#### <u>abstract</u>

# **ENDOCRINE DISORDERS**



Unintentional weight loss is a common problem among communitydwelling older adults. Although a slight decline in body weight is considered a normal part of the aging process, clinically significant weight loss (>5% of usual body weight) has harmful consequences on functional status and quality of life, and is associated with excess mortality over a three- to twelve-month period. A variety of physical and psychological conditions, along with age-related changes, can lead to weight loss. In up to one-quarter of patients, there is no identifiable cause. A rational approach to clinical investigation of these patients can facilitate arriving at a diagnosis and minimize unnecessary diagnostic procedures.

Key words: weight loss, older adults, mortality, epidemiology, diagnosis

## An Approach to the Diagnosis of Unintentional Weight Loss in Older Adults, Part One: Prevalence Rates and Screening

*Karen L. Smith, MSc, Kunin Lunenfeld Applied Research Unit, Baycrest and Department of Nutritional Sciences, University of Toronto, Toronto, ON.* 

*Carol Greenwood, PhD, Kunin Lunenfeld Applied Research Unit, Baycrest and Department of Nutritional Sciences, University of Toronto, Toronto, ON.* 

*Helene Payette, PhD,* Research Center on Aging, Health & Social Services Center – University Institute of Geriatrics of Sherbrooke, Faculty of Medicine and Health Sciences, University of Sherbrooke, Sherbrooke, QC.

Shabbir M.H. Alibhai, MD, MSc, Division of General Internal Medicine & Clinical Epidemiology, University Health Network; Geriatric Program, Toronto Rehabilitation Institute; Departments of Medicine and Health Policy, Management and Evaluation, University of Toronto, Toronto, ON.

#### Introduction

Unintentional weight loss is described as an involuntary decrease in body weight over time. Although a slight decline in body weight is considered a normal part of aging, clinically significant weight loss (frequently defined as >5% of usual body weight over six to twelve months<sup>1</sup>) is a common finding among communitydwelling older adults. Among older adults who receive homecare services, unintentional weight loss is encountered in up to 27% of frail people 65 years of age or older.<sup>2</sup> Fundamentally, weight loss occurs as a result of inadequate caloric intake given the energy needs of the individual. Among older adults, the causes of weight loss appear to be quite heterogeneous and depend largely on the presence of underlying health problems, poor nutritional status, or both. Weight loss may occur in isolation but is often a symptom of one or more diagnosed or undiagnosed illnesses. Epidemiological studies have consistently found that weight loss in older adults is associated with increased mortality, which can range from 9% to 38% within 1 to 2.5 years after the weight loss occurred.<sup>3–5</sup> High-risk populations, such as frail older adults,<sup>6</sup> individuals with low initial body weights,<sup>6-8</sup> individuals who have Alzheimer's disease<sup>9</sup> and older adults recently admitted to hospital, are particularly susceptible to increased mortality.<sup>10,11</sup> Weight loss is also associated with an increased risk of in-hospital complications,<sup>12,13</sup> a decline in activities of daily living or physical function,<sup>14,15</sup> higher rates of admission to an institution<sup>2,10</sup> and poor quality of life.<sup>16</sup>

This article is the first installment of a two-part clinical review of unintentional weight loss in older adults. In this article, the prevalence of weight loss in community-dwelling older adults and the impact of weight loss on morbidity and mortality are reviewed. Screening tools that identify individuals at high risk of malnutrition are also reviewed and several diagnostic aids that may help clinicians distinguish among the different causes of weight loss are highlighted. Portions of this article are reviewed in greater detail elsewhere.<sup>17</sup>

#### The Prevalence of Weight Loss in Community-Dwelling Older People

There is a large body of epidemiological literature examining the prevalence of weight loss in the adult population in general<sup>18-27</sup> and among older adults (generally defined as 65 years of age or older) in particular.<sup>7,24,26,28–30</sup> Several important conclusions can be made from these studies. Most adults age 65 or older experience little change in weight, on average, over a period of five to ten years. For example, in Canadian,<sup>31</sup> European,<sup>32</sup> and American<sup>15</sup> prospective studies of community-dwelling older adults, little to no change in group mean body weight or weight change was observed over a three- to five-year period, suggesting reasonably stable body weights in most study participants. However, there was significant heterogeneity in body weight status over time, and a nonnegligible proportion of study participants experienced clinically significant weight loss. The European study reported that 16% of men and 16% of women lost at least 5 kg, whereas 9% of men and 10% of women gained at least 5 kg.32 The American study reported that 16.2% of men and 18.7% of women lost at least 5% of their weight over three years, while 11.1% of men and 15.9% of women gained at least 5% of their weight over three years.<sup>15</sup> Similar results have been demonstrated in other longitudinal studies of older adults.28-30,33,34

