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# ASSOCIATION BETWEEN ADIPOSITY AND DISABILITY IN THE Lc65+ COHORT

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**Abstract:** *Objectives:* To examine the longitudinal association between body mass index (BMI) and waist circumference (WC) with mortality and incident disability in Lc65+ cohort. *Design:* Population-based cohort of non-institutionalized adults with up to 8.9 years of follow-up. *Setting:* City of Lausanne, Switzerland. *Participants:* 1,293 individuals aged 65 to 70 at baseline (58% women). *Measurements:* BMI, WC and covariates were measured at baseline in 2004-2005. Vital status was obtained up to the 31st December 2013 and difficulty with basic activities of daily living (BADL) was reported in a self-administered questionnaire sent to participants every year. Main outcomes were total mortality and disability, defined as difficulty with BADL for ≥2 years or institutionalization. Cox regression was used with BMI/WC quintiles 2 as the reference. *Results:* 130 persons died over a median follow-up of 8.47 years (crude mortality rate, men: 16.5/1,000 person-years, women: 9.7/1,000 person-years). In Cox regression adjusted for age, sex, education, financial situation, smoking and involuntary weight loss (IWL) at baseline, mortality was significantly associated with neither BMI nor WC, but there were trends towards non-significant J-curves across both BMI and WC quintiles. Disability (231 cases) tended to increase monotonically across both BMI and WC quintiles and was significantly associated with BMI quintile 5 (HR=2.44, 95% CI [1.65-3.63]), and WC quintiles 4 (HR=1.81 [1.15-2.85]) and 5 (HR=2.58, [1.67-4.00]). *Conclusion:* Almost half of the study population had a substantially increased HR of disability, as compared to the reference BMI/WC categories. This observation emphasizes the need for life-long strategies aimed at preventing excess weight, muscle loss and functional decline through adequate nutrition and regular physical activity, starting at early age and extending throughout life.

**Key words:** Body mass index, waist circumference, adiposity, disability, mortality.

## Introduction

In many developed countries, including Switzerland, overweight and obesity prevalence peaks between 60 and 75 years of age (1, 2). Mortality associated with body mass index (BMI) differs according to age and is weaker after age 65 years (3-8). Some studies suggest that mortality is not increased among older persons with high BMI (3, 4). At this age, adults with BMI <25 kg/m$^2$ might be of a lower socio-economic status and/or suffer from malnutrition or disease. Low BMI seems to be associated with increased mortality in old age (9) through mechanisms including weight loss, chronic diseases, frailty, and cachexia (10). Low BMI and high body fat percentage were independently associated with increased mortality in a large cohort (10); according to its authors, BMI is often used as a proxy for adiposity even though it more closely reflects lean mass than fat mass. Increasing BMI might reflect higher fitness levels and greater metabolic reserve, leading to higher survival. Body composition changes and abdominal fat increases with increasing age, especially among women (11). Waist circumference (WC) is often used as a surrogate measure of fat mass distribution, both intra-abdominal and overall body fat (12). In an important cohort study with 16 years of follow-up, high WC was strongly and positively associated with cardio-vascular disease mortality, independently of BMI (13). Yet, a systematic review (including mainly cross-sectional studies) (14) compared the discriminatory power of BMI, WC, and waist:hip ratio in terms of cardiovascular risk and concluded that no adiposity measure had superior discriminatory capability. There is a long-standing controversy on which adiposity indicator performs best in predicting cardiovascular risk (15-18).

Studies aimed at assessing the shape of the association between adiposity and mortality usually require large samples in order to ensure sufficient numbers of persons with very low and very high BMI/WC values (e.g. >4,000 participants) (7, 19-21), and studies relating adiposity with mortality in older persons should ideally also account for adiposity (e.g. BMI) at middle age in order to avoid several potential biases like reverse causation or survival bias (22).

Obesity seems to have a negative impact on a person's independence in basic activities of daily living (BADL) among the young old (i.e. at age 65-70 years), in particular because muscle mass decreases with advancing age (23, 24). While life expectancy is increasing in most populations, disability-free life expectancy evolves differently across developed countries (25, 26), but a common finding is that years spent with disability tend to increase (12, 27-29). Because obesity is likely to be associated with disability, the obesity pandemic (30) might increase the burden of dependent persons in the future. Unlike obesity, the effect of overweight on disability is more controversial: some studies have shown either no (31, 32) or

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moderate effect on disability. Furthermore, several definitions of disability exist in the medical literature (28, 33). According to Linda Fried (34), "disability is defined as difficulty or dependency in carrying out activities essential to independent living, including essential roles, tasks needed for self-care and living independently in a home, and desired activities important to one's quality of life." In this report, difficulty with BADL (35) will be used for assessment of disability.

To which extent overweight is associated with mortality and disability is still uncertain after age 65. This study aims to identify which BMI and WC quintiles are associated with the longest preservation of autonomy in BADL (primary aim) and survival (secondary aim) after a follow-up of up to 8.9 years in a Swiss cohort aged 65-70 years at baseline.

## Methods

The Lc65+ cohort has been described previously (36-39). Briefly, a population-based sample of residents of Lausanne aged 65-70 years were invited to be examined and enrolled in the cohort in 2005. Exclusion criteria at baseline included being institutionalized or unable to respond because of advanced dementia. Of the 3,056 persons who were initially mailed a questionnaire, 2,096 (69%) replied, of whom 1,564 (75%) agreed to participate [36]. Overall, nonparticipants had demographic characteristics (sex, birth year) similar to participants (36) and participants' socio-economic characteristics closely reflected the Lausanne general population in the same age category in aggregate statistics from the Population Office or the 2000 Swiss national census (proportions with foreign nationality, marital status, place of birth, living arrangement, professional activity). Of the 1,564 respondents to the initial questionnaire, 1,524 (97.4%) were still eligible and 1,307 (85.8%) participated in the baseline physical examination in 2005 at the study centre.

All participants were asked to complete and return a postal questionnaire every year, and to undergo an interview and a physical examination every 3 years since 2005. Trained medical assistants conducted the performance tests and examination using standardized protocols (36).

Body weight, height, and waist circumference (WC) were measured and body mass index (BMI) was calculated. The participants' financial situation was assessed by the self-report of financial difficulties (construction of the variable: see tables' footnotes).

### *Mortality*

We updated the vital status of the participants by checking every year the electronic records of the office in charge for population registration in the Canton of Vaud. Among all 1,307 participants examined in 2004 and 2005, 14 (1.1%) persons with missing data for BMI (N=5) and/or WC (N=12) were excluded. Therefore, this study includes 1,293 participants examined at baseline (see Flow chart in Figure 1A). In the Kaplan-Meyer survival curves, person-years at risk were calculated from the date of the first examination (in 2005) to date of death or 31 December 2013, whichever came first (time unit: day).

