Attribution of Causes of Weight Loss and Weight Gain to 3-Year Mortality in Older Adults: Results From the Longitudinal Aging Study Amsterdam

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Background. Weight loss is associated with a higher mortality risk in old age, but the underlying cause may impact this association. We examined associations between causes of intentional and unintentional weight loss and weight gain and mortality.

Methods. We used data of five triannual examination rounds of the Longitudinal Aging Study Amsterdam (age ≥ 55 years, n = 2,645) and two examination rounds of a new cohort (n = 909). Self-reported weight loss or gain and causes were measured during a personal interview. Time-dependent Cox regression was used to model the association between weight loss and gain causes and subsequent 3-year mortality.

Results. At baseline, 16% reported weight loss (mean = 4.7 kg, SD = 3.7) in 6 months. After adjustment for potential confounders, an increased mortality risk was observed for unintentional weight loss due to medical reasons (<72 years: hazard ratio = 2.43 [95% confidence interval: 1.52–3.88]; ≥72 years: 1.62 [1.23–2.14]), unknown reasons (1.98 [1.49–2.62]), and change in eating pattern (1.89 [1.12–3.18]). No association was found for unintentional weight loss due to social reasons, intentional weight loss (dieting or physical activity), or weight gain. Weight loss due to medical or social reasons was often regained in subsequent 3 years while weight loss due to other causes was not.

Conclusions. Weight loss due to social reasons was not associated with mortality suggesting that not all unintentional weight loss is harmful. The increased mortality risk of other causes of unintentional weight loss may be related to underlying disease. Intentional weight loss was not associated with mortality.

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The association between weight loss and a higher mortality risk in older adults is well established (1–12), although one study found no (13) and one a reversed (14) association. The association probably differs for unintentional and intentional weight loss. Important questions are whether the association between unintentional weight loss and mortality is solely due to underlying disease or partly causal and whether intentional weight loss in overweight or obese older adults is beneficial. Differentiating between the causes of intentional and unintentional weight loss may help to address these questions.

A few observational studies that examined associations with mortality (follow-up range: 2–12 years) (2,3,7,8,14) differentiated for the intentionality of weight loss. Most found that unintentional weight loss in old age was associated with a higher mortality risk (2,7,8,12), but one found an association with a lower mortality risk (14). For intentional weight loss, two studies found no association (7,8), while two found an increased mortality risk (2,12). Two randomized controlled trials examined the effect of a weight loss intervention on mortality among obese older adults (15,16). One found that the weight loss intervention resulted in a statistically significantly lower 8-year mortality risk, while the other study found no effect on mortality (16).

Thus far, none of the observational studies examined the attribution of causes of intentional and unintentional weight loss in association with mortality. This may explain differences between study results and may add valuable information to the causality discussion. Therefore, the aim of this study is to examine associations between causes of
intentional and unintentional weight loss and weight gain and mortality in old age.

METHODS

Study Design

The study sample was derived from the Longitudinal Aging Study Amsterdam, an ongoing multidisciplinary study focusing on physical, emotional, cognitive, and social functioning in an older population. Details on the sampling and data collection have been described elsewhere (17). A random sample of individuals aged 55–85 years, stratified by age, sex, level of urbanization, and expected 5-year mortality, was drawn from 11 municipalities in the west, northeast, and south of the Netherlands. The baseline examination wave (1992–1993) of the first study cohort included 3,107 participants. Follow-up examinations were performed every 3 years. In 2002/2003, a new study cohort (n = 1,002, age 55–65 years), sampled from the same sampling frame as the original cohort, was included. Each examination wave included a self-administered questionnaire, a general interview in the individuals home, and after 4–6 weeks a medical interview including medical tests. The Longitudinal Aging Study Amsterdam was conducted according to the guidelines laid down in the Declaration of Helsinki and all procedures involving human participants were approved by the Medical Ethics Committee of the VU University Medical Center. Written informed consent was obtained from all respondents.