These studies also highlight factors associated with weight loss. Among older adults, increasing age, disability, coexisting medical illnesses, prior hospitalization, low income and/or educational attainment, presence of cognitive impairment, low levels of physical activity, smoking, heavy drinking, low body weight, prior unintentional weight loss, and medically or self-prescribed dieting were associated with a higher likelihood of weight loss in various studies.<sup>28–30,33–36</sup>

Among individuals seeking health care, the incidence of unintentional weight loss is typically lower than the results of longitudinal studies would suggest. In one study of adults seen in an internal medicine clinic, approximately 8% of 1,200 consecutive patients reported having unintentionally lost at least 2.3 kg (5 lbs) within the last six months.<sup>4</sup> In three studies of hospitalized adults using slightly different definitions of weight loss, incidence rates varied from 1.3% to 3%.<sup>3,5,37</sup> In the only study examining rapid and severe weight loss among older adults (age 63 or older), 45 of approximately 10,000 patients (0.45%) had lost at least 7.5% of their baseline body weight within six months and did not have a definitive cause of weight loss recorded at initial presentation.<sup>38</sup> These incidence data, in the 1-3% range, contrast sharply with figures from other settings. For example, in a study of community-dwelling older men, the annual incidence of at least a 5% decline in weight was 7.8%.39 In free-living frail older adults receiving community services (n=290), the prevalence of reported unintentional weight loss of more than 5 kg in the previous 12 months was 27%.<sup>2</sup> This suggests significant differences in the population of older adults with weight loss who come to the attention of health care professionals, with greater vulnerability apparent in those who are already frail (see below).

#### Weight Loss and the Associated Risks

Given that weight loss is reasonably common among older adults, when does weight loss become a clinically significant condition that requires intervention by health care professionals? The clinical importance of unintentional weight loss can be demonstrated by its association with increased mortality risk, need for increased health care, and adverse consequences on physical function and quality of life. Prospective studies report that weight loss of 4-5% or more of body weight within one year, or 10% or more over five to ten years or longer, is associated with increased mortality or morbidity or both.<sup>7,28,36,39,40</sup> This association has also been seen in numerous epidemiologic and clinical studies that adjusted for age, gender, comorbidities, disability,

smoking, alcohol use, or level of physical activity and that excluded deaths within the first few years of weight loss to account for undiagnosed illness. In addition, recent weight loss has been associated with increased in-hospital mortality and one-year mortality in several groups of older adults admitted to hospital.<sup>10,11,13,41</sup> Among surgical patients 60 years of age or older undergoing a variety of surgical procedures, weight loss of at least 10 lbs within six months prior to surgery was associated with an 11-fold increased mortality risk.<sup>12</sup> Weight loss has also been associated with an increased risk of in-hospital complications,<sup>13</sup> decline in activities of daily living or physical function,14,15,42 increased likelihood of institutionalization<sup>2</sup> and poor quality of life.<sup>16</sup> Adverse effects of weight loss are particularly significant among individuals with low body weight.<sup>7,16,19,22,23,25,26,40,43-45</sup> In frail older populations, even a small degree of weight loss (e.g., 1 kg,<sup>46</sup> or 3% of body weight<sup>42</sup>) may be significant. Evidence that weight loss per se, irrespective of its origins, is harmful comes from studies demonstrating that even voluntary weight loss among older adults is associated with increased risk of death and of hip fracture, which highlights the importance of maintaining weight with age.47