Deaths among all participants continuously residing in the Canton de Vaud could be ascertained by the Population's Office until December 31st, 2013, except for 8 of 1,293 cases (0.6%), who had left the Canton de Vaud and for whom vital status is unknown. For these persons, the date of the last contact was kept as the censoring date.

### *Disability*

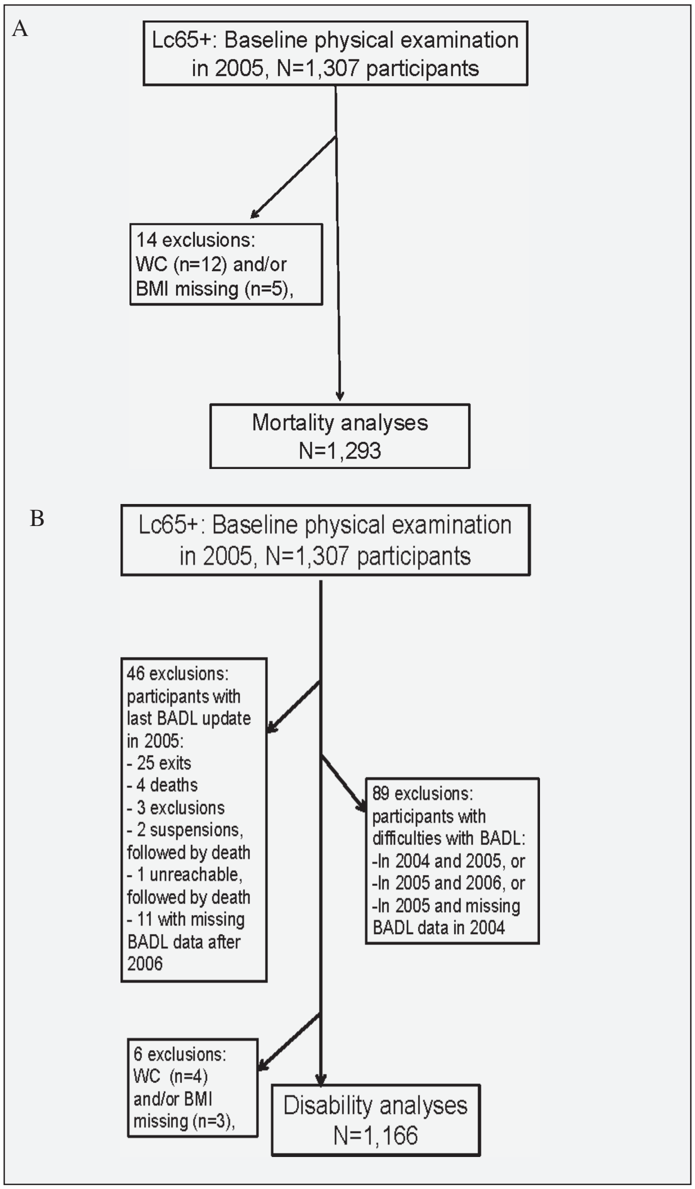
Difficulty with basic activities of daily living (BADL) was reported every year in a self-administered questionnaire sent at home, except in 2011, where the same questions were asked by the interviewer during the visit at the study centre; the following questions where used about five BADLs defined by Katz (35): "Do you have difficulty, or do you usually receive help with performing the following activities?: a) getting dressed, including putting on socks and shoes, b) taking a bath or a shower, c) eating, including cutting foodstuffs, d) getting in/out of bed, e) getting on and off toilet? Each question allowed for three answers: "No difficulty at all; difficulties but no help; and I receive help". Participants who reported any difficulty or received help for ≥ one of the five items were considered to have difficulty with BADL.

Difficulty with BADL is reversible from year to year. Therefore, in the statistical analysis, the outcome "difficulty with BADL" was considered to have occurred if it had been reported for at least 2 consecutive years.

The outcome «disability» was defined as the occurrence of difficulty with ≥1 of 5 BADLs for ≥2 consecutive years or institutionalization (time unit: year). Institutionalization is included in the definition of this outcome because older adults' admission in nursing homes in the study area implies functional limitations. Time at risk for this outcome was considered from baseline until the first year of occurrence of either difficulties with BADL or institutionalization or until the last year with information on the status of the participant. Since this outcome had to last at least 2 consecutive years, the follow-up for disability ended on the 31st December 2012, hence a follow-up of up to 7 years.

Among the 1,307 participants assessed in 2005, information on difficulty with BADL on subsequent years was not available in 46 and these persons were excluded from all analyses about difficulty with BADL (see Flow chart in Figure 1B). In addition, 89 persons were excluded because they already reported difficulty with BADL or had missing information on difficulty with BADL at baseline. Furthermore, 6 participants with missing data on baseline exposures (weight, height, WC) were excluded. As a result, the analysis of the disability outcome is based on data in 1,166 participants. A flow chart about inclusion of participants appears in Figure 1B.

**Figure 1**
Flow Chart of the Participants Included in the Mortality Analysis (A) and in the Disability Analysis (B)




***Statistical analysis***

Statistical analyses were performed using Stata 14 (Stata Corp, College Station, TX). Differences in proportions were tested with the Chi-square test. Mortality and disability were compared across baseline BMI and WC quintiles, using Cox regression analysis. Sex-specific BMI and WC quintiles were re-aggregated (Tables 1, 3, 4, and Figures 2 and 3). Unadjusted Kaplan-Meyer survival curves were produced and differences in univariate comparisons of survival distributions were tested with the log rank test. The assumption of proportional hazards was verified and confirmed for all exposure and adjustment variables with a test of Schoenfeld residuals and with graphical validation. The number of cases of deaths (130) was lower than the number of cases of disability (231); therefore the power to detect differences was higher for the analyses of disability than mortality. BMI and WC were highly correlated and were therefore analyzed in distinct Cox models.

***Mortality***

Confounders were chosen if they were known to be associated with BMI (or WC) and mortality (40). Initial Cox models were adjusted for age and sex only, and sex interactions were tested. Subsequent models were additionally adjusted for education, financial difficulties, involuntary weight loss during the 12 months before baseline (IWL) (41), and smoking status (42). The final model was adjusted for all covariates.

Because obesity requires many years to result in harmful effects on health (8, 43) and many chronic conditions are associated with weight loss (43), studies on the association between obesity and obesity-related outcomes generally exclude subjects with weight loss (43) or pre-existing diseases and/or mortality in the first few years (44). To minimize potential bias and/or a reverse causation effect related to preexisting disease (45), we adjusted i) for IWL in all analyses (41) and ii) we also ran analyses after exclusion of participants who died within the first 3 years of follow-up (45).

