myers J, Abella J, et al. Body mass, fitness and survival in veteran patients: another obesity paradox? Am J Med 2007;120:518–24.
- Menotti A, Kromhout D, Nissinen A, et al. Short-term all-cause mortality and its determinants in elderly male populations in Finland, The Netherlands, and Italy: the FINE Study. Finland, Italy, Netherlands Elderly Study. Prev Med 1996;25: 319–26.
- 26. Al Snih S, Ottenbacher KJ, Markides KS, et al. The effect of obesity on disability vs mortality in older Americans. Arch Intern Med 2007;167:774–80.
- 27. Wassertheil-Smoller S, Fann C, Allman RM, et al. Relation of low body mass to death and stroke in the systolic hypertension in the elderly program. The SHEP Cooperative Research Group. Arch Intern Med 2000;160:494–500.
- 28. Kinney E, Caldwall J. Relationship between body weight and mortality in men aged 75 years and older. South Med J 1990;83:1256–8.

- 29. Weiss A, Beloosesky Y, Boaz M, et al. Body mass index is inversely related to mortality in elderly subjects. J Gen Intern Med 2007;23:19–24.
- 30. Takata Y, Ansai T, Soh I, et al. Association between body mass index and mortality in an 80-year-old population. J Am Geriatr Soc 2007;55:913–7.
- Dolan C, Kraemer H, Browner W, et al. An intermediate body mass index (23 to 30 kg/m<sup>2</sup>) was associated with the most favorable mortality in older women. Am J Public Health 2007;97:93–8.
- Mazza A, Zamboni S, Tikhonoff V, et al. Body mass index and mortality in elderly men and women from general population: the experience of Cardiovascular Study in the Elderly (CASTEL). Gerontology 2007;53:36–45.
- 33. Woo J, Ho S, Yu A, et al. Is waist circumference a useful measure in predicting health outcomes in the elderly? Int J Obes 2002;26:1349–55.
- 34. Price GM, Uauy R, Breeze E, et al. Weight, shape, and mortality risk in older persons: elevated waist-hip ratio, not high body mass index, is associated with a greater risk of death. Am J Clin Nutr 2006;84:449–60.
- Heitmann BL, Erikson H, Ellsinger BM, et al. Mortality associated with body fat, fat-free mass and body mass index among 60-year-old Swedish men-a 22-year follow-up. The study of men born in 1913. Int J Obes Relat Metab Disord 2000; 24:33–7.
- 36. Janssen I, Bacon E. Effect of current and midlife obesity status on mortality risk in the elderly. Obesity (Silver Spring) 2008;16:2504–9.
- 37. Lahmann PH, Lissner L, Gullberg B, et al. A prospective study of adiposity and all-cause mortality: the Malmo Diet and Cancer Study. Obes Res 2002;10:361–9.
- Corrada MM, Kawas CH, Mozaffar F, et al. Association of body mass index and weight change with all-cause mortality in the elderly. Am J Epidemiol 2006;163: 938–49.
- 39. McTigue KM, Hess R, Ziouras J. Obesity in older adults: a systematic review of the evidence for diagnosis and treatment. Obesity (Silver Spring) 2006;14:1485–97.
- 40. Bales C, Buhr G. Is obesity bad for older persons? A systematic review of the pros and cons of weight reduction in later life. J Am Med Dir Assoc 2008;9:302–12.
- Heiat A, Vaccarino V, Krumholz HM. An evidence-based assessment of federal guidelines for overweight and obesity as they apply to elderly persons. Arch Intern Med 2001;161:1194–203.
- 42. Zamboni M, Mazzali G, Zoico E, et al. Health consequences of obesity in the elderly: a review of four unresolved questions. Int J Obes 2005;29:1011–29.
- 43. Heiat A. Impact of age on definition of standards for ideal weight. Prev Cardiol 2003;6:104–7.
- 44. Villareal DT, Apovian CM, Kushner RF, et al. Obesity in older adults: technical review and position statement of the American Society for Nutrition and NAASO, the Obesity Society. Obes Res 2005;13:1849–63.