A number of mechanisms have been suggested to explain the association between weight loss and various adverse outcomes. Weight loss exacerbates loss of fat-free mass, known as sarcopenia (Figure 1), associated with aging,48 leading to decreased functional capacities<sup>49,50</sup> and increased probability of mobility disability and osteoporotic fractures.<sup>51</sup> Many older patients with unintentional weight loss experience concomitant malnutrition<sup>52-54</sup> and thereby have cachexia.<sup>55</sup> Cachexia is associated with a disproportionate loss of skeletal muscle rather than body fat, even in the absence of weight loss and is generally defined as a profound and marked state of constitutional disorder, general ill health, and malnutrition. A decline of 10% of skeletal muscle mass may be associated with a decline in physical function (e.g.,

#### Figure 1: **Physiology of Sarcopenia**

#### sarcopenia

Sarcopenia is the age-related loss of muscle mass, strength, and function. It may also accompany diet-induced weight loss. With aging and inactivity, the most atrophy is seen in the fast-twitch fibres that are recruited during high-intensity, anaerobic movements. Although sarcopenia is mostly seen in physically inactive individuals, it is also evident in individuals who remain physically active throughout their lives



Branches of motor neuron

Muscle fibres

#### the motor unit

Age-related changes in the neuromuscular system may play a role in the onset of sarcopenia. The number of spinal cord motor neurons and functioning motor units decline with age. Human nerve cells have a predetermined life span and the decline in these cells is dependent on the location in the body, age, and presence of disease. The motor neurons are responsible for sending signals from the brain to the muscles to initiate movement. A motor unit consists of the motor neuron and all of the muscle fibres that it connects to or innervates.

The loss of muscle fibres begins with the loss of motor neurons. Motor neurons will die with age, resulting in a denervation of the muscle fibres within the motor unit. This denervation causes the muscle fibres to atrophy and eventually die, leading to a decrease in muscle mass.

### the role of the satellite cell

Satellite cells are adult stem cells specific to skeletal muscle fibres. Satellite cells are found in the mature muscle, between the sarcolemma and basement membrane of the muscle fibres. These cells are involved in the normal growth of muscle, as well as regeneration following injury or disease. They are able to proliferate in response to injury and give rise to regenerated muscle and to more satellite cells.

MOTOR UNIT

The biological mechanism of sarcopenia appears to be in the decreased ability of satellite cells to propagate themselves. Satellite cells are required to fuse into skeletal muscle fibres, and help in settings where repair and regeneration are required. Therefore aging muscle loses its ability to respond to anabolic stimuli.

decreased exercise tolerance or difficulty performing activities of daily living).<sup>56</sup> In addition, cachexia is associated with a systemic inflammatory response, elevated cytokine levels, and compromised immunity, all of which are thought to contribute to adverse outcomes, including early death.<sup>57,58</sup>

#### Approach to Diagnosis of Clinically Significant Weight Loss

In general, causes of weight loss among older adults can be classified as organic (e.g., neoplastic, nonneoplastic, and agerelated changes), psychological (e.g., depression, dementia, anxiety disorders) or nonmedical (e.g., socioeconomic conditions) (Table 1). Up to one-quarter of all cases have no identifiable cause, despite extensive investigation. People with no known cause of weight loss generally have a better prognosis than people with known causes, particularly when the cause is neoplastic.

Often a combination of factors,

rather than a single cause, will lead to weight loss in older adults, particularly frail individuals 75 years or older. Studies suggest that when a definitive diagnosis can be established, the most common causes of unintentional weight loss include depression, gastrointestinal illnesses (e.g., peptic ulcers or motility disorders), and cancer.<sup>1</sup> Many factors contributing to weight loss are not associated with traditional medical diseases (see "Meals on Wheels" sidebar), while other factors may be related to age-associated physiologic changes, collectively known as the "anorexia of aging." The importance of medications in contributing to weight loss cannot be overstated. Many older adults take medications, mostly for chronic conditions, which may have a variety of side effects that hinder their desire and/or ability to eat (Table 2).