***Disability***

IWL has also been associated with rapid functional decline (46, 31). Models in Table 4 included the same adjustment variables as models in Table 3 (mortality). In addition, all possible interactions involving BMI or WC quintiles were tested.

All participants had given written informed consent and the ethics committee of the Faculty of Biology and Medicine of the University of Lausanne has approved the study protocol.

## Results

This study included 531 men and 762 women (total N=1,293). The prevalence of overweight and obesity at baseline was 53.3% and 24.1% in men, respectively 35.3% and 23.5% in women. The prevalence of IWL in 2005, educational level and the financial situation were significantly and linearly negatively associated with BMI and WC quintiles (Table 1). The correlation coefficient between BMI and WC was 0.89 in men and 0.85 in women.

***Mortality***

Of the 1,293 participants at baseline, 130 persons died over a total follow-up period of 10,447 person-years of observation, a crude mortality rate of 12.4 per 1,000 person-years (16.5 among men, 9.7 among women, Table 2). The mean, median and maximal follow-up durations were respectively 8.1, 8.5 and 8.9 years. In crude analyses (Figure 2, 1st column, upper graph), mortality rates tended to follow a J-curve with highest mortality in the first BMI quintile and lowest mortality rate in the second

**Table 1**
Baseline Characteristics of Participants according to Baseline BMI (a) and WC (b) Quintiles (N=1,293)

| a) | BMI quintiles | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Baseline characteristics | Q 1 | Q 2 | Q 3 | Q 4 | Q 5 | | | Total |
| | N=260 | N=258 | N=259 | N=258 | N=258 | | | 1,293 |
| BMI range (kg/m$^2$) | | | | | | | | |
| Men | 18.7-24.8 | 24.8-26.4 | 26.5-28.3 | 28.3-30.6 | 30.6-46.7 | | | |
| Women | 15.0-22.5 | 22.5-24.8 | 24.8-27.3 | 27.3-30.7 | 30.7-53.6 | | | |
| | *N(%)* | *N(%)* | *N(%)* | *N(%)* | *N(%)* | *Chi 2 P* | *Test for trend P-value (across quintiles)* | *N(%)* |
| Women | 153 (58.9) | 152 (58.9) | 153 (59.1) | 152 (58.9) | 152 (58.9) | | | 762 (58.9 ) |
| Age at baseline visit (2005)* | 69.1 (1.5) | 68.9 (1.4) | 69.0 (1.4) | 69.2 (1.5) | 68.9 (1.5) | 0.274 | | 69.0 (1.5 ) |
| Education: high school or more | 126 (48.5) | 97 (37.6) | 97 (37.9) | 73 (28.6) | 65 (25.3) | 0.001 | <0.001 | 458 (35.6 ) |
| Financial difficulties (0/1) | 53 (20.4) | 67 (26.0) | 63 (24.3) | 78 (30.2) | 92 (35.7) | 0.001 | <0.001 | 353 (27.3 ) |
| IWL in 2005 (12 mo.) | 44 (16.9) | 24 (9.3) | 21 (8.1) | 9 (3.5) | 16 (6.2) | <0.001 | <0.001 | 114 (8.8 ) |
| Smoking status | | | | | | | | |
| Never | 104 (40.3) | 127 (49.8) | 116 (45.7) | 116 (45.1) | 105 (41.5) | 0.004 | 0.222 | 568 (44.5 ) |
| Former | 86 (33.3) | 69 (27.1) | 94 (37.0) | 97 (37.7) | 107 (42.3) | | | 453 (35.5 ) |
| Current | 68 (26.4) | 59 (23.1) | 44 (17.3) | 44 (17.1) | 41 (16.2) | | | 256 (20.1 ) |

| b) | WC quintiles | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| Baseline characteristics | Q 1 | Q 2 | Q 3 | Q 4 | Q 5 | | | Total |
| | N=263 | N=259 | N=256 | N=259 | N=256 | | | 1,293 |
| WC range (cm) | | | | | | | | |
| Men | 70.0-91.9 | 92.0-97.5 | 97.6-103.0 | 103.2-109.5 | 109.6-147.2 | | | |
| Women | 58.8-77.0 | 77.1-83.0 | 83.2-90.0 | 90.2-99.0 | 99.1-150.0 | | | |
| | *N(%)* | *N(%)* | *N(%)* | *N(%)* | *N(%)* | *Chi 2 P* | *Test for trend P-value (across quintiles)* | *N(%)* |
| Women | 156 (59.3) | 152 (58.7) | 150 (58.6) | 153 (59.1) | 151 (59.0) | | | 762 (58.9) |
| Age at baseline visit (2005)* | 69.0 (1.5) | 68.9 (1.5) | 69.1 (1.4) | 69.0 (1.4) | 69.0 (1.5) | 0.451 | | 69.0 (1.5) |
| Education: high school or more | 118 (45.0) | 110 (42.5) | 78 (30.7) | 81 (31.4) | 71 (28.1) | <0.001 | <0.001 | 458 (35.6) |
| Financial difficulties (0/1) | 58 (22.1) | 54 (20.9) | 74 (28.9) | 77 (29.7) | 90 (35.2) | 0.001 | <0.001 | 353(27.3) |
| IWL in 2005 (12 mo.) | 36 (13.7) | 26 (10.0) | 20 (7.8) | 13 (5.0) | 19 (7.4) | 0.008 | 0.002 | 114 (8.8) |
| Smoking status | | | | | | | | |
| Never | 122 (46.6) | 131 (51.8) | 111 (43.7) | 110 (42.6) | 94 (37.6) | 0.001 | 0.173 | 568 (44.5) |
| Former | 79 (30.2) | 78 (30.8) | 82 (32.3) | 98 (38.0) | 116 (46.4) | | | 453 (35.5) |
| Current | 61 (23.3) | 44 (17.4) | 61 (24.0) | 50 (19.4) | 40 (16.0) | | | 256 (20.1) |

Sex-specific BMI and WC quintiles have been re-aggregated; *mean (SD) and Kruskall-Wallis test P-value; Financial difficulties were considered if any of the following criteria was fulfilled: 1) current income clearly lower than others, 2) sometimes difficulty to make ends meet, 3) subsidy for health insurance, or 4) complementary subsidy (from old age insurance). IWL in 2005 was assessed (in the postal questionnaire) by the question: "In the last 12 months, have you involuntarily lost weight?" (yes/no)

BMI quintile. The mortality rates across BMI quintiles were the following: BMI quintile 1) 16.5 per 1,000 person-years (p*y) (95% confidence interval (CI) 11.8-23.1), 2) 9.0 (5.7-14.1), 3) 11.5 (7.7-17.1), 4) 11.9 (8.0-17.6), and 5) 13.5 (9.3-19.6). The differences were not significant according to the log rank test (P=0.256).