- 45. Kalantar-Zadeh K, Horwich TB, Oreopoulos A, et al. Risk factor paradox in wasting diseases. Curr Opin Clin Nutr Metab Care 2007;10:433–42.
- 46. Kalantar-Zadeh K, Kilpatrick RD, Kuwae N, et al. Reverse epidemiology: a spurious hypothesis or a hardcore reality? Blood Purif 2005;23(1):57–63.
- Smith SC Jr, Allen J, Blair SN, et al. AHA/ACC guidelines for secondary prevention for patients with coronary and other atherosclerotic vascular disease: 2006 update endorsed by the National Heart, Lung, and Blood Institute. J Am Coll Cardiol 2006;47:2130–9.
- Pi-Sunyer FX. Clinical guidelines on the identification, evaluation, and treatment of overweight and obesity in adults. Bethesda (MD): National Institutes of Health; 1998. Publication NIH 98-4083.

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- Sorkin JD, Muller DC, Andres R. Longitudinal change in height of men and women: implications for interpretation of the body mass index: the Baltimore Longitudinal Study of Aging. Am J Epidemiol 1999;150:969–77.
- 50. Elia M. Organ and tissue contribution to metabolic rate. New York: Raven Press; 1992.
- 51. Baumgartner RN, Heymsfield SB, Roche AF. Human body composition and the epidemiology of chronic disease. Obes Res 1995;3:73–95.
- 52. Villareal DT, Banks M, Siener C, et al. Physical frailty and body composition in obese elderly men and women. Obes Res 2004;12:913–20.
- 53. Zamboni M, Armellini F, Harris T, et al. Effects of age on body fat distribution and cardiovascular risk factors in women. Am J Clin Nutr 1997;66:111–5.
- 54. Bjorntorp P. Portal adipose tissue as a generator of risk factors for cardiovascular disease and diabetes. Arteriosclerosis 1990;10:493–6.
- 55. Turcato E, Bosello O, Di Francesco V, et al. Waist circumference and abdominal sagittal diameter as surrogates of body fat distribution in the elderly: their relation with cardiovascular risk factors. Int J Obes Relat Metab Disord 2000;24:1005–10.
- 56. Harris TB, Visser M, Everhart J, et al. Waist circumference and sagittal diameter reflect total body fat better than visceral fat in older men and women. The Health, Aging and Body Composition Study. Ann N Y Acad Sci 2000;904:462–73.
- 57. Segal K, Dunaif A, Gutin B, et al. Body composition, not body weight, is related to cardiovascular disease risk factors and sex hormone levels in men. J Clin Invest 1987;80:1050–5.
- Andres R, Elahi D, Tobin JD, et al. Impact of age on weight goals. Ann Intern Med 1985;103:1030–3.
- 59. Hallfrisch J, Muller D, Drinkwater D, et al. Continuing diet trends in men: the Baltimore Longitudinal Study of Aging (1961–1987). J Gerontol 1990;45:M186–91.
- 60. Elia M, Ritz P, Stubbs RJ. Total energy expenditure in the elderly. Eur J Clin Nutr 2000;54(Suppl 3):S92–103.
- 61. Corpas E, Harman SM, Blackman MR. Human growth hormone and human aging. Endocr Rev 1993;14:20-39.
- 62. Matsumoto AM. Andropause: clinical implications of the decline in serum testosterone levels with aging in men. J Gerontol A Biol Sci Med Sci 2002;57:M76–99.
- 63. Moller N, O'Brien P, Nair KS. Disruption of the relationship between fat content and leptin levels with aging in humans. J Clin Endocrinol Metab 1998;83:931–4.
- 64. Fontaine K, Redden D, Wang C, et al. Years of life lost due to obesity. JAMA 2003;289:187–93.
- 65. Stevens J, Cai J, Pamuk ER, et al. The effect of age on the association between body-mass index and mortality. N Engl J Med 1998;338:1–7.
- 66. Jee SH, Sull JW, Park J, et al. Body-mass index and mortality in Korean men and women. N Engl J Med 2006;355:779–87.