In clinical practice, it is important to establish first the presence of weight loss. A significant proportion of older adults with documented weight loss may not complain about losing weight or, less

Table 1: Common Causes of Unintentional Weight Loss in Older Adults

Cause	Range of occurrence (%)
Malignant disease	16–36
Psychiatric disorder (especially depression)	9–42
Gastrointestinal disease	6–19
Endocrine disorder (especially hyperthyroidism)	4–11
Cardiovascular disease	2–9
Nutritional disorders or alcoholism	4–8
Respiratory disease	~6
Neurologic disorder	2–7
Chronic infection	2–5
Renal disease	~4
Connective tissue disease	2–4
Drug-induced weight loss (medication side effect)	~2
Unknown	10–36
Source: Alibhai SMH et al., 2005. <sup>17</sup> Reprinted with permission of the publisher. © 2005 Canadian Medical Association	

commonly, may mistakenly attribute weight loss to successful diet or lifestyle modifications. Furthermore, disturbed eating behaviours and negative body image (e.g., anorexia tardive) among some older individuals may lead them to regard weight loss as desirable and therefore not worth reporting. Conversely, up to half of people who claim to have lost weight have no documented evidence of weight loss.<sup>4</sup> If it is not possible to measure weight directly, true weight loss can be qualitatively established by a change in clothing size, corroboration of weight loss by a relative or friend, or a numerical estimate of weight loss provided by the patient. A careful medical history

"Meals on Wheels": A Mnemonic for Common Treatable Causes of Unintentional Weight Loss in Older Adults

M Medication effects

	inculation chects
E	Emotional problems, especially depression
A	Anorexia tardive (nervosa), alcoholism
L	Late-life paranoia
S	Swallowing disorders
0	Oral factors (e.g., poorly fitting dentures, caries)
Ν	No money
W	Wandering and other dementia- related behaviours
Η	Hyperthyroidism, hypothyroidism, hyperparathyroidism, hypoadrenalism
E	Enteric problems (e.g., malabsorption
E	Eating problems (e.g., inability to feed self)
L	Low-salt, low-cholesterol diets
S	Social problems (e.g., isolation, inability to obtain preferred foods)
Sou	rce: Morley JE et al. 1995. <sup>68</sup> Reprinted by

permission of Annals of Internal Medicine.

may elicit localizing symptoms (e.g., changes in defecation frequently imply involvement of the gastrointestinal tract) that may guide further investigations in almost half of patients.<sup>3,59</sup> All older adults experiencing unintentional weight loss should undergo screening using common assessment tools for dementia (e.g., the Mini-Mental State Examination)60 and depression (e.g., the Geriatric Depression Scale).<sup>61</sup> Specific features on physical examination, such as cachexia, lymphadenopathy, or palpable masses, may suggest a physical cause of weight loss (e.g., malignant disease).<sup>3,4</sup> The diagnostic utility of the medical history and physical examination in identifying the cause of weight loss, however, has not been adequately evaluated.

Although few studies have systematically evaluated the utility of screening methods for weight loss, the most useful noninvasive procedures appear to include a complete blood count, tests of liver enzyme levels (including alkaline phosphatase and bilirubin), measurement of lactate dehydrogenase level, and chest radiography. Individuals with irondeficiency anemia or symptoms likely originating in the gastrointestinal tract, and individuals with elevated liver enzyme levels on initial screening, should undergo investigation of their gastrointestinal tract (either endoscopy or upper gastrointestinal series) or an abdominal ultrasound, respectively.

Three scoring systems have been developed to help clinicians identify which patient with weight loss is likely to have a physical<sup>3,4</sup> or malignant<sup>62</sup> cause as opposed to a psychological or unknown cause. None of these scoring systems has been validated in independent populations presenting with weight loss. As such, none can be recommended presently for routine clinical use.

When weight loss is apparent in an older individual with no evidence of an organic disorder, primary malnutrition (i.e., resulting from inadequate food intake) must be considered as a contributor. In general, older adults are at increased risk of malnutrition due to insufficient food intake (quantity) rather

than inappropriate food selection (quality). Two screening tools, ENS (www.dietitians.ca/seniors/content/oth er/clsc\_overview.asp) and SCREEN (www.dietitians.ca/seniors/index.asp), have been developed and validated in Canada to identify community-dwelling older adults who are at risk of malnutrition. The Mini Nutritional Assessment (www.mna-elderly.com) and the Nutrition Screening Initiative (www.aafp.org/x16081.xml) are two other assessment tools designed for nutritional assessment of older adults. All four of these assessments are freely available online. While the Canadiandeveloped screening tools are questionnaire-based, the other assessment tools are of varying complexity and attempt to identify multiple factors associated with nutritional status. Under investigation are even simpler tools, such as the short, appetite-specific questionnaire the Simplified Nutritional Appetite Questionnaire (SNAQ), which appears to reliably predict weight loss in older, community-dwelling individuals.63 The