The mortality rates across WC quintiles were the following: WC quintile 1) 11.7 per 1,000 p*y (95% CI 7.9-17.4), 2) 12.9 (8.9-18.9), 3) 10.5 (6.9-16.0), 4) 8.0 (5.0-12.8), and 5) 19.4 (14.2-26.6, Figure 2, 1st column, lower graph, log rank test chi2 P=0.016). There was some trend towards a J-curve, with the lowest mortality in fourth quintile and highest mortality in the

**Table 2**
Numbers of Incident Cases for each Outcome

| Outcomes | MEN N | WOMEN N | ALL N | Total N | Specific exclusion criteria |
|---|---|---|---|---|---|
| | | | | | *Starting with N=1,307, then exclusion of 14 persons with missing BMI/WC* |
| N | 531 | 762 | 1,293 | | =Sample included for mortality analyses |
| Mortality (until 31 December 2013) | | | | | |
| Number of deaths | 70 | 60 | 130 | 1,293 | |
| Time at risk (p*y) | 4,244 | 6,202 | 10,447 | | |
| Mortality rate (per 1,000 p*y) | 16.49 | 9.67 | 12.44 | | |
| Mean follow-up (years) | | | 8.1 | | |
| Median follow-up (years) | | | 8.5 | | |
| Maximum follow-up (years) | | | 8.9 | | |
| | | | | | *Starting with N=1,172, then exclusion of 6 persons with missing BMI/WC* |
| N | 489 | 677 | 1,166 | | =Sample included for analyses of disability |
| Disability* (until 31 December 2012) | | | | | |
| Number of incident cases | 96 | 135 | 231 | 1,166 | |
| Time at risk (p*y) | 2,830 | 4,028 | 6,858 | | |
| Incidence rate (per 1,000 p*y) | 33.92 | 33.52 | 33.68 | | |
| Mean follow-up (years) | | | 5.9 | | |
| Median follow-up (years) | | | 7.0 | | |
| Maximum follow-up (years) | | | 7.0 | | |

* Difficulty with BADL for ≥2 years or institutionalization

fifth.

In Cox regression analysis adjusting for age at study entry, sex, education, financial difficulties, IWL, and smoking, there was no statistically significant difference in mortality across both BMI quintiles (Table 3A), and WC quintiles (Table 3B). There were again non-significant trends towards J-curve relations with BMI with highest mortality in the highest quintile and lowest mortality in the second quintile (hazard ratio (HR) 1.59, 1.00, 1.22, 1.42 and 1.62 in the five quintiles, respectively); as well as with WC with highest mortality in the 5th quintile and lowest mortality in the fourth quintile (HR 0.75, 1.00, 0.69, 0.59, and 1.36, Figure 3, first column). Except for the first BMI quintile (HR =0.99 (95% CI 0.45-2.18) in men, HR =3.10 (1.23-7.81) in women), the results were very similar in both sexes. The interaction of BMI with sex was not significant. Whereas absolute mortality rates differed strongly between men and women (Table 2), the associations between adiposity and mortality were similar in both sexes.

The correlations between all adjustment variables were calculated. The highest correlation in absolute value was between sex and smoking status (Cramér's V=0.30).

No significant interactions were found between BMI, WC and the potential confounders included in the models. In the fully adjusted models (Table 3), male sex, IWL in 2005, and current smoking were significantly associated with higher mortality.

The same analyses were carried out after exclusion of 31 participants deceased during the first three years of their follow-up; after this exclusion, mortality rates remained similar across all BMI and WC quintiles.

***Disability***

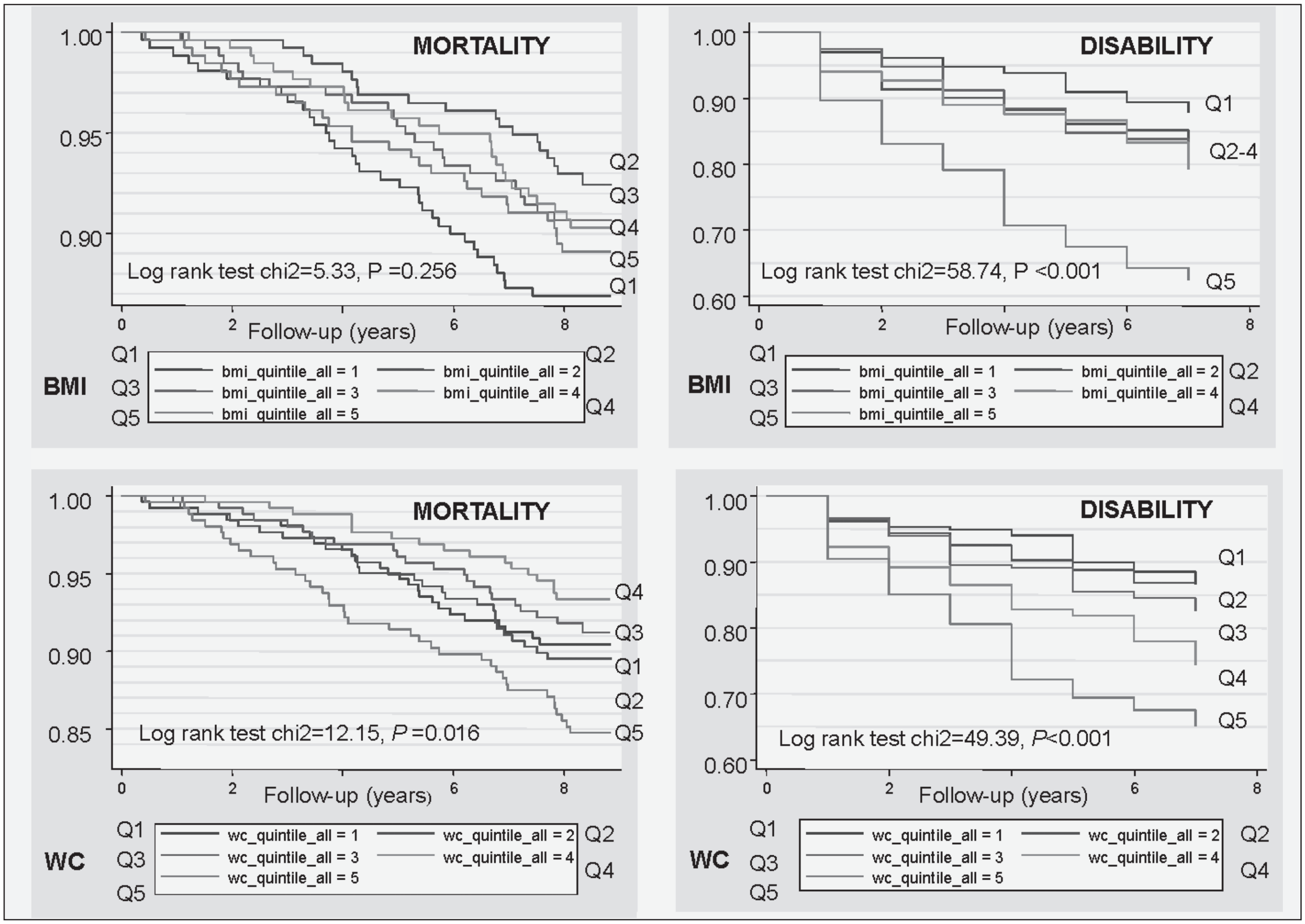
Of 1,166 disability-free participants at baseline (489 men and 677 women), 231 experienced disability. The crude incidence rate of disability was 33.7 per 1,000 p*y (33.9/1,000 p*y in men, 33.5/1,000 p*y in women, Table 2). The mean, median and maximal follow-up durations were respectively 5.9, 7.0 and 7.0 years.

