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A SYSTEMATIC REVIEW OF THE LITERATURE CONCERNING THE RELATIONSHIP BETWEEN OBESITY AND MORTALITY IN THE ELDERLY

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Abstract

Introduction—Obesity is a risk factor for chronic diseases and premature mortality, but the extent of these associations among the elderly is under debate. The aim of this systematic literature review (SR) is to collate and critically assess the available information of the impact of obesity on mortality in the elderly.

Methods—In PubMed, there are three-hundred twelve papers on the relationship between obesity and mortality among older adults. These papers were analysed on the basis of their abstracts, and sixteen studies were considered suitable for the purpose of the study. It was possible to perform a pooled estimate for aggregated data in three different studies.

Conclusion—The results of this SR document that an increased mortality in obese older adults. The limitation of BMI to index obesity and the noted protective action of a moderate increase in BMI on mortality are highlighted. Waist circumference is an indicator of central adiposity and potentially as good a risk factor for mortality as BMI in obese elderly adults.

Keywords

Obesity; elderly; BMI; mortality; sarcopenic obesity

Introduction

Obesity is a world-wide health problem across the lifespan that also affects the elderly in developed and emerging countries. In these countries, their populations have proportionally greater numbers of older adults living to older ages, and the prevalence of obesity is

increasing rapidly even at these oldest ages. In the United States, the prevalence of obesity in the elderly ranges from 42.5% in women aged 60–69 years to 19.5% in those aged 80 years or older. The prevalence of obesity is 38.1% in men aged 60–69 years and 9.6% for those men aged 80 years or older. In Europe, the prevalence is slightly lower but it is still a significant health issue. In the United Kingdom for example, 22% of women and 12% of men aged 75 years or older are obese (1, 2). These statistics bode ill as the proportion of world's elderly population continues to increase.

Absolute and relative fat redistribution, sarcopenia, limited physical activity, poor fitness, chronic inflammation and hormonal changes occur frequently in the latter stages of the aging process. These are all clinical markers and risk factors for obesity, and overweight, obesity and abdominal obesity are risk factors for numerous chronic diseases and premature mortality throughout adulthood. These clinical determinants and their interactions are important in the aetiology, onset, duration, health management and consequences of obesity in old age. Combinations of these risk factors accelerate senescence and increase the cost of acute and chronic rehabilitation and palliative care in the elderly. However, epidemiological data suggest that obesity among the elderly is protective against some health risks and morbid conditions such as hip fractures. Nevertheless, an increasing proportion of obese elderly in a population is a significant health concern, and its impact on the treatment and financial aspects of a health-care system must be carefully examined (3, 4).

In young and middle-aged adults, obesity presents as an excess of body weight and adipose tissue, but among the elderly, obesity is more physiologically and anatomically complex and not so clearly quantifiable. Changes in body composition throughout the ageing process increase variation in the amounts and distribution of muscle and fat among race and ethnic groups that are not present at younger ages. The expression of obesity in young and middle-aged adults includes an increase in fat and fat-free mass, but in the elderly, the decrease of fat-free mass as part of the aging process can produce an obesity characterized by a high percentage of body fat but a stable or low body weight (3, 4). As a result, elderly adults have a greater proportion of fat than younger adults at the same body mass index (BMI) (5, 6). Among these elderly adults, body fat distribution also changes with an increased centralization of fatness from the limbs to the trunk while total fat remains constant (2) even in the oldest individuals (7), and there is an additional increase in fatty infiltration of muscle tissues (2). As a result of these changes and in conjunction with chronic disease and developing frailty, some elderly can develop a condition defined as a new nosographic entity, “sarcopenic obesity”. Those elderly classified as sarcopenic-obese have a significantly high prevalence of physical impairment and disability as well as a high prevalence of metabolic syndrome and co-morbidity (8).

Obesity in adulthood is associated with increased mortality, and data from the Framingham Heart Study report that obese adults (BMI ≥ 30) at age 40 years lived 6–7 years less than did their normal-weight counterparts (8). Another study based on several U.S. data sets (US Life Tables (1999), the third National Health and Nutrition Examination Survey (NHANES III), NHANES I and II, and the NHANES II Mortality Study) also reported that obesity reduces life expectancy, particularly so in younger adults. For example, in obese (BMI ≥ 45) white men and women aged 20–30 years, the minimum years of life lost was 13 and 8 years,

respectively (9). However, the relationship between body weight and mortality in the elderly is controversial because optimal weight varies by age, race and sex, and weight is positively associated with longevity in older populations (10). Much of the current literature reports a curvilinear relationship where the risk of death increases among the very heavy and the very lean, but overweight, healthy adults have a reduced risk of death. However, in most of these studies it is unclear if the increased longevity of the overweight elderly is a result of comparisons to lean (or malnourished) or to normal-weight subjects.

The aim of this systematic literature review (SR) is to collate, review and critically assess current scientific and clinical information on the impact of obesity on mortality in the elderly so as to help clarify and improve our understanding of the complex relationship between the increasing health problem of obesity in elderly adults and the risk of mortality. This knowledge can help to reduce the cost of health care and improve the quality of life in this segment of the world's population.