Table 2: Side Effects of Drugs and Supplements that Can Contribute to Weight Loss			
Side effect	Drug or supplement		
Anorexia	Amantadine, amphetamines, antibiotics (e.g., atovaquone), anticonvulsants, benzodiazepines, decongestants, digoxin, gold, levodopa, metformin, neuroleptics, nicotine, opiates, SSRIs, theophylline		
Dry mouth	Anticholinergics, antihistamines, clonidine, loop diuretics		
Dysgeusia or dysosmia or both	Acetazolamide, alcohol, allopurinol, amphetamines, ACE inhibitors, antibiotics (e.g., atovaquone, ciprofloxacin, clarithromycin, doxycycline, ethambutol, griseofulvin, metronidazole, ofloxacin, pentamidine, rifabutin, tetracycline), anticholinergics, antihistamines, calcium-channel blockers, carbamazepine, chemotherapeutic agents, chloral hydrate, cocaine, etidronate, gold, hydralazine, hydrochlorothiazide, iron, levodopa, lithium, methimazole, metformin, nasal vasoconstrictors, nitroglycerin, opiates, penicillamine, pergolide, phenytoin, propranolol, selegiline, sodium cromoglycate, spironolactone, statins, terbinafine, tobacco products, triazolam, tricyclics		
Dysphagia	Antibiotics (e.g., doxycycline), anticholinergics, bisphosphonates, chemotherapeutic agents, corticosteroids, gold, iron, levodopa, NSAIDs, potassium, quinidine, theophylline		
Nausea or vomiting or both	Amantadine, antibiotics, bisphosphonates, digoxin, dopamine agonists, hormone replacement therapy, iron, levodopa, metformin, metronidazole, nitroglycerin, opiates, phenytoin, potassium, SSRIs, statins, theophylline, tricyclics		
Note: SSRI = serotonin-specific reuptake inhibitor, ACE = angiotensin-converting enzyme, NSAID = nonsteroidal anti-inflammatory drug.			
Source: Source: Alibhai SMH et al., 2005. <sup>17</sup> Reprinted with permission of the publisher. © 2005 Canadian Medical Association			

#### **Key Points**

Clinically significant weight loss (frequently defined as  $\geq$  5% of usual body weight over six to twelve months) is a common finding among community-dwelling older adults.

Among older adults, the causes of weight loss appear to be quite heterogeneous and depend largely on the presence of underlying health problems, poor nutritional status, or both.

Weight loss in older adults is associated with increased mortality, an increased risk of in-hospital complications, a decline in activities of daily living or physical function, higher rates of admission to an institution, and poor quality of life.

Common causes of weight loss include cancer, benign gastrointestinal illness, depression, and a variety of other medical conditions. However, up to one-quarter of all cases have no identifiable cause, despite extensive investigation.

Contributing factors to weight loss include disease and age-associated physiologic changes; another important source are medications, which may have a variety of side effects that hinder many older adults' desire and/or ability to eat.

All older adults experiencing unintentional weight loss should undergo screening, using common assessment tools, for dementia and depression.

Routine nutritional screening is an effective way to identify those at nutritional risk and may aid in timely intervention, which has the potential to prevent higher health care costs associated with malnutrition-related morbidity.

routine use of nutritional screening, especially with those tools that are solely questionnaire-based and can be completed by the patient, such as the SCREEN and SNAQ, or by field clinical staff, such as ENS, provides an effective way to identify those at nutritional risk and may aid in timely nutritional intervention. Early nutrition intervention has the potential to prevent higher health care costs associated with malnutrition-related morbidity.