The crude disability incidence rate increased monotonically across BMI baseline quintiles: 18.3/1,000 p*y (95% CI 12.4-26.8), 26.0 (18.8-35.8), 27.2 (19.8-37.4), 32.8 (24.5-43.9), and 68.5 (55.4-84.7, Figure 2, 2nd column, upper graph, log rank test chi2 P<0.001).

The crude disability incidence rate also increased

**Figure 2**

Kaplan-Meyer Survival Curves for Mortality (1st Column, N=1,293) and Disability Incidence (2nd column, N=1,166) by BMI Quintiles (Upper Graphs) and WC Quintiles (Lower Graphs)




"bmi_quintile_all" is the label indicating that the sex-specific BMI quintiles have been reagreggated to give BMI quintiles including men and women. In the same way, "wc_quintile_all" is the label indicating WC quintiles including men and women. For example, wc_quintile_all=5 indicates the 5th WC quintile. "Disability-free survival" indicates survival with neither difficulty with BADL for ≥2 years nor institutionalization.

monotonically across WC baseline quintiles: 20.3/1,000 p*y (95% CI 14.2-29.0), 20.8 (14.5-30.0), 27.3 (20.0-37.4), 42.2 (32.5-54.9), and 62.4 (49.9-78.1, Figure 2, 2nd column, lower graph, log rank test chi2 P<0.001).

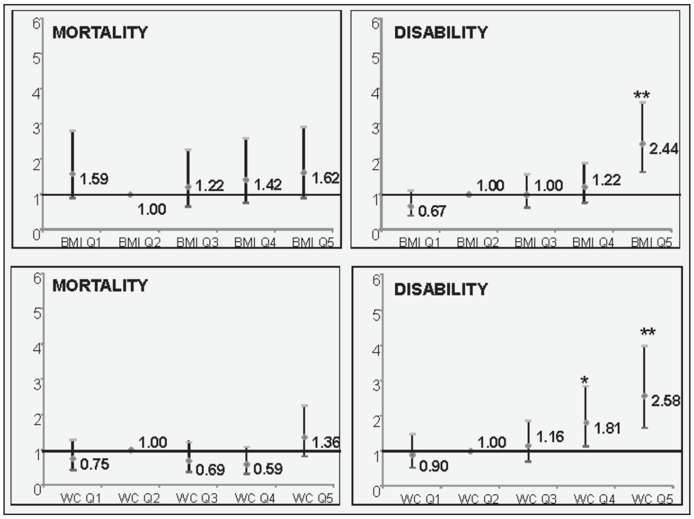
Fully adjusted Cox models also showed that disability tended to increase monotonically across BMI quintiles (HRs: 0.67, 1.00, 1.00, 1.22, and 2.44) and was significantly associated with BMI quintile 5 (HR=2.44, (95% CI 1.65-3.63), p<0.001, Table 4A and Figure 3, 2nd column, upper graph). Disability also tended to increase monotonically across WC quintiles (HRs: 0.90, 1.00, 1.16, 1.81, and 2.58) and was significantly associated with WC quintile 4 (HR=1.81, (1.15-2.85), p=0.011) and quintile 5 (HR=2.58, (1.67-4.00), p<0.001, Table 4B and Figure 3, 2nd column, lower graph). The results were very similar in both sexes.

The range of BMI quintile 5 was 30.5-41.8 kg/m$^2$ in men, and 30.3-47.4 kg/m$^2$ in women. Therefore, overweight (BMI 25.0-29.9 kg/m$^2$) was not significantly associated with incident disability although there were, as mentioned above, non-significant trends towards monotonically upward increases in disability across both BMI and WC quintiles.

Older age at baseline, low education, financial difficulties, and IWL were significantly associated with disability. There were no statistically significant interactions involving disability.

Of note, we have also carried out the analyses of Tables 3 and 4 and Figure 3 (results not shown, tables available upon request) while stratifying data by sex. Results stratified by sex were nearly identical to sex-adjusted aggregated results, except that BMI/WC quintiles 4 and 5 were slightly more significantly associated with disability in women than in men in the stratified analyses. In addition, the first BMI quintile was significantly associated with mortality in women (HR=3.10 [1.23-7.81], P=0.017), but not in men, in the sex-stratified analyses.

**Figure 3**
Association between Mortality (1st Column) and Disability (2nd Column) with BMI (Upper Graphs) and WC quintiles (Lower Graphs)




Hazard ratios and 95% CI are adjusted for age, sex, education, financial situation, involuntary weight loss, and smoking status. In this Figure, hazards ratios and 95% CI stem from the 3rd columns of Tables 3 and 4; N=1,270 and median follow-up=8.5 years for mortality; N=1,147 and median follow-up=7.0 years for disability; *P<0.05; **P<0.001; Sex-specific BMI and WC quintiles have been aggregated.

In summary, the BMI-mortality and the WC-mortality relationships were J-shaped; the optimal values in terms of mortality were unclear because of an insufficient study power. By contrast, disability increased monotonically with both BMI and WC; larger samples would be needed to assess whether this association is linear or curved.

## Discussion

In this cohort study of community-dwelling adults aged 65 to 70 years at baseline, BMI and WC had a non-significant J-shaped association with mortality after 8 years of follow-up. Disability increased monotonically with both BMI and WC and a statistical difference was found when comparing the fifth BMI and WC quintiles vs. quintile 2. However, the study lacked sufficient power to assess whether this relationship was linear or curved.