Material and Methods

This SR was conducted following steps codified by Egger and colleagues (11).

1. Creation of the working group at three institutions
 - a. "Sapienza" University of Rome: one methodological operator (expert in statistics: AR) and three clinical operators (LMD, CS, EG) two of whom were senior researchers experienced in clinical geriatric nutrition.
 - b. INSERM U558, Service de Nutrition, Pôle cardiovasculaire et métabolique, CHU Toulouse (F) one senior investigator (PR) of energy metabolism in the elderly.
 - c. Lifespan Health Research Center, Boonshoft School of Medicine Dayton, Ohio, (USA) one senior investigator (WCC) experienced in body composition and nutritional assessment in the elderly.
2. Formulation and revision of questions based on evidence presented in the introduction: obesity in the elderly and its relation to mortality.
3. Identification of relevant studies and development of a research strategy plan.
 - a. In PubMed (Public Medline run by the National Center of Biotechnology Information (NCBI) of the National Library of Medicine of Bethesda (USA), through:
 - i. selection of key words such as obesity, aged, elderly BMI, mortality that defines of the interest field of the documents to search, grouped in inverted commas ("...") and used separately or in combination;
 - ii. use of the Boolean "AND" operator to allow logical relations among concepts;
 - iii. use of research modalities such as advanced search.

iv. limitations

1. a time limit of papers published in the last 10 years
 2. papers on human subjects
 3. studies of Caucasian subjects > 65 years of age
 4. papers in English, French or Italian
- b.** Senior researchers experienced in geriatric clinical nutrition through revision of reviews and individual articles on nutrition and geriatrics published in reviews qualified in the Index Medicus:
- i.** clinical nutrition reviews in journals such as Nutrition, American Journal of Clinical Nutrition, Nutrition Reviews, British Journal of Nutrition, Journal of Nutrition Health & Aging
 - ii.** geriatric reviews in Journals such as Age & Aging, Journal of the American Geriatric Society, Journals of Gerontology,
- 4.** Definition of the selection criteria of the studies to be included in the SR:
- a.** Studies exploring the impact of obesity in the elderly on mortality
 - b.** Study design based upon clinical trials, randomized controlled trials
 - c.** Studies with end-points of morbid and mortal events
 - d.** Study outcome with identifying parameters and covariates correlated with obesity morbidity and mortality
- 5.** The quality of the selected publications was further critiqued based up on the following characteristics:
- a.** Study duration (temporal, up to an event (death, ...));
 - b.** Enrollment criteria (random, all present at a certain time, ...);
 - c.** Description of the sample and analysis of drop-outs
 - d.** Analysis of the interaction of covariates and confounding variables conditioning the relation between obesity and mortality (sex, age, economic level), pathologies (number or severity of current pathologies), drugs (number and typology of drugs prescribed), depression;
- 6.** Analysis and presentation of study outcomes were compared:
- a.** The data extrapolated from the selected publications were collated and tabulated to allow for comparisons.

1.89; 95% CI: 1.62–2.21). As expected, the shape and magnitude of the BMI and mortality relationship was substantially modified by a history of both smoking and disease, which are predictive factors of leanness and poor survival. Also, Adams and colleagues identified a “U” shaped curve that characterized the relationship between obesity and mortality in men, aged 66 to 71 years where the highest mortality rate was correlated with high values of BMI ($> 40 \text{ kg/m}^2$), and the lowest mortality rate was for a BMI of between 25 and 26.4 kg/m^2 (17).

A “U” shaped curve relationship between BMI and mortality for men and women from ages 70 to 85 years was also demonstrated in the findings of by Dey and Rothenberg (13), during a follow-up of 15 years. The lowest mortality risk was in the middle quintile of BMI for the men of between 24.7 to 26.4 kg/m^2 and for the women between 24.6 and 26.5 kg/m^2 . The nadir of the curve was at a BMI of 27 – 29 kg/m^2 for men and between 25 – 27 kg/m^2 for women. The mortality risk significantly increased for BMI values of between 28.6 – 39.2 kg/m^2 for men and between 29.3 – 39.8 kg/m^2 for women.

The study of Wassertheil-Smoller and colleagues (18) included a sample of 3,975 older adults with hypertension (systolic blood pressure $\geq 160 \text{ mmHg}$ and diastolic blood pressure $\geq 90 \text{ mmHg}$ who were treated with atenolol and chlorthalidone), noted that the relation between BMI and cerebro-cardiovascular accidents confirmed the “U” shaped curve relationship between BMI and mortality. In this study, the nadir of this curve was at a BMI of 27.7 kg/m^2 , and the lowest mortality risk was at a BMI of 25.8 kg/m^2 in men and of 29.6 kg/m^2 for women. Similar values were found for those who had never smoked (nadir of 27.9 kg/m^2) or for current or recently stopped smokers (nadir of 29.1 kg/m^2). For a BMI over 30 kg/m^2 , the mortality risk rises significantly for both men and women.