- 67. Su D. Body mass index and old-age survival: a comparative study between the Union Army Records and the NHANES-I Epidemiological Follow-Up Sample. Am J Hum Biol 2005;17:341–54.
- 68. Janssen I, Mark AE. Elevated body mass index and mortality risk in the elderly. Obes Rev 2007;8:41–59.
- Wannamethee SG, Shaper AG, Lennon L, et al. Decreased muscle mass and increased central adiposity are independently related to mortality in older men. Am J Clin Nutr 2007;86:1339–46.
- Janssen I, Katzmarzyk P, Ross R. Body mass index is inversely related to mortality in older people after adjustment for waist circumference. J Am Geriatr Soc 2005;52:2112–8.

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- 71. Bigaard J, Tjonneland A, Thomsen BL, et al. Waist circumference, BMI, smoking, and mortality in middle-aged men and women. Obes Res 2003;11: 895–903.
- 72. Kalmijn S, Curb JD, Rodriguez BL, et al. The association of body weight and anthropometry with mortality in elderly men: the Honolulu Heart Program. Int J Obes Relat Metab Disord 1999;23:395–402.
- 73. Baik I, Ascherio A, Rimm EB, et al. Adiposity and mortality in men. Am J Epidemiol 2000;152:264–71.
- 74. Taylor DH Jr, Ostbye T. The effect of middle- and old-age body mass index on short-term mortality in older people. J Am Geriatr Soc 2001;49:1319–26.
- 75. Yan LL, Daviglus ML, Liu K, et al. Midlife body mass index and hospitalization and mortality in older age. JAMA 2006;295:190–8.
- Adams KF, Schatzkin A, Harris TB, et al. Overweight, obesity, and mortality in a large prospective cohort of persons 50 to 71 years old. N Engl J Med 2006; 355:763–78.
- 77. Newman AB, Yanez D, Harris T, et al. Weight change in old age and its association with mortality. J Am Geriatr Soc 2001;49:1309–18.
- 78. Heo M, Pietrobelli A, Fontaine KR, et al. Depressive mood and obesity in US adults: comparison and moderation by sex, age, and race. Int J Obes (Lond) 2006;30:513–9.
- 79. Barberger-Gateau P, Fabrigoule C. Disability and cognitive impairment in the elderly. Disabil Rehabil 1997;19:175–93.
- Sakakura K, Hoshide S, Ishikawa J, et al. Association of body mass index with cognitive function in elderly hypertensive Japanese. Am J Hypertens 2008;21: 627–32.
- Deschamps V, Astier X, Ferry M, et al. Nutritional status of healthy elderly persons living in Dordogne, France, and relation with mortality and cognitive or functional decline. Eur J Clin Nutr 2002;56:305–12.
- Han C, Jo SA, Seo JA, et al. Adiposity parameters and cognitive function in the elderly: application of "Jolly Fat" hypothesis to cognition. Arch Gerontol Geriatr 2009;49:e133–8.
- Felson DT, Zhang Y, Hannan MT, et al. Effects of weight and body mass index on bone mineral density in men and women: the Framingham study. J Bone Miner Res 1993;8:567–73.
- Schoptt A, Cormier C, Hans D, et al. How hip and whole-body bone mineral density predict hip fracture in elderly women: the EPIDOS prospective study. Osteoporos Int 1998;8:247–54.
- Imbeault P, Tremblay A, Simoneau JA, et al. Weight loss-induced rise in plasma pollutant is associated with reduced skeletal muscle oxidative capacity. Am J Physiol Endocrinol Metab 2002;282:E574–9.
- 86. Nelson KJ, Coulston AM, Sucher KP, et al. Prevalence of malnutrition in the elderly admitted to long-term-care facilities. J Am Diet Assoc 1993;93:459–61.
- Chlebowski RT, Grosvenor M, Lillington L, et al. Dietary intake and counseling, weight maintenance, and the course of HIV infection. J Am Diet Assoc 1995; 95:428–32 [quiz 433–435].