<table>
<thead>
<tr>
<th>Examination wave</th>
<th>N Medical Interview</th>
<th>Excluded (Reason: N)</th>
<th>N Analytical sample by 'weight change'</th>
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*Excluded because of weight loss or gain due to diuretics or dehydration, edema or ascites, or quitting prednisone.

Figure 1. Selection of the analytical sample of the first and second study cohort by examination wave: the Longitudinal Aging Study Amsterdam (LASA).
Measurements

Mortality.—Vital status and date of death were traced until June 1, 2011. Mortality was reported through the registrars of municipalities in which the participants were living.

Weight loss and causes.—Self-reported weight change in the past 6 months was assessed by the question: “Did your weight change in the past 6 months?” (answer categories: not changed; gained weight; lost weight). The estimated amount of weight change (kilograms) and causes of weight change were also obtained. Answer categories for causes of weight change were: sickness; diet; social reasons; physical activity; do not know; or other reasons, namely (...). This open “other reasons” category was recoded afterward by two independent researchers. Reasons for weight loss were then recoded as: (1) unintentional weight loss due to social reasons (“social reasons” or “other reasons” like moving, stress, death of spouse, or sickness of a family member); (2) unintentional weight loss due to medical reasons (“sickness” or “other reasons” like depression, pain, operation, not feeling well, medication, or hospitalization); (3) unintentional weight loss due to unknown reasons (“do not know” or “other reasons” like no taste or smell, not hungry, or old age); (4) intentional weight loss due to dieting (“diet” or “other reasons” like eat less candy, eat fewer snacks, eat less fat, or more healthy diet); (5) intentional weight loss due to increased physical activity (“physical activity” or “other reasons” like more physical activity, walk more, more activities, or sports); (6) intentional or unintentional weight loss due to a change in eating pattern (“other reasons” like eating less, ate to little, or almost stopped eating). It was not clear whether the change in eating pattern was intentional or unintentional. Reasons for weight gain were recoded as: (1) weight gain due to medical reasons (“sickness” or “other reasons” like pain, operation, medication, and hospitalization); (2) weight gain due to increased caloric intake (“diet” or “other reasons” like eating more, eating more candy, eating more snacks); (3) weight gain due to decreased physical activity (“physical activity” or “other reasons” like walk less, exercise less, less physical activity); (4) weight gain due to increased caloric intake and decreased physical activity (“other reasons” including a combination of increased caloric intake and decreased physical activity); (5) weight gain due to other reasons (“do not know” or “other reasons” like older age, social factors like moving, busy, life events). Participants that changed weight because of use of diuretics, dehydration, edema or ascites, or quitting prednisone were excluded (Figure 1).

Covariates.—Height (0.001 m) was measured using a stadiometer. Weight (0.1 kg) was measured using a calibrated scale. Body mass index (BMI) was calculated as body weight divided by height squared. Educational level was categorized in: low (elementary not completed, elementary education); medium (lower vocational education, general intermediate education, intermediate vocational education, general secondary education); and high education (higher vocational education, college education, university education). Depression was measured with the Dutch translation of the Center for Epidemiologic Studies Depression scale (18), applying a cutoff of ≥16 to define presence of depressive symptoms (19). Cognitive functioning was measured with the Mini-Mental State Examination (20), applying a cutoff of ≤23 to define poor cognitive functioning (21). Presence of chronic diseases was determined by explicitly asking the participants if they had any of the following diseases: cardiac diseases (including myocardial infarction), peripheral atherosclerosis, stroke, diabetes mellitus, obstructive lung disease (asthma, chronic bronchitis, or pulmonary emphysema), arthritis (rheumatoid arthritis or osteoarthritis), or cancer. Self-report data for these diseases as compared with general practitioners’ information was shown to be adequate (22). Number of chronic diseases was categorized into: no chronic diseases; one chronic disease; two or more chronic diseases. Smoking status was categorized into: current smoker; ex-smoker; and never smoker (including ex-smokers who stopped more than 15 years ago) (23).