Stevens (14) conducted a study of a sample of 62,116 men and 262,019 women, including 46,954 who were aged 65 years and older (9,816 men and 37,138 women). For the group of 65–74 year old women with a BMI of 19.0 to 21.9 kg/m^2 , there were 1,494 deaths per 100,000 person-years due to cardiovascular disease, compared with 1,854 deaths per 100,000 person-years among subjects with a BMI of 29.0 to 31.9 kg/m^2 . For men and women aged over 75 years, the mortality rate did not increase with BMI; for women 75–84 years of age at a BMI of 19 to 21.9 kg/m^2 , there were 5,259 deaths per 100,000 person-years due to cardiovascular disease, compared to 5,227 deaths per 100,000 person-years into the group with same age, same sex, but at a BMI of 29 to 31.9 kg/m^2 . Although mortality increased with increasing BMI, the relative risk in these older adults is lower than that of younger adults. The BMI value corresponding to the nadir of the risk of mortality was of 27.4 kg/m^2 among those over 75 years of age and 28.5 kg/m^2 for those over 80 years of age.

Hillier et al (19), analyzed a sample of 9,704 U.S. women aged 65 years and older and reported that the risk of developing cardiovascular and coronary disease is twice as high for women with the metabolic syndrome (NCEP criteria - National Cholesterol Education Panel - or World Health Organization criteria). Sixty-one percent of women with the metabolic syndrome died during the follow-up, compared to 34% of deaths among women without metabolic syndrome. In the study by Diehr et al (15) conducted on a sample of 5,201 old adults, a decrease in mortality was again noted with increasing BMI, but this effect was

reversed for values of BMI between 32 and 34 kg/m² for both men and women. Among men the number of deaths per 100,000 person-years, starting from values of 5,977 for a BMI between 20 and 22 kg/m², reached values of 2,260 per 100,000 person-years for a BMI 30.1 to 32 kg/m², and decreased to 3,931 per 100,000 person-years when the BMI was between 32.1 and 34 kg/m². For women, the same trend was observed, with a mortality of 1,710 deaths per 100,000 person-years for a BMI between 20 and 22 kg/m², arriving at 1,429 deaths per 100,000 person-years when BMI was between 30.1 and 32 kg/m². For values of BMI between 32.1 and 34 kg/m², the mortality rate increased again. Once more the relationship between BMI and mortality was represented by a “U” shaped curve.

The relationship between BMI and mortality was similar in the study of Dorn et al (20) where in a sample of 1,308 men and women, aged between 20 and 96 years with a follow up period of 29 years, there were 91 and 95 deaths among men and women respectively 65–96 years of age. A “U” shaped curve described the relationship between BMI and mortality associated with cardiovascular diseases in this sample. For the men, the lowest mortality was linked to BMI values of between 25.2 and 27.4 kg/m².

An increased risk of mortality associated with an increased BMI was also identified by the analysis conducted by Ajani and collaborators (21). In their study of older adults aged between 70 and 80 years, the highest relative risk of mortality occurred for BMI values above 30 kg/m², but there was a reduced risk of mortality for BMI between 27.5 and 29.9 kg/m². According to the study conducted in 1994 by Taylor et al (22) in 4,208 institutionalized elderly adults, BMI and mortality were linked by a “J” shaped curve, with the nadir of the curve corresponding to values of BMI between 30 and 34.9 kg/m² for subjects aged between 65 and 84 years, and between 25 and 29.9 kg/m² for subjects aged 85 years. The results from this study indicate that the lowest mortality risk was associated with a BMI corresponding to the first degree of obesity based on international guidelines (23).

In contrast to the findings of previous studies, analysis of the Longitudinal Study of Aging (LSOA) conducted by Grabowski et al (24), noted a decreased mortality in obese older adults. Within this sample, malnourished subjects at BMI values of <19.4 kg/m² who represents less than 10% of the population, had the highest mortality (53.9%; HR 1.46), followed by the normal-weight subjects (37%); whereas, the overweight-obese group (BMI > 28.5 kg/m²) had the lowest mortality (33.5%; HR 0.86). This low mortality in the obese group persisted despite controlling for several confounders such as demographic factors, health service utilisation and functional status.

According to the studies conducted by Janssen (25, 26) with a follow-up of 9 years in a cohort from the Cardiovascular Health Study (CHS), after adjusting for confounding variables (age, sex, race, socio-economic status, physical activities and prevalent diseases), the risk for all-cause mortality was 11% lower in the overweight group (BMI 25 to 29.9 kg/m²) and 17% lower in the obese group (BMI 30 kg/m²) compared with the normal-weight group (BMI 24.9 kg/m²). The effect of an elevated BMI on decreasing mortality risk was particularly evident in the oldest (> 75 years) and those in the lowest smoking exposure category.