- Yeh S, Wu SY, Levine DM, et al. Quality of life and stimulation of weight gain after treatment with megestrol acetate: correlation between cytokine levels and nutritional status, appetite in geriatric patients with wasting syndrome. J Nutr Health Aging 2000;4:246–51.
- 89. Horwich T, Fonarow GC, Hamilton MA, et al. The relationship between obesity and mortality in patients with heart failure. J Am Coll Cardiol 2001;38:789–95.

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- Kalantar-Zadeh K, Block G, Humphreys MH, et al. Reverse epidemiology of cardiovascular risk factors in maintenance dialysis patients. Kidney Int 2003; 63:793–808.
- 91. Elia M. Hunger disease. Clin Nutr 2000;19:379-86.
- 92. DeFronzo RA, Ferrannini E. Insulin resistance: a multifaceted syndrome responsible for NIDDM, obesity, hypertension, dyslipidemia, and atherosclerotic cardiovascular disease. Diabetes Care 1991;14:173–94.
- Ramsay SE, Whincup PH, Shaper AG, et al. The relations of body composition and adiposity measures to ill health and physical disability in elderly men. Am J Epidemiol 2006;164:459–69.
- Oppert JM, Charles MA, Thibult N, et al. Anthropometric estimates of muscle and fat mass in relation to cardiac and cancer mortality in men: the Paris Prospective Study. Am J Clin Nutr 2002;75:1107–13.
- 95. Ensrud KE, Nevitt MC, Yunis C, et al. Correlates of impaired function in older women. J Am Geriatr Soc 1994;42:481–9.
- 96. Lang IA, Llewellyn DJ, Alexander K, et al. Obesity, physical function, and mortality in older adults. J Am Geriatr Soc 2008;56:1474–8.
- 97. Reynolds SL, Saito Y, Crimmins EM. The impact of obesity on active life expectancy in older American men and women. Gerontologist 2005;45:438–44.
- Sternfeld B, Ngo L, Satariano WA, et al. Associations of body composition with physical performance and self-reported functional limitation in elderly men and women. Am J Epidemiol 2002;156:110–21.
- Janssen I, Heymsfield SB, Ross R. Low relative skeletal muscle mass (sarcopenia) in older persons is associated with functional impairment and physical disability. J Am Geriatr Soc 2002;50:889–96.
- 100. DiPietro L. Physical activity, body weight, and adiposity: an epidemiologic perspective. Exerc Sport Sci Rev 1995;23:275–303.
- 101. McAuley PA, Myers JN, Abella JP, et al. Exercise capacity and body mass as predictors of mortality among male veterans with type 2 diabetes. Diabetes Care 2007;30:1539–43.
- 102. Haapanen-Niemi N, Miilunpalo S, Pasanen M, et al. Body mass index, physical inactivity and low level of physical fitness as determinants of all-cause and cardiovascular disease mortality: 16 y follow-up of middle-aged and elderly men and women. Int J Obes Relat Metab Disord 2000;24:1465–74.
- 103. Dziura J, Leon C, Kasl S, et al. Can physical activity attenuate aging-related weight loss in older people. Am J Epidemiol 2004;159:759–67.
- 104. Whelton PK, Appel LJ, Espeland MA, 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.
- Rejeski WJ, Focht BC, Messier SP, et al. Obese, older adults with knee osteoarthritis: weight loss, exercise, and quality of life. Health Psychol 2002;21:419–26.
- 106. Messier SP, Loeser RF, Miller GD, et al. Exercise and dietary weight loss in overweight and obese older adults with knee osteoarthritis: the Arthritis, Diet, and Activity Promotion Trial. Arthritis Rheum 2004;50:1501–10.
- Chao D, Espeland MA, Farmer D, et al. Effect of voluntary weight loss on bone mineral density in older overweight women. J Am Geriatr Soc 2000;48:753–9.
- 108. Daly R, Dunstan D, Owen N, et al. Does high-intensity resistance training maintain bone mass during moderate weight loss in older overweight adults with type 2 diabetes? Osteoporos Int 2005;16:1703–12.

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