The finding of a non-significant association between adiposity and mortality was expected in view of the limited study power. There are a number of entangled issues that prevent straightforward interpretation of the relationship between adiposity (e.g. BMI, WC) and mortality in older persons, including survival bias (8), collider bias, competing risks, reverse causation (normal weight participants at study entry who had previously been obese have very high mortality rates) (47), the obesity paradox (applying to individuals who have a disease) (10, 19, 48), and differential meaning of BMI versus WC at different ages and in men vs. women. These phenomena might contribute to explain why the higher BMI and WC quintiles were not significantly associated with mortality in our analyses.

It is likely that adiposity status at midlife (22) or maximum lifetime BMI (47) may better predict mortality, at least as far as causation is concerned, as they are less prone to the aforementioned biases (47). In the present study, we adjusted for involuntary weight loss but this issue is inherently difficult to account for because weight loss related to disease can be insidious and take place over many years. Ideally, the lifetime duration of exposure to obesity should be recorded. In spite of the limited sample size of our study, the observation of an apparent J-shape association between BMI and mortality is consistent with results of larger studies (49, 50). The observation of different nadirs for BMI (2nd quintile) and WC (4th quintile) might reflect the different significance of BMI and WC at this age: e.g. different links with the nutritional state, socio-economic status, life-course lifestyles, and local adiposity standard and customs.

In the present study, we observed no gender difference in the disability incidence rates, while in the literature disability prevalence or incidence is usually higher in women than in men (51-53). However, gender differences are usually more marked in instrumental activities than in basic activities of daily living (BADL) (52-54), while the present study focused exclusively on the latter (i.e. BADL). Men might be less inclined to report functional limitations (54), although some studies suggest that they do so with reasonably good reliability (55). Women might truly have a higher frequency of disability or perceive and report that they do. Moreover, in Lc65+ at baseline, the prevalence of overweight was 53% in men, but 35% in women.

We found a monotonous association between adiposity and disability, which may be consistent with either a linear relationship or a slightly J-curved association. Both shapes have been described in the literature for the association between adiposity (BMI or WC) and disability: linear (56) and J-shaped (57-59). An underlying explanation for the graded relation is that increasing body weight can decrease a person's functional autonomy and mobility because of increased weight to carry, and it can increase the risk of disability (60). Whether subcutaneous or abdominal, excess weight is also likely to have a negative impact on the osteoarticular system, e.g. arthrosis of the backbone, knees, hips, and feet.

Our study suggests that overweight and obesity may result in a substantial morbidity related to disability. Almost half of our study population had a substantially increased HR of disability, as compared to the reference category. This finding has implications on health care of older persons who either stay at home or need to be institutionalized. This observation emphasizes the need for preventive measures aimed at preventing overweight with a life-course perspective (i.e. starting at early age and extending throughout a person's life). Yet, the potentially negative impact of excess weight with regards to disability must be weighted against the apparent survival advantage of high vs. low body weight at an old

**Table 3**
Univariate and Multivariate Associations between Mortality and A) BMI Quintiles and B) WC Quintiles Measured at Baseline, during 8-Year Follow-up

| MORTALITY | Univariate N=1,293 Crude HR (95% CI) | P>z | Multivariate N=1,293 HR (95% CI) | P>z | Multivariate N=1,270 HR (95% CI) | P>z | Multivariate after exclusion of early deaths N=1,240 HR (95% CI) | P>z |
|---|---|---|---|---|---|---|---|---|
| A)BMI quintiles | | | | | | | | |
| Q1 (Men: 18.7-24.8; Women: 15.0-22.5) | 1.85 [1.06-3.25] | 0.031 | 1.82 [1.04-3.20] | 0.036 | 1.59[0.90-2.81] | 0.114 | 1.30[0.69-2.43] | 0.418 |
| Q2 (Men: 24.8-26.4; Women: 22.5-24.8) | 1 (ref) | | 1 (ref) | | 1 (ref) | | 1 (ref) | |
| Q3 (Men: 26.5-28.3; Women: 24.8-27.3) | 1.28 [0.70-2.34] | 0.418 | 1.26 [0.69-2.30] | 0.452 | 1.22[0.66-2.27] | 0.523 | 0.91[0.46-1.84] | 0.803 |
| Q4 (Men: 28.3-30.6; Women: 27.3-30.7) | 1.32 [0.73-2.40] | 0.356 | 1.30 [0.72-2.37] | 0.385 | 1.42[0.77-2.60] | 0.259 | 1.24[0.65-2.38] | 0.519 |
| Q5 (Men: 30.6-46.7; Women: 30.7-53.6) | 1.51 [0.85-2.71] | 0.163 | 1.51 [0.84-2.70] | 0.167 | 1.62[0.90-2.92] | 0.108 | 1.23[0.64-2.36] | 0.541 |
| Age at first visit (2005), linear | 1.05[0.94-1.18] | 0.400 | 1.05[0.93-1.18] | 0.434 | 1.03[0.91-1.17] | 0.610 | 1.07[0.93-1.23] | 0.341 |
| Female sex | 0.58[0.41-0.82] | 0.002 | 0.58[0.41-0.82] | 0.002 | 0.69[0.48-0.99] | 0.043 | 0.65[0.43-0.99] | 0.047 |
| Education: ≥high school | 0.84 [0.58-1.21] | 0.354 | | | 0.84[0.57-1.22] | 0.360 | 0.73[0.47-1.13] | 0.160 |
| Financial difficulties (0/1) | 1.50[1.05-2.15] | 0.026 | | | 1.32[0.91-1.92] | 0.147 | 1.12[0.72-1.74] | 0.606 |
| IWL in 2005 (12 mo.) | 3.71[2.48-5.56] | <0.001 | | | 3.39[2.20-5.22] | <0.001 | 2.91[1.74-4.87] | <0.001 |
| Smoking status | | | | | | | | |
| Never | 1 (ref) | | | | 1 (ref) | | 1 (ref) | |
| Former | 1.78[1.15-2.75] | 0.009 | | | 1.46[0.93-2.30] | 0.102 | 1.66[0.98-2.80] | 0.058 |
| Current smoker | 2.98[1.91-4.64] | <0.001 | | | 2.58[1.63-4.08] | <0.001 | 2.90[1.70-4.95] | <0.001 |