Measurements of Obesity

In some of the studies reviewed, it was questioned whether BMI is an adequate descriptive indicator of mortality among elderly adults when compared to waist circumference (WC), which is strongly related to both visceral and total fat at the same age group. The risk relationship of BMI and WC on mortality in both women and men were examined with particular attention to independent predictive value of these two anthropometric variables (27). Janssen et al (26) showed that death rates per 1,000 person-years (adjusted for age and sex) were highest in those older adults who had a high WC (96.4±8 and 107.4±8 cm) within the overweight and obese BMI categories (27.2±1 and 32.6±2 kg/m²). Within the low (82.0±7 cm) and moderate (91±7 cm) WC categories, death rates were lower in the BMI overweight (25.4±2 kg/m²) and obese (28.9±4 kg/m²) adults, than in those with a normal BMI (22.8±2 kg/m²). After controlling for WC, mortality risk decreased 21% for every standard deviation increase in BMI; whereas, after controlling for BMI, mortality risk increased only 13% for every standard deviation increase in WC. Another study, conducted by Visscher et al (28), maintains that high values of WC are a better predictor of mortality than BMI. WC values between 90 and 102 cm and greater than 102 cm are associated with increased mortality and indicate that WC is able to predict mortality risk more specifically than BMI.

Some studies have used other measures or indices of obesity. Miller and collaborators in an earlier study conducted (29) on a population of 1,396 elderly adults used corrected arm muscle area (the ratio between the average circumference of the arm and triceps skinfold) which had a greater predictive value for mortality among during a 8 year follow up, but it is very prone to measurement error. In addition, Volpato et al (30) conducted a study on 344 subjects aged between 65 and 99 years in a nursing home in Padua (Italy) where the lowest mortality risk was associated with a BMI of between 23.6 and 29.2 kg/m². However, the association loses force if body cell mass (BCM) was considered in the analysis. With high BCM values, subjects with a low BMI (19.3–23.5 kg/m²), intermediate BMI (23.6 to 29.2 kg/m²) or high BMI (> 29.2 kg/m²) had the same probability of surviving.

Meta-analysis and pooled estimated

It was possible to conduct a meta-analysis using separate data stratified by age, gender, classes of BMI and mortality from three of the studies conducted by Adams (17), Calle (16) and Diehr (15). Through a pooled estimate (12), we obtained a new estimate of the relation between obesity and mortality in older adults simultaneously using all the information achieved from the three studies (Table 4). BMI was stratified into the following classes: 20, 20–25, 25–30 and >30 kg/m². The mortality rate was highest among malnourished subjects, decreased with increasing BMI but rose again when the values of BMI were over 30 kg/m². The analysis of the data from these three studies, included 58,227 deaths (30,036 deaths among men and 28,191 deaths among women), over the follow-up period which demonstrated a clear a “U” shaped curve association between BMI and mortality. The lowest mortality rate was for 2,108 deaths per 100,000 person-years for men and 1,366 deaths per 100,000 person-years for the women at a BMI of 25–30 and 20–25 kg/m², respectively. These findings indicate that a lower BMI may be more protective against mortality for women rather than men.

Discussion

The results of this SR present data that show an increased mortality in obese and older adults. The limitation of BMI to index obesity and the noted protective action of a moderate increase in BMI on mortality have been highlighted.

Limitations of BMI as a measure of geriatric adiposity

BMI is an epidemiological index that can categorizes a population into underweight (BMI 18.5 kg/m^2), normal weight (BMI between 18.5 and 24.9 kg/m^2), overweight (BMI between 25 and 29.9 kg/m^2) and obese (BMI $\geq 30 \text{ kg/m}^2$) (31) based on validated measures of body composition. BMI is a well-accepted index of body fatness, but it lacks specificity in clinical practice (32). It is significantly correlated with fat mass ($r = 0.6\text{--}0.7$), and with fat-free mass ($r = 0.5\text{--}0.6$) (33, 34), and it has low sensitivity in subjects with increased fat mass (35). Furthermore, the correlation of BMI with the fat mass decreases with age, race, in athletes, in those with pathological conditions and in weight loss (36). Body composition changes affect the application of BMI in the elderly, because the aging process modifies both the numerator (weight) and the denominator (stature). Several studies documented in this review, reported that the well recognized age-related decline in stature induces a false BMI value resulting from an increase of 1.5 kg/m^2 in men and 2.5 kg/m^2 in women despite minimal changes in body weight (38). Studies conducted by Wassertheil-Smoller (18), Stevens (14), Diehr (15) and Miller (29) all demonstrated that ranges of BMI from a young adult population are not a suitable health risk reference for an elderly population. There is an increase in mortality with increasing BMI in younger adults, but among the elderly, the relative risk is lower than that of young and middle-aged adults.