#### Conclusion

Unintentional weight loss is common in older adults and is associated with significant adverse health outcomes, increased mortality and progressive disability. The differential diagnosis is broad, ranging from reduced food intake to organic causes to psychological disorders, such as dementia and depression. Medications may also contribute to weight loss, as may social or economic factors. In up to one in four older adults with unintentional weight loss, there will be no obvious medical cause. In others, a limited set of initial symptom-oriented investigations may reveal the underlying causes. In part two of this review, nonpharmacological and pharmacological strategies to counter unintentional weight loss among older adults in clinical practice will be discussed. ga

No competing financial interests declared for all authors.

#### References

- Wallace JI, Schwartz RS. Epidemiology of weight loss in humans with special reference to wasting in the elderly. Int J Cardiol 2002;85:15–21.
- Payette H, Coulombe C, Boutier V, et al. Nutrition risk factors for institutionalization in a free-living functionally dependent elderly population. J Clin Epidemiol 2000;53:579–87.
- Bilbao-Garay J, Barba R, Losa-Garcia JE, et al. Assessing clinical probability of organic disease in patients with involuntary weight loss: a simple score. Eur J Intern Med 2002;13:240–5.
- Marton KI, Sox HC, Jr., Krupp JR. Involuntary weight loss: diagnostic and prognostic significance. Ann Intern Med 1981;95:568–74.
- Rabinovitz M, Pitlik SD, Leifer M, et al. Unintentional weight loss. A retrospective analysis of 154 cases. Arch Intern Med 1986;146:186–7.
- Payette H, Guigoz Y, Vellas BJ. Study design for nutritional assessments in the elderly. In: Yu BP, ed. Methods in Aging Research. Boca Raton: CRC Press LLC; 1999:301–20.
- Cornoni-Huntley JC, Harris TB, Everett DF, et al. An overview of body weight of older persons, including the impact on mortality. The National Health and Nutrition Examination Survey I—Epidemiologic Follow-up Study. J Clin Epidemiol 1991;44:743–53.
- Somes GW, Kritchevsky SB, Shorr RI, et al. Body mass index, weight change, and death in older adults: the systolic hypertension in the elderly program. Am J Epidemiol 2002;156:132–8.

9. White H, Pieper C, Schmader K. The associa-

tion of weight change in Alzheimer's disease with severity of disease and mortality: a longitudinal analysis. J Am Geriatr Soc 1998;46:1223–7.

- 10. Satish S, Winograd CH, Chavez C, et al. Geriatric targeting criteria as predictors of survival and health care utilization. J Am Geriatr Soc 1996;44:914–21.
- Verdery R, Levy K, Roberts N, et al. Natural history of failure to thrive, weight loss, and functional disability in elderly people after hospitalization. Age & Nutrition 1996;7:70–4.
- Seltzer MH, Slocum BA, Cataldi-Betcher EL, et al. Instant nutritional assessment: absolute weight loss and surgical mortality. J Parenter Enteral Nutr 1982;6:218–21.
- Sullivan DH, Patch GA, Walls RC, et al. Impact of nutrition status on morbidity and mortality in a select population of geriatric rehabilitation patients. Am J Clin Nutr 1990;51:749–58.
- Launer LJ, Harris T, Rumpel C, et al. Body mass index, weight change, and risk of mobility disability in middle-aged and older women. The epidemiologic follow-up study of NHANES I. JAMA 1994;271:1093–8.
- 15. 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.
- Fine JT, Colditz GA, Coakley EH, et al. A prospective study of weight change and health-related quality of life in women. JAMA 1999;282:2136–42.
- Alibhai SM, Greenwood C, Payette H. An approach to the management of unintentional weight loss in elderly people. CMAJ 2005;172:773–80.
- Andres R, Muller DC, Sorkin JD. Long-term effects of change in body weight on all-cause mortality. A review. Ann Intern Med 1993;119:737–43.