Statistical Analyses

Time-dependent Cox proportional hazard regression (24) was used to examine the association between causes of weight loss or gain and subsequent 3-year mortality. A categorical variable “causes of weight loss or gain” was included as a time-dependent variable with “weight stable” as the reference category and each weight loss or gain cause as a separate category. Models were adjusted for dependency of observations within participants by including a “subject variable” in the model. Effect modification was examined for sex, age, and BMI by subsequently adding an interaction term with the variable “causes of weight loss or gain” to the model. When there was interaction (p < .05), associations were presented stratified by the effect modifier. The model was cumulatively adjusted for sex, age, educational level (model 1), BMI (model 2), the absolute value of kilograms of self-reported weight change (model 3), depressive symptoms, cognitive functioning, number of chronic diseases, and smoking (model 4). All covariates were included in a time-dependent manner. Two sensitivity analyses were performed on the fully adjusted model: (i) applying a cutoff for weight loss (≥5%) and (ii) analyzing 6-year mortality. In addition, we examined weight change in the next 3 years between the 1992–1993 and 1995–1996 by cause of weight loss. Analyses were performed using SPSS (version 18.0; SPSS, Inc., Chicago, IL) and STATA software (version 10.1; StataCorp., College Station, TX).

RESULTS

Table 1 shows the characteristics of the study participants by examination wave. Across the examination waves, 3-year mortality rates varied between 10.3%–14.1% (first study cohort) and 2.1%–2.5% (second study cohort). Self-report of weight
Table 1. Characteristics of the Analytical Sample of the First and Second Study Cohort by Examination Wave: The Longitudinal Aging Study Amsterdam (LASA)

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<tbody>
<tr>
<td></td>
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<td>Mean (SD) or %</td>
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<td>Mean (SD) or %</td>
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<tr>
<td>Female sex</td>
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<td>51.1</td>
<td>1,501</td>
<td>51.8</td>
<td>1,356</td>
<td>55.1</td>
<td>1,281</td>
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<tr>
<td>Age, y</td>
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<td>70.4 (8.7)</td>
<td>1,501</td>
<td>75.9 (6.7)</td>
<td>1,356</td>
<td>76.3 (7.4)</td>
<td>1,281</td>
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<tr>
<td>3-y mortality</td>
<td>2,645</td>
<td>10.9</td>
<td>1,501</td>
<td>14.1</td>
<td>1,356</td>
<td>14.0</td>
<td>1,281</td>
</tr>
<tr>
<td>Weight change in past 6 mo</td>
<td>2,645</td>
<td>15.5</td>
<td>1,501</td>
<td>16.4</td>
<td>1,356</td>
<td>17.1</td>
<td>1,281</td>
</tr>
<tr>
<td>BMI (kg/m²)</td>
<td>2,560</td>
<td>26.8 (4.0)</td>
<td>1,474</td>
<td>26.9 (4.3)</td>
<td>1,326</td>
<td>27.3 (4.2)</td>
<td>1,251</td>
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<tr>
<td>Education</td>
<td>2,645</td>
<td>42.5</td>
<td>1,500</td>
<td>40.7</td>
<td>1,356</td>
<td>36.6</td>
<td>1,280</td>
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<td>Low</td>
<td>45.7</td>
<td>45.1</td>
<td>1,356</td>
<td>47.8</td>
<td>1,280</td>
<td>49.9</td>
<td>961</td>
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<tr>
<td>Medium</td>
<td>11.6</td>
<td>12.1</td>
<td>1,356</td>
<td>11.5</td>
<td>1,280</td>
<td>13.4</td>
<td>961</td>
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<tr>
<td>High</td>
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<td>13.4</td>
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<td>15.7</td>
<td>1,346</td>
<td>20.5</td>
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<td>Poor cognitive status (MMSE ≤ 23)</td>
<td>2,642</td>
<td>35.8</td>
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<td>1,278</td>
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<tr>
<td>Chronic diseases</td>
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<td>26.6</td>
<td>1,356</td>
<td>21.9</td>
<td>1,278</td>
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<td>One</td>
<td>One</td>
<td>37.1</td>
<td>1,356</td>
<td>36.0</td>
<td>1,278</td>
<td>35.3</td>
<td>961</td>
</tr>
<tr>
<td>Two or more</td>
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<td>36.3</td>
<td>1,356</td>
<td>42.1</td>
<td>1,278</td>
<td>39.5</td>
<td>961</td>
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Notes: BMI = body mass index; CES-D = Center for Epidemiologic Studies Depression scale; MMSE = Mini-Mental State Examination.
loss in the past 6 months remained fairly stable (15.5%–18.9%). Figure 2 shows the causes of weight loss and gain across examination waves. Medical reasons (20.1%–37.4%) and dieting (21.6%–34%) were the most often reported causes of weight loss. Increased caloric intake was the most often reported cause of weight gain. The average amount of weight loss in 6 months varied between 2.2 and 6.8 kg, without a clear pattern across causes. Those who intentionally lost weight due to dieting had the highest BMI (Table 2).