The literature reviewed in this report confirms that abdominal fatness, even in geriatric age groups, is more strongly linked to morbidity and mortality than peripheral fat deposits (26, 39, 40). Data for waist circumference indicates that it is as effective as BMI as a risk factor, if not more so in assessing abdominal fatness and mortality risk in the elderly obese. In fact, according to the studies of Janssen (26) and Visscher (28), higher BMI values indicated lower mortality risk once the risk attributable to WC was accounted for. BMI indicating overweight or obese individuals is associated with reduced mortality risk when waist circumference is less than 93 cm for men and 79 cm for women (41, 42). This data may be attributed to the consideration that BMI is a reflection of lean mass for individuals with the same WC; whereas, WC is a reflection of fat mass for individuals with the same BMI. Therefore, WC predicts abdominal subcutaneous and visceral fat and the weighted evidence suggest that abdominal fatness is strongly related to morbidity than peripheral fatness, whereas accumulation of fat and lean mass in the arms and legs seems to be protective against cardiovascular risk factors

The study of Volpato (30) reaches similar conclusions taking into account a different body composition parameter which is the BCM where, the association between BMI and mortality loses strength, indicating that the BCM can better predict survival independently than BMI values. BMI may remain unchanged despite changes in body composition in old age, while BCM can decrease, although the weight (and thus BMI) remains unchanged.

Relation between BMI and mortality in elderly

The majority of studies reviewed in this report noted an increased risk of mortality in obese older adults with high BMI. This is confirmed primarily by the study that defines obesity based on WC and by the results of the meta-analysis we conducted. The two studies reviewed that arrive at different conclusions have limitations in their designs. The study of Grabowski (24) considered a broad range of BMI values so that the high mortality appears to be associated with BMI ranging from 19.5 to 28.4 kg/m², but thus includes malnourished or obese subjects. Moreover, this study makes no distinction between men and women in the classes of BMI as does the study of Janssen (25). Furthermore, in another study conducted in 2007, the same research group (26) noted that a BMI indicating overweight is associated with a small increased risk of disease, but at the same time it is also associated with a reduction in mortality risk. This confirms once again that the threshold values for classes of BMI cannot be transposed purely and simply on a geriatric age group. Therefore, it is not easy to show a protective effect of obesity in the geriatric age as much as the ineffectiveness of the tools at our disposal (BMI above all) to highlight just a state of obesity.

BMI range at lower risk of mortality in elderly

Almost all the studies in this SR confirmed that the lowest mortality is correlated with an average BMI of between 23.5 and 27.5 kg/m², higher than that in young and middle-aged adults (3, 43–46). Also, the pooled estimate confirms that a U-shaped curve continues to describe the relationship between BMI and mortality in old age, but the nadir is shifted toward higher values of BMI (47) because subjects who are susceptible to the effects of excess body fat die before reaching old age (9, 48, 49). Older adults with a high BMI are resistant to the effect of an excess of adiposity (50). On the other hand, a moderately high BMI is a protective factor (increased fat mass and/or lean body mass) against acute events that occur frequently in geriatric age groups (51).

Conclusions

Obesity is a mortality risk in old age, but with threshold values to be defined taking into account the protective effect that a mild increase of fat mass seems to have against mortality. Clearly, further research is needed to better define the characteristics of obesity in the elderly, to identify the ranges of BMI associated with lower risk of mortality, distinguishing between men and women. It is also important to identify and/or to develop more effective tools in risk assessment related to adiposity excess in geriatric age. Finally, it remains to evaluate the cost/benefit ratio that measures of reduction of body fat have on the quality of life of elderly obese.

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Table 1

General Characteristics of selected studies

	Design	Setting	Selection criteria	Limits of the study
NON-INSTITUTIONALISED				
Janssen I et al: JAGS 2005; 53: 2112–8	Cohort longitudinal study	Participants to the Cardiovascular Health Study (CHS)	M and F 65 yrs old	Participants were predominately white, and more than half were women All-cause mortality was the only outcome examined
Wassertheil-Smoller S et al: Arch Intern Med 2000; 160: 494–500	Randomized clinical trial	Participants to the Systolic Hypertension in the Elderly Program trial (SHEP)	M and F 60 yrs old; SBP > 160 mmHg and DBP < 90 mmHg	Despite randomization, the control and treatment groups differed in important unknown confounders
Grabowski DC et al: JAGS 2001; 49: 968–979	Retrospective cohort study	Participants to the Longitudinal Study of Aging (LSOA)	M and F 70 yrs old	It was not possible to examine the effects of smoking, exercise or aerobic capacity in this dataset. Self-reported heights and weights were used to compute BMI
Hillier TA et al: Diabetes Care 2005; 28: 2258–60	Prospective cohort study	Participants to the Study of osteoporotic fractures (SOF)	M and F 70 yrs old	Not reported
Stevens J. et al: N Engl J Med 1998; 338: 1–7	Prospective cohort study	Participants to the American Cancer Society's Cancer Prevention Study I	analysis was restricted to subjects who had never smoked, who had no history of cancer, heart disease or stroke, Involuntary weight loss 4.5 kg in past 2 yr	Self-reported heights and weights were used to compute BMI BMI was estimated only once, at one age, for each subject the number of years of follow-up was the same in the cohort of 30-year-old subjects and among 85-year-old subjects
Diehr P. et al: Am J Public Health 1998; 88: 623–629	Cohort longitudinal study	Participants to the Cardiovascular Health Study (CHS)	M and F > 65 yrs old who had never smoked	Too short follow-up Exclusion of the sickest and thinnest people
Calle E. et al: N Engl J Med 1999; 341: 1097–105	Prospective cohort study	Participants to the American Cancer Society's Cancer Prevention Study II	M and F > 30 yrs old	The increased risk of death from specific causes that was associated with leanness in this and other studies may reflect pre-existing, but unrecognized, disease processes Unable to control for long-term weight loss Self-reported heights and weights were used to compute BMI No direct measure of adiposity or of lean body mass, and no measure of central adiposity
Janssen I: Obesity 2007; 15: 1827–40	Prospective cohort study	Participants to the Cardiovascular Health Study (CHS)	M and F > 65 yrs old	No measure of adiposity distribution Participants were predominately white