| MORTALITY | Univariate N=1,293 Crude HR (95% CI) | P>z | Multivariate N=1,293 HR (95% CI) | P>z | Multivariate N=1,270 HR (95% CI) | P>z | Multivariate after exclusion of early deaths N=1,240 HR (95% CI) | P>z |
|---|---|---|---|---|---|---|---|---|
| B)WC quintiles | | | | | | | | |
| Q1 (Men: 70.0-91.9 cm; Women: 58.8-77.0 cm) | 0.91[0.53-1.57] | 0.730 | 0.91[0.53-1.56] | 0.724 | 0.75[0.43-1.29] | 0.296 | 0.79[0.42-1.47] | 0.450 |
| Q2 (Men: 92.0-97.5 cm; Women: 77.1-83.0 cm) | 1 (ref) | | 1 (ref) | | 1 (ref) | | 1 (ref) | |
| Q3 (Men:97.6-103.0 cm; Women: 83.2-90.0 cm) | 0.81[0.46-1.42] | 0.461 | 0.80[0.45-1.40] | 0.434 | 0.69[0.38-1.22] | 0.202 | 0.68[0.35-1.32] | 0.256 |
| Q4 (Men: 103.2-109.5 cm; Women: 90.2-99.0 cm) | 0.61[0.33-1.13] | 0.115 | 0.61[0.33-1.12] | 0.108 | 0.59[0.32-1.09] | 0.093 | 0.69[0.35-1.35] | 0.277 |
| Q5 (Men: 109.6-147.2 cm; Women: 99.1-150.0 cm) | 1.50[0.92-2.45] | 0.104 | 1.51[0.92-2.46] | 0.102 | 1.36[0.82-2.26] | 0.239 | 1.19[0.66-2.17] | 0.558 |
| Age at first visit (2005), linear* | 1.05[0.94-1.18] | 0.400 | 1.06[0.94-1.19] | 0.343 | 1.04[0.92-1.17] | 0.532 | 1.08[0.94-1.24] | 0.307 |
| Female sex | 0.58[0.41-0.82] | 0.002 | 0.58[0.41-0.81] | 0.002 | 0.69[0.48-1.00] | 0.048 | 0.66[0.43-1.00] | 0.051 |
| Education: ≥high school | 0.84 [0.58-1.21] | 0.354 | | | 0.86[0.59-1.25] | 0.433 | 0.74[0.48-1.16] | 0.189 |
| Financial difficulties (0/1) | 1.50[1.05-2.15] | 0.026 | | | 1.29[0.89-1.88] | 0.184 | 1.10[0.71-1.71] | 0.670 |
| IWL in 2005 (12 mo.) | 3.71[2.48-5.56] | <0.001 | | | 3.50[2.30-5.34] | <0.001 | 2.99[1.80-4.96] | <0.001 |
| Smoking status | | | | | | | | |
| Never smoker | 1 (ref) | | | | 1 (ref) | | 1 (ref) | |
| Former smoker | 1.78[1.15-2.75] | 0.009 | | | 1.43[0.91-2.26] | 0.125 | 1.62[0.96-2.75] | 0.073 |
| Current smoker | 2.98[1.91-4.64] | <0.001 | | | 2.66[1.68-4.22] | <0.001 | 2.98[1.74-5.09] | <0.001 |

HR: hazard ratio from Cox regression models; N indicated in the first line represents the number of participants included in the model; Sex-specific BMI and WC quintiles have been aggregated; Adjustment variables: sex, age at first visit (linear), education ≥high school (0/1), financial difficulties (0/1), involuntary weight loss during the past 12 months (IWL) in 2005 (0/1); smoking status (never/former/current smoker); Financial difficulties were considered if any of the following criteria was fulfilled: 1) current income clearly lower than others, 2) sometimes difficulty to make ends meet, 3) subsidy for health insurance, or 4) complementary subsidy (from old age insurance); IWL in 2005 was assessed (in the postal questionnaire) by the question: "In the last 12 months, have you involuntarily lost weight?" (yes/no)

**Table 4**
Univariate and Multivariate Associations between Disability (i.e. Difficulty with BADL for ≥2 Years or Institutionalization) and A) BMI Quintiles and B) WC Quintiles Measured at Baseline, during 7-Year Follow-up

| DISABILITY | Univariate N=1,166 Crude HR (95% CI) | P>z | Multivariate N=1,166 HR (95% CI) | P>z | Multivariate N=1,147 HR (95% CI) | P>z |
|---|---|---|---|---|---|---|
| A)BMI quintiles | | | | | | |
| Q1 (Men: 18.7-24.8; Women: 15.0-22.4)) | 0.70[0.43-1.16] | 0.167 | 0.68[0.41-1.13] | 0.138 | 0.67[0.41-1.12] | 0.126 |
| Q2 (Men: 24.8-26.4; Women: 22.5-24.6) | 1 (ref) | | 1 (ref) | | 1 (ref) | |
| Q3 (Men: 26.4-28.3; Women: 24.6-27.0) | 1.04[0.66-1.64] | 0.857 | 1.00[0.64-1.58] | 0.996 | 1.00[0.63-1.58] | 0.997 |
| Q4 (Men: 28.3-30.5; Women: 27.0-30.2) | 1.26[0.81-1.94] | 0.304 | 1.21[0.78-1.87] | 0.401 | 1.22[0.78-1.90] | 0.390 |
| Q5 (Men: 30.5-41.8; Women: 30.3-47.4) | 2.58[1.75-3.80] | <0.001 | 2.53[1.72-3.72] | <0.001 | 2.44[1.65-3.63] | <0.001 |
| Age at first visit (2005) | 1.12[1.02-1.22] | 0.015 | 1.12[1.02-1.22] | 0.013 | 1.12[1.02-1.22] | 0.015 |
| Female sex | 0.99[0.76-1.29] | 0.949 | 0.98[0.76-1.28] | 0.906 | 0.94[0.71-1.25] | 0.662 |
| Education: ≥high school | 0.53[0.39-0.71] | <0.001 | | | 0.62[0.45-0.84] | 0.003 |
| Financial difficulties (0/1) | 1.54[1.17-2.03] | 0.002 | | | 1.35[1.02-1.79] | 0.038 |
| IWL in 2005 (12 mo.) | 2.02[1.39-2.94] | <0.001 | | | 2.49[1.70-3.66] | <0.001 |
| Smoking status | | | | | | |
| Never | 1 (ref) | | | | 1 (ref) | |
| Former | 1.07[0.80-1.44] | 0.643 | | | 1.00[0.72-1.37] | 0.985 |
| Current smoker | 1.26[0.89-1.77] | 0.187 | | | 1.30[0.91-1.85] | 0.152 |
| **DISABILITY** | **Univariate N=1,166 Crude HR (95% CI)** | **P>z** | **Multivariate N=1,166 HR (95% CI)** | **P>z** | **Multivariate N=1,147 HR (95% CI)** | **P>z** |
| B)WC quintiles | | | | | | |
| Q1 (Men: 70.0-91.8 cm; Women: 58.8-76.8 cm) | 0.98[0.59-1.63] | 0.936 | 0.97[0.58-1.61] | 0.893 | 0.90[0.54-1.50] | 0.687 |
| Q2 (Men: 91.9-97.5 cm; Women: 77.0-82.5 cm) | 1 (ref) | | 1 (ref) | | 1 (ref) | |
| Q3 (Men:97.6-103.0 cm; Women: 82.6-89.5 cm) | 1.32[0.81-2.13] | 0.261 | 1.28[0.79-2.07] | 0.317 | 1.16[0.71-1.88] | 0.560 |
| Q4 (Men: 103.2-109.0 cm; Women: 89.8-97.2 cm) | 2.01[1.29-3.15] | 0.002 | 1.98[1.26-3.10] | 0.003 | 1.81[1.15-2.85] | 0.011 |
| Q5 (Men: 109.1-138.5 cm; Women: 97.3-150.0 cm) | 2.95[1.92-4.52] | <0.001 | 2.89[1.89-4.43] | <0.001 | 2.58[1.67-4.00] | <0.001 |
| Age at first visit (2005) | 1.12[1.02-1.22] | 0.015 | 1.11[1.01-1.21] | 0.022 | 1.10[1.01-1.20] | 0.035 |
| Female sex | 0.99[0.76-1.29] | 0.949 | 0.99[0.76-1.29] | 0.945 | 0.92[0.70-1.22] | 0.571 |
| Education: ≥High school | 0.53[0.39-0.71] | <0.001 | | | 0.59[0.43-0.80] | 0.001 |
| Financial difficulties (0/1) | 1.54[1.17-2.03] | 0.002 | | | 1.35[1.02-1.79] | 0.038 |
| IWL in 2005 (12 mo.) | 2.02[1.39-2.94] | <0.001 | | | 2.30[1.57-3.36] | <0.001 |
| Smoking status | | | | | | |
| Never | 1 (ref) | | | | 1 (ref) | |
| Former | 1.07[0.80-1.44] | 0.643 | | | 0.90[0.66-1.24] | 0.535 |
| Current smoker | 1.26[0.89-1.77] | 0.187 | | | 1.19[0.84-1.70] | 0.322 |