- 19. Avons P, Ducimetiere P, Rakotovao R. Weight and mortality. Lancet 1983;1:1104.
- Diehr P, Bild DE, Harris TB, et al. Body mass index and mortality in nonsmoking older adults: the Cardiovascular Health Study. Am J Public Health 1998;88:623–9.
- French SA, Folsom AR, Jeffery RW, et al. Prospective study of intentionality of weight loss and mortality in older women: the Iowa Women's Health Study. Am J Epidemiol 1999;149:504–14.
- 22. French SA, Jeffery RW, Folsom AR, et al. Relation of weight variability and intentionality of weight loss to disease history and healthrelated variables in a population-based sample of women aged 55–69 years. Am J Epidemiol 1995;142:1306–14.
- 23. Lee IM, Paffenbarger RS, Jr. Change in body weight and longevity. JAMA 1992;268:2045–9.
- 24. Meltzer AA, Everhart JE. Unintentional weight loss in the United States. Am J Epidemiol 1995;142:1039–46.
- Pamuk ER, Williamson DF, Serdula MK, et al. Weight loss and subsequent death in a cohort of U.S. adults. Ann Intern Med 1993;119:744–8.
- 26. Sidney S, Friedman GD, Siegelaub AB. Thinness and mortality. Am J Public Health 1987;77:317–22.
- 27. Williamson DF. Descriptive epidemiology of body weight and weight change in U.S. adults. Ann Intern Med 1993;119:646–9.
- Deeg DJ, Miles TP, Van Zonneveld RJ, et al. Weight change, survival time and cause of death in Dutch elderly. Arch Gerontol Geriatr 1990;10:97–111.
- Harris TB, Savage PJ, Tell GS, et al. Carrying the burden of cardiovascular risk in old age: associations of weight and weight change with prevalent cardiovascular disease, risk factors, and health status in the Cardiovascular Health Study. Am J Clin Nutr 1997;66:837–44.
- Vellas BJ, Hunt WC, Romero LJ, et al. Changes in nutritional status and patterns of morbidity among free-living elderly persons: a 10-year longitudinal study. Nutrition 1997;13:515–9.
- 31. Shatenstein B, Kergoat MJ, Nadon S. Weight change, nutritional risk and its determinants among cognitively intact and demented elderly Canadians. Can J Public Health 2001;92:143–9.
- de Groot CP, Perdigao AL, Deurenberg P. Longitudinal changes in anthropometric characteristics of elderly Europeans. SENECA Investigators. Eur J Clin Nutr 1996;50 Suppl 2:S9–15.
- Chumlea WC, Garry PJ, Hunt WC, et al. Distributions of serial changes in stature and weight in a healthy elderly population. Human Biology 1988;60:917–25.
- 34. Friedlaender JS, Costa PT, Jr., Bosse R, et al. Longitudinal physique changes among healthy white veterans at Boston. Human Biology 1977;49:541–58.
- 35. Lee JS, Kritchevsky SB, Harris TB, et al. Shortterm weight changes in community-dwelling

older adults: the Health, Aging, and Body Composition Weight Change Substudy. Am J Clin Nutr 2005;82:644–50.

- Knudtson MD, Klein BE, Klein R, et al. Associations with weight loss and subsequent mortality risk. Ann Epidemiol 2005;15:483–91.
- Lankisch P, Gerzmann M, Gerzmann JF, et al. Unintentional weight loss: diagnosis and prognosis. The first prospective follow-up study from a secondary referral centre. J Intern Med 2001;249:41–6.
- Thompson MP, Morris LK. Unexplained weight loss in the ambulatory elderly. J Am Geriatr Soc 1991;39:497–500.
- Wallace JI, Schwartz RS, LaCroix AZ, et al. Involuntary weight loss in older outpatients: incidence and clinical significance. J Am Geriatr Soc 1995;43:329–37.
- Losonczy KG, Harris TB, Cornoni-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.
- Sullivan DH, Walls RC, Lipschitz DA. Protein-energy undernutrition and the risk of mortality within 1 y of hospital discharge in a select population of geriatric rehabilitation patients. Am J Clin Nutr 1991;53:599–605.
- Tully CL, Snowdon DA. Weight change and physical function in older women: findings from the Nun Study. J Am Geriatr Soc 1995;43:1394–7.
- Blair SN, Shaten J, Brownell K, et al. Body weight change, all-cause mortality, and causespecific mortality in the Multiple Risk Factor Intervention Trial. Ann Intern Med 1993;119:749–57.
- Ho SC, Woo J, Sham A. Risk factor change in older persons, a perspective from Hong Kong: weight change and mortality. J Gerontol 1994;49:M269–72.
- Rhoads GG, Kagan A. The relation of coronary disease, stroke, and mortality to weight in youth and in middle age. Lancet 1983;1:492–5.
- Payette H, Coulombe C, Boutier V, et al. Weight loss and mortality among free-living frail elders: a prospective study. J Gerontol A Biol Sci Med Sci 1999;54:M440–5.
- Ensrud KE, Ewing SK, Stone KL, et al. Intentional and unintentional weight loss increase bone loss and hip fracture risk in older women. J Amer Geriatr Soc 2003;51:1740–7.
- Payette H, Roubenoff R, Jacques PF, et al. Insulin-like growth factor-1 and interleukin 6 predict sarcopenia in very old communityliving men and women: the Framingham Heart Study. J Am Geriatr Soc 2003;51:1237–43.
- Baumgartner RN, Koehler KM, Gallagher D, et al. Epidemiology of sarcopenia among the elderly in New Mexico. Am J Epidemiol 1998;147:755–63.
- Rosenberg IH. Sarcopenia: origins and clinical relevance. Journal of Nutrition 1997;127(5 Suppl):990S–1S.
- Melton LJ 3rd, Khosla S, Crowson CS, et al. Epidemiology of sarcopenia. J Am Geriatr Soc 2000;48:625–30.