	Design	Setting	Selection criteria	Limits of the study
Adams KF et al N Engl J Med 2006; 355: 763–78	Prospective cohort study	Participants to the National Institutes of Health (NHI)-A ARP Diet and Health Study	M and F aged 50–71 years	Not reported
Ajani UA et al: Ann Epidemiol 2004; 10: 731–739	Randomized placebo-controlled trial	Participants to the Physicians' Health Study	M and F aged 40–84 years	Self-reported heights and weights were used to compute BMI
Dorn JM et al: Am J Epid 1997; 919–931	Prospective cohort study	Participants to the Buffalo Blood Pressure Study	M and F aged 20–96 years, who had no history of cancer, heart disease or stroke, diabetes	Self-reported heights and weights were used to compute BMI BMI and other characteristics were determined only at 146: baseline No measures of body composition or fat distribution were available
Miller MD et al: JAGS 2002; 50: 1272–1277	Prospective cohort study	Participants to the Australian Longitudinal Study of Aging	M and F > 70 yrs old	Some of the most ill people may have been excluded due to selection criteria Men were significantly older than women
Visscher TLS et al: Int J of Obes 2001; 25: 1730–1735	Prospective cohort study	Participants to the Rotterdam Study	M and F aged 55–102 years	No informations about weight loss or health status
INSTITUTIONALISED and FREE-LIVING SUBJECTS				
Dey DK et al: Eur J Clin Nutr. 2001; 55: 482–492	Prospective cohort study	Subjects enrolled at the Göteborg University (Sweden)	M and F > 70 yrs old	Chronic diseases were not considered
INSTITUTIONALISED SUBJECTS				
Volpato S et al: JAGS 29004; 52: 886–891	Prospective cohort study	M and F institutionalised in the "Istituto di riposo per anziani" of Padua (Italy)	M and F aged 65–99 years, who had no history of acute diseases in the last 30 days	Body composition was obtained from Bioelectrical impedance analysis No informations about muscle mass, physical activity, and weight loss The sample was mainly constituted by women
Taylor DH et al: JAGS 2001; 49: 1319–1326	Cross-sectional study	Participants to the National Long Term Care Survey (NLTC)	M and F > 65 yrs old	Confounders factors (smoking habits, alcohol consumption) were not considered

Legend: BMI: body mass index

Table 2

Characteristics of the sample analysed in the studies selected in the systematic review

	Subjects	Study duration	Drop out
FREE-LIVING SUBJECTS			
Janssen I et al: JAGS 2005; 53: 2112–8	5200 M and F; 94,7% whites	Enrollement: 1989–1990. 9 yrs follow-up	Not indicated
Wassertheil-Smoller S et al: Arch Intern Med 2000; 160: 494–500	4736 M and F, black and white	5 yrs follow-up	47 participants (BMI not available)
Grabowski DC et al: JAGS 2001; 49: 968–979	7,527 participants: black, white (91,4%) and hispanic	Enrollement: 1984 8 yrs follow-up	Not indicated
Hillier TA et al: Diabetes Care 2005; 28: 2258–60	9704 F (99% non-hispanic white)	Enrollement: 1986–1988 12 yrs follow-up	Functionally impaired subjects
Stevens J. et al: N Engl J Med 1998; 338: 1–7	62.116 M and 262.019 F (46.954 elderly participants: 9.816 M, 37.138 F) 100% white	Enrollement: 1959–1960 13 years follow-up	Not indicated
Diehr P. et al: Am J Public Health 1998; 88: 623–629	4317 M and F 95% white	Enrollement: 1989 5 yrs follow-up	Not indicated
Calle E. et al: N Engl J Med 1999; 341: 1097–105	457.785 M, 588.369 F: white and black	Enrollement: 1982 14 years follow up	Not indicated
Janssen I: Obesity 2007; 15: 1827–40	4968 M and F White: 94,8%	Enrollement: 1989–90 9 years follow up	Not indicated
Adams KF et al N Engl J Med 2006; 355: 763–78	527265 participants (313047 M, 214218 F) 90% white	Enrollement: 1995–6 10 years follow up	Not indicated
Ajani UA et al: Ann Epidemiol 2004; 10: 731–739	85078 M 100% white	Enrollement: 1983 5 years follow up	Not indicated
Dorn JM et al: Am J Epid 1997; 146: 919–931	1308 participants (611 M, 697 F) 100% white	Enrollement: 1960–61 29 years follow up	Not indicated
Miller MD et al: JAGS 2002; 50: 1272–1277	1396 M and F 100% white	Enrollement: 1992 8 years follow up	Not indicated
Visscher TLS et al: Int J of Obes 2001; 25: 1730–1735	6296 M and F 100% white	Enrollement: 1990–93 5 years follow up	Not indicated
INSTITUTIONALISED and FREE-LIVING SUBJECTS			
Dey DK et al: Eur J Clin Nutr. 2001; 55: 482–492	2628 subjects (1225 U, 1403 F)	Enrollement: 1971–1981 15 years follow up	35 subjects (15 M, 20 F) weight and stature not available 3 F with BMI 40 Neoplastic subjects (77 M and 108 F)
INSTITUTIONALISED SUBJECTS			
Volpato S et al: JAGS 29004; 52: 886–891	344 subjects (272 F, 72 U)	Enrollement: 1990 4 years follow up	Not indicated
Taylor DH et al: JAGS 2001; 49: 1319–1326	4208 M and F 100% white	Enrollement: 1994	Not indicated 1 year follow up