Unintentional weight loss overall was associated with an increased 3-year mortality risk (hazard ratio [HR] = 1.67; 95% confidence interval [CI] = 1.39–2.01), compared with stable weight. No association was found for intentional weight loss (HR = 1.17; 95% CI = 0.85–1.61) or weight gain (HR = 0.91; 95% CI = 0.72–1.14; results not shown in tables).

Table 3 presents the 3-year mortality risk by cause of weight loss gain. In the fully adjusted model, an increased mortality risk was observed for unintentional weight loss due to medical reasons (<72 years: HR = 2.43; 95% CI = 1.52–3.88; ≥72 years: HR = 1.62; 95% CI = 1.23–2.14), unintentional weight loss due to unknown reasons (HR = 1.98; 95% CI = 1.49–2.62), and weight loss due to a change in eating pattern (either unintentional or intentional; HR = 1.89; 95% CI = 1.12–3.18). No association was found for unintentional weight loss due to social reasons, intentional weight loss due to dieting, and intentional weight loss due to increased physical activity. For weight gain, only weight gain due to medical reasons was associated with an increased mortality risk in men (HR = 1.96; 95% CI = 1.30–2.96). No effect modification for BMI was found. The results of model 4 did not markedly change when applying a cutoff of ≥5% for weight loss and gain or analyzing 6-year mortality (results not shown in tables). For example, the HR for unintentional weight loss due to social reasons was 0.95 (95% CI: 0.53–1.70; cutoff of ≥5%) or 1.06 (95% CI: 0.73–1.54; 6-year mortality). The HR for unknown reasons was 1.85 (95% CI: 1.16–2.94) or 1.65 (95% CI: 1.14–2.37). Only exception was the association between intentional weight
loss due to dieting and 6-year mortality that became stronger (HR = 1.96; 95% CI: 1.15–2.17).

Weight loss due to medical or social reasons (1992–1993) was mostly followed by weight regain in the subsequent 3 years: mean +1.3 kg (SD = 5.8, n = 53) and +0.4 kg (SD = 5.0, n = 38), respectively. Weight loss due to unknown reasons or a change in eating pattern was mostly followed by more weight loss: mean −2.0 kg (SD = 4.7, n = 21) and −3.1 kg (SD = 3.8, n = 18), respectively. This was also the case for intentional weight loss due to dieting (mean −0.7 kg, SD = 3.7, n = 13). The weight stable group also lost weight: mean −0.7 kg (SD = 4.0, n = 922; results not shown in tables).

**DISCUSSION**

The present study shows that unintentional weight loss in the past 6 months due to medical or unknown reasons or due to a change in eating pattern (unintentional or intentional) is associated with an increased 3-year mortality risk among community-dwelling older men and women. No association is found for unintentional weight loss due to social reasons,
intentional weight loss due to dieting or increased physical activity, and weight gain.

Consistent with previous studies (2,7,8,12) except one (14), we found an increased mortality risk for unintentional weight loss. Separated by underlying cause, we found an increased mortality risk for unintentional weight loss due to medical but not social reasons. The association with weight loss due to medical reasons was adjusted for number of chronic disease but may still be explained by disease severity. Unintentional weight loss due to unknown reasons or a change in eating pattern were also associated with an increased mortality risk. For a change in eating pattern, we assume that this was mostly unintentional given the increased mortality risk and because participants did not indicate being on a diet. These causes may reflect weight loss due to (unknown) disease or due to age-related physiological changes like decrease in taste and smell and altered satiety mechanisms (25). It remains to be established if the increased mortality risk with unintentional weight loss is then due to unknown underlying disease or weight loss per se.