- Hardy C, Wallace C, Khansur T, et al. Nutrition, cancer, and aging: an annotated review. II. Cancer cachexia and aging. J Am Geriatr Soc 1986;34:219–28.
- 53. Kotler DP. Cachexia. Ann Intern Med 2000;133:622–34.
- Morley JE. Anorexia and weight loss in older persons. J Gerontol A Biol Sci Med Sci 2003;58:131–7.
- Roubenoff R, Heymsfield SB, Kehayias JJ, et al. Standardization of nomenclature of body composition in weight loss. Am J Clin Nutr 1997;66:192–6.
- 56. Reife CM. Involuntary weight loss. Med Clin North Am 1995;79:299–313.
- 57. Roubenoff R, Parise H, Payette HA, et al. Cytokines, insulin-like growth factor 1, sarcopenia, and mortality in very old community-dwelling men and women: the Framingham Heart Study. Am J Med 2003;115:429–35.
- Volpato S, Guralnik JM, Ferrucci L, et al. Cardiovascular disease, interleukin-6, and risk of mortality in older women: the women's health and aging study. Circulation 2001;103:947–53.
- Hernandez JL, Riancho JA, Matorras P, et al. Clinical evaluation for cancer in patients with involuntary weight loss without specific symptoms. Am J Med 2003;114:631–7.
- Folstein MF, Folstein SE, McHugh PR. "Minimental state." A practical method for grading the cognitive state of patients for the clinician. J Psych Res 1975;12:189–98.
- Yesavage JA, Brink TL, Rose TL, et al. Development and validation of a geriatric depression screening scale: a preliminary report. J Psych Res 1983;17:37–49.
- Hernandez JL, Matorras P, Riancho JA, et al. Involuntary weight loss without specific symptoms: a clinical prediction score for malignant neoplasm. Q J Med 2003;96:649–55.
- Wilson MM, Thomas DR, Rubenstein LZ, et al. Appetite assessment: simple appetite questionnaire predicts weight loss in communitydwelling adults and nursing home residents. Am J Clin Nutr 2005;82:1074–81.
- Huerta G, Viniegra L. Involuntary weight loss as a clinical problem. Rev Invest Clin 1989;41:5–9.
- Levine MA. Unintentional weight loss in the ambulatory setting: etiologies and outcomes [abstract]. Clin Res 1991;39:580A.
- Lin HW, Li CM, Lee YC, et al. Differences in diagnostic approach between family physicians and other specialists in patients with unintentional body weight loss. Fam Pract 1999;16:586–90.
- 67. Huffman GB. Evaluating and treating unintentional weight loss in the elderly. Am Fam Physician 2002;65:640–50.
- Morley JE, Silver AJ. Nutritional issues in nursing home care. Ann Intern Med 1995;123:850–9.
- Ackerman BH, Kasbekar N. Disturbances of taste and smell induced by drugs. Pharmacotherapy 1997;17:482–96.
- Carr-Lopez SM, Phillips SL. The role of medications in geriatric failure to thrive. Drugs Aging 1996;9:221–5.