Legend: BMI: body mass index

Table 3

Correlation between mortality and obesity

	Mortality analysis	Correlation between mortality and obesity
FREE-LIVING SUBJECTS		
Janssen I et al: JAGS 2005; 53: 2112–8	Cox-proportional hazards model, considering sex, age, ethnicity, socioeconomic status, smoking habits, physical activity, health status Mortality rates per 1000 person-year	BMI and WC were both negative predictors of mortality. BMI and WC examined simultaneously, BMI was a negative predictor of mortality, whereas WC was a positive predictor of mortality. After controlling for WC, mortality risk decreased 21% for every standard deviation increase in BMI. After controlling for BMI, mortality risk increased 13% for every standard deviation increase in WC. The patterns of associations were consistent by sex, age, and disease status.
Wassertheil-Smoller S et al: Arch Intern Med 2000; 160: 494–500	Cox-proportional hazard analysis, considering age, ethnicity, sex, educational level Mortality rates per 1000 person-year	The relation between BMI and cerebro-cardiovascular accidents, confirms the “U” shaped relation between BMI and mortality The nadir of this curve is at a BMI of 27.7 kg/m ² The lowest mortality risk is associated with a BMI of 25.8 kg/m ² in men and of 29.6 kg/m ² for women. Similar values for patients who had never smoked (nadir of 27.9 kg/m ²) or for patients who smoke now or in the recent past (nadir of 29.1 kg/m ²) For BMI over 30 kg/m ² , the mortality risk rises significantly for both men and women.
Grabowski DC et al: JAGS 2001; 49: 968–979	Cox proportional hazard model	Decreased mortality in obese older people. The group of malnourished subjects (BMI <19.4 kg/m ²) has the highest mortality (53.9%; HR 1.46), followed by the normal-weight subjects (37%), whereas the overweight-obese group (BMI > 28.5 kg/m ²) has the lowest mortality (33.5%; HR 0.86). Lowest mortality in obese older people persists despite controlling for different confounders: demographic factors, health service utilisation and functional status.
Hillier TA et al: Diabetes Care 2005; 28: 2258–60	Cox proportional hazard model considering age and smoking habits	61% of elderly women with metabolic syndrome died during the follow-up, compared to 34% of deaths among women without metabolic syndrome.
Stevens J. et al: N Engl J Med 1998; 338: 1–7	Proportional-hazard analysis (PROC PHREG, SAS Institute, Cary, N.C.) Likelihood-ratio test Weighted linear regression analysis	For 65–74 years old women with a BMI of 19.0 to 21.9 kg/m ² , 1,494 deaths per 100,000 person-years due to cardiovascular disease, compared with 1854 deaths per 100,000 person-years among subjects with a BMI of 29.0 to 31.9 kg/m ² . For men and women aged over 75 years, the mortality rate does not increase with BMI: within the group of women 75–84 years with BMI of 19 to 21.9 kg/m ² . Although there is an increase in mortality with increasing BMI, the RR is lower than that of younger individuals. The BMI value corresponding to the nadir of the risk of mortality is of 27.4 kg/m ² among the ultra seventy-five and 28.5 kg/m ² among the ultra eighty.
Diehr P. et al: Am J Public Health 1998; 88: 623–629	Mortality rate (5 years-person) Logistic regression model	Relation between BMI and mortality is represented by a “U” shaped curve (decrease in mortality with increasing BMI; reversed effect for values of BMI between 32 and 34 kg/m ² for both men and women) Men: death rate per 100,000 person-years is of 5977 for a BMI between 20 and 22 kg/m ² , 2260 for a BMI 30.1 to 32 kg/m ² , 3931 when the BMI is between 32.1 and 34 kg/m ² Women: mortality rate of 1710 for a BMI between 20 and 22 kg/m ² , 1429 when the BMI is between 30.1 and 32 kg/m ² . For values of BMI between 32.1 and 34 kg/m ² , the rate increases again.
Calle E. et al: N Engl J Med 1999; 341: 1097–105	Mortality rate considering age Cox proportional hazard model	A high BMI is associated with higher rates of death from all causes among men and women (“U” shaped relation): <ul style="list-style-type: none"> the lowest death rate per 100,000 person-years was within the class of BMI between 20.5 and 21.9 kg/m² for age between 65 and 74 years, and the BMI class of 23.5 to 24.9 kg/m² for subjects > 75 years the highest mortality in all cases was at BMI 35 kg/m² both for men (RR 2.68; 95% CI: 1.76–4.08) and women (RR: 1.89; 95% CI: 1.62–2.21). The association between BMI and mortality is substantially modified by a history of both smoking and disease, factors that are predictive of leanness and poor survival.