HR: hazard ratio from Cox regression models; N indicated in the first line represents the number of participants included in the model; Sex-specific BMI and WC quintiles have been aggregated; Adjustment variables: sex, age at first visit (linear), education ≥high school (0/1), financial difficulties (0/1), involuntary weight loss during the past 12 months (IWL) in 2005 (0/1); smoking status (never/former/current smoker); Financial difficulties were considered if any of the following criteria was fulfilled: 1) current income clearly lower than others, 2) sometimes difficulty to make ends meet, 3) subsidy for health insurance, or 4) complementary subsidy (from old age insurance); IWL in 2005 was assessed (in the postal questionnaire) by the question: "In the last 12 months, have you involuntarily lost weight?" (yes/no) age. To further address this issue, one should also be able to distinguish leanness due to disease in older persons from leanness maintained during a whole life-course among fully healthy persons, which would incur the use of more complex measurements (e.g. dual-energy X-ray absorptiometry or abdominal CT scan) that often exceed what is acceptable and/or feasible in epidemiological studies. Nonetheless, our findings, consistent with evidence in the literature, stress the need to prevent functional decline and muscle loss in older adults through adequate nutrition (e.g. a number of older persons tend to lessen their intake of protein and other important nutrients) and encourage them to sustain regular physical activity, including resistance training at all ages (8, 61). Another practical issue applicable for all older persons, but likely even more for older individuals with overweight, is to adapt the living environment to facilitate daily life movements and activities, including for the prevention of falls, e.g. by installing chairs in the shower, anti-slide mats, electronic devices for seeking help in case of fall, medical walkers.

This study has some limitations. First, of all 3,056 individuals initially contacted, 1,307 participated at the baseline physical examination and 1,293 of them (42% of the initial sample) could be included in the 8-year mortality analyses. This final participation rate was comparable with other surveys involving community-dwelling individuals (rather than hospitalized persons) in Western countries (62-64); for example, in the Cardiovascular Health Study in the USA (65), 31% of those contacted in the randomly selected sample were initially enrolled. Differential participation of population subgroups in Lc65+ is likely to be small since only 8% of those refusing to participate attributed their refusal to poor health (36, 37). Participants and non-participants showed no significant difference in their distribution of sex and year of birth. Furthermore, the social characteristics of participants closely reflected the local population of same age according to data from the population census.

Extreme quintiles might include persons with very different BMI or WC values (e.g. BMI in fifth quintile ranging between 31 and 54 $kg/m^2$, as mentioned in Table 1). In mortality analyses, 21 men (with a BMI in quintile 5) had a BMI ≥35 $kg/m^2$ and among them, 4 men had a BMI ≥40 $kg/m^2$; 53 women (with a BMI in quintile 5) had a BMI ≥35 $kg/m^2$ and among them, 18 women had a BMI ≥40 $kg/m^2$. We preferred to use quintiles over quartiles despite fairly small size numbers, in order to better examine the associations of outcomes (BADL, mortality) with low and high BMI/waist, as a major contemporary question precisely relates to the shape of the associations of outcomes with BMI/waist at such extreme low and high values in older persons. In addition, the use of quintiles allows better assessing a graded effect. Our study lacked statistical power to demonstrate a relationship between BMI/WC and mortality and to assess whether the graded relationship with disability was linear or J-curved. However, despite the relatively small sample size, our study had a fairly long follow-up time, which allowed accumulating a large number of person-years to be used in denominators. The consistency of our results in both univariate and multivariate analyses suggests that the J-shape association between adiposity and mortality and a graded association between adiposity and disability in our study are true. The limited study power explains why only extreme quintiles showed statistically significant associations with disability. Inversely, precise assessment of disability as done in our study has not been often performed in large studies so that our results are informative. Further studies aiming at clarifying the relation between BMI/WC and disability will need to include larger sample sizes (31) and/or longer follow-ups. Our study also has strengths. BMI and WC were measured and not self-reported. Another important strength (41) is our explicit adjustment for involuntary weight loss at baseline, while most other similar studies reported weight loss with no distinction of participants' intention (31, 43). The truly population-based nature of our sample is another strength.

In conclusion, we found that adiposity markers tended to show a J-shaped relation with mortality and a graded relation with disability in "young old" adults aged 65 to 70 years at baseline. Studies with larger sample sizes and/or longer follow-up should further clarify the exact shapes of these associations, including by assessing the role of exposures (adiposity) measured at different ages (31) on later health outcomes and the potentially different predictive values of different adiposity markers (BMI, WC), which may represent different phenotypes (e.g. overall adiposity versus abdominal adiposity). The findings emphasize the need for life-long strategies to maintain a healthy weight during the entire life course and, specifically, the need for supportive tools for older persons with excess weight in order to reduce their functional limitations and improve their quality of life.

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*Ethical standard:* This study complies with Switzerland' current laws.

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