An important explanatory factor in the association between unintentional weight loss and mortality may be the reversibility of weight loss. A previous study among relatively healthy older adults showed that most 6–12-month weight loss is resolved within 6 months except for unintentional weight loss (26). We found that those who lost weight due to medical or social reasons mostly regained weight in the subsequent 3 years while those who lost weight due to unknown reasons or a change in eating pattern mostly continued to lose weight. Although those who died were not included and numbers were small, this suggests that reversibility of weight loss differs by unintentional weight loss cause. Unintentional weight loss due to social reasons mostly reversed in the next 3 years and was not associated with mortality, suggesting that reversible unintentional weight loss is not harmful in old age. The increased mortality risk for reversible weight loss due to medical causes may then be explained by disease (severity) and not by weight loss per se.

Intentional weight loss in overweight and obese older adults is associated with short-term health benefits like improvements in cardiometabolic risk profile (27) but also physical functioning (28). Controversy still exists as to whether intentional weight loss is beneficial in the long term in old age. We found that intentional weight loss—due to diet or increased physical activity and independent of current BMI—was not associated with 3-year mortality, comparable to previous studies with 3- and 7-year follow-up (7,8). Although sensitivity analyses showed an increased 6-year mortality risk for weight loss due to dieting, this may be due to chance as we expected weaker long-term associations. One of these studies found that men who lost weight as a result of personal choice (vs intentional weight loss because of illness or physician’s advice) had a lower mortality risk (8), suggesting that weight loss may be beneficial in a subsample of healthy overweight or obese older men. Two other studies found an increased mortality risk for intentional weight loss after 4- and 12-year follow-up (2,12). Two randomized controlled trials are published on the effects of intentional weight loss on long-term mortality in old age (15,16). In older adults with knee osteoarthritis, those randomized to a 18-month dietary weight loss intervention lost more weight and had a lower 8-year mortality risk compared with controls (15). The other randomized controlled trial was also effective with respect to weight loss but found no effect on 12-year mortality after a 28-month dietary weight loss intervention among overweight and obese older adults (16). In both studies, weight change after the intervention period was unknown. Summarizing current evidence, intentional weight loss in overweight or obese older adults does not seem to result in a higher mortality risk.

With respect to weight gain in old age, our results are in accordance with most previous studies that found no association with mortality (3,6,12,13), although two studies found an association with a higher mortality risk (4,11). Gaining weight due to medical reasons was associated with a higher mortality risk in men which is likely explained by disease and not so much by weight gain itself.

To our knowledge, this is the first study to describe causes of unintentional and intentional weight loss and gain in association with mortality in old age. Strong features are the large, representative study sample of older men and women and use of weight loss over 6 months, a clinically important unit of time for weight loss in older persons (29,30). Limitations are use of self-report weight loss and causes. It may be difficult for participants to pinpoint the cause of their weight loss. Moreover, causes of weight loss are likely multifactorial and participants were only allowed to indicate the main cause. This probably resulted in random misclassification of the causes of weight loss, weakening the existing associations. Another limitation is that we had no information on weight regain within 6 months after weight loss. This may be an important modifying or confounding factor in the association between (causes of) weight loss and mortality. Finally, observational studies cannot be used to establish causation.

We conclude that the association between unintentional weight loss and mortality differs by underlying cause. Unintentional weight loss due social reasons was not associated with mortality and often reversed in the next 3 years, suggesting that reversible unintentional weight loss is not harmful in old age. Unintentional weight loss due to unknown causes or change in eating pattern more often continued in the next 3 years and was associated with an increased mortality risk. It remains to be established if this is due to unknown underlying disease or the weight loss per se. Intentional weight loss was not associated with mortality.
WEIGHT LOSS AND MORTALITY IN OLD AGE

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References