	Mortality analysis	Correlation between mortality and obesity
Janssen I: Obesity 2007; 15: 1827–40	Cox proportional hazard model	Compared with the normal-weight group, the risks of myocardial infarction, stroke, sleep apnea, urinary incontinence, cancer, and osteoporosis is not different in the overweight group ($p < 0.05$). The risks for arthritis and physical disability are modestly increased in the overweight group ($p < 0.05$), whereas the risk for type 2 diabetes is increased by 78% in the overweight group ($p < 0.01$). After adjusting for all relevant covariates, all cause mortality risk was 11% lower in the overweight group ($p < 0.05$).
Adams KF et al N Engl J Med 2006; 355: 763–78	Mortality rates per 100.000 person-year	Cox regression analysis, considering ethnicity, educational level, smoking habits, alcohol consumption, chronic diseases Increased risk of death for the highest and lowest categories of BMI among both men and women, in all racial or ethnic groups, and at all ages.
Ajani UA et al: Ann Epidemiol 2004; 10: 731–739	Proportional hazard regression model	The highest RR of mortality occurs for BMI above 30 kg/m ² whereas there is a reduced risk of mortality for BMI between 27.5 and 29.9 kg/m ² .
Dorn JM et al: Am J Epid 1997; 146: 919–931	Cox proportional hazard model	“U” shaped curve correctly described the relation between BMI and mortality associated with cardiovascular diseases As regards men, the lowest mortality is linked to a range of BMI between 25.2 and 27.4 kg/m ² .
Miller MD et al: JAGS 2002; 50: 1272–1277	Cox proportional hazard regression model	After adjustment for potential confounders (baseline age, gender, marital status, smoking, self-rated health, ability to conduct activities of daily living, comorbidity, cognition performance, and presence of depression), those older Australians with a low CAMA (Corrected Arm Muscle Area) had an increased risk of mortality at 8-year follow-up (HR 1.94, 95% CI 1.25–3.00) There was no increased risk in 8-year mortality identified for those with a high or low BMI.
Visscher TLS et al: Int J of Obes 2001; 25: 1730–1735	Cox proportional hazard model	U shaped curve describes the relation between BMI and mortality An increased risk is present for BMI 30 A linear correlation is present between WC and mortality.
INSTITUTIONALISED and FREE-LIVING SUBJECTS		
Dey DK et al: Eur J Clin Nutr. 2001; 55: 482–492	Cox proportional hazard regression model	“U” shaped relation between BMI and mortality The lowest mortality risk has been found in the middle quintile of BMI (24.7 to 26.4 kg/m ²) for men and women The nadir of the curve is at 27–29 kg/m ² for men and at 25–27 kg/m ² for women. The mortality risk significantly increases for values of BMI between 28.6 and 39.2 kg/m ² for men and between 29.3 and 39.8 kg/m ² for women.
INSTITUTIONALISED SUBJECTS		
Volpato S et al: JAGS 29004; 52: 886–891	Kaplan-Meier Curves Cox Proportional Hazard Model	After adjustment for age and sex, subjects with low BMI had significantly higher mortality than those with higher BMI levels. In a fully adjusted regression model, there was no association between BMI levels and risk of mortality, with subjects in the top tertile having the same likelihood of mortality as subjects in the lowest tertile (RR 0.94, 95% CI 0.61–1.43).
Taylor DH et al: JAGS 2001; 49: 1319–1326	Mortality rates per 1000 person-year Multivariate logistic regression	BMI and mortality are linked by a “J” shaped curve, with the nadir of the curve corresponding to values of BMI between 30 and 34.9 kg/m ² for subjects aged between 65 and 84 years, and between 25 and 29.9 kg/m ² for subjects aged 85 years.

Legend: BMI: body mass index; WC: waist circumference; CVD: cardio vascular diseases; BCM: body cell mass

Table 4

Pooled estimate of mortality rate per 100,000 person-years stratified by gender and classes of BMI

	BMI (kg/m ²)	Mortality rate	95% CI
Men	20,0	3500,5	3311,2–3689,9
	20–25	2200,3	2156,6–2243,9
	25–30	2108,0	2072,9–2143,1
	>30	2781,2	2704,8–2857,7
Women	20,0	1795,3	1736,2–1854,4
	20–25	1366,3	1343,1–1389,4
	25–30	1524,2	1490,1–1558,4
	>30	1974,9	1910,2–2039,6

Legend: BMI: body mass index; CI: confidence interval