Changes in Body Mass Index and Waist circumference and concurrent mortality among Swedish women

Nina Roswall[1,2*], Yingjun Li[1,3*], Sven Sandin[1], Peter Ström[1], Hans-Olov Adami[1,4,5] and Elisabete Weiderpass[1,6,7,8]

[1] *Department of Medical Epidemiology and Biostatistics, Karolinska Institutet, Stockholm, Sweden*

[2] *Danish Cancer Society Research Center, Copenhagen, Denmark*

[3] *Department of Epidemiology and Health Statistics, Zhejiang University School of Public Health, Hangzhou, China*

[4] *Department of Epidemiology, Harvard T. H. Chan School of Public Health, Boston, MA, USA*

[5] *Institute of Health and Society, University of Oslo, Oslo, Norway*

[6] *Department of Community Medicine, Faculty of Health Sciences, University of Tromsø, The Arctic University of Norway, Tromsø, Norway*

[7] *Genetic Epidemiology Group, Folkhälsan Research Center, Helsinki, Finland*

[8] *The Cancer Registry of Norway – Institute of Population Based Cancer Research, Oslo, Norway*

* These authors contributed evenly to the project and share first authorship

Key words: Epidemiology; Body Mass Index; Waist circumference; Mortality; Weight Change

Running title: Changes in BMI/waist circumference and mortality

Corresponding author: Nina Roswall, Danish Cancer Society Research Center, Strandboulevarden 49. DK-2100 Copenhagen Ø, Denmark. E-mail: roswall@cancer.dk

Word count: 2,843 words

Funding: This study was funded by the Swedish Research Council. (Grant number 521-2011-2955)

Disclosure: The authors declare that they have no conflict of interest.

Study Importance Questions

What is already known about this subject?

- Obesity is known to be a strong and independent risk factor for several cancers, cardiovascular disease, and all-cause mortality, with the association between Body Mass Index and all-cause mortality being J-or U-shaped.
- It has been suggested that the association between fat tissue and mortality is modified by the location of body fat: Waist Circumference appears to be more strongly associated with the risk of type 2 diabetes, cardiovascular disease and mortality than Body Mass Index.
- Few studies have assessed the association between changes in Body Mass Index and/or waist circumference and concurrent mortality, and most studies doing so have focused on young adult populations or the elderly.

What does your study add?

- The present study is one of few studies, which examines the association between changes in Body Mass Index and waist circumference over time, rather than a single time-point measure of these.
- Furthermore, it stands out by examining the association in a mid-life adult population, rather than in the elderly. The associations in these different age-groups may not be directly comparable and thus the study adds considerably to the research area of weight change in mid-life adults.
- Finally, a limited body of literature has focused on habitual weight gain over adult life, as does the present study. Most of the existing literature on weight and mortality centres on the effects of weight loss in overweight/obese individuals, which entails different metabolic effects, and thus a different association with concurrent mortality.

Abstract

Objective

Most studies on obesity and mortality use a single anthropometric measure. Less is known about the effects of weight change on mortality. This study examined changes in Body Mass Index (ΔBMI) and waist circumference (ΔWC), and subsequent all-cause, and cause-specific mortality.

Methods

The study was conducted in the Women's Lifestyle and Health cohort, using self-reported anthropometric measures from 1991-92 and 2003. We calculated Hazard Ratios of mortality and 95% confidence intervals using Cox proportional hazards models. ΔBMI and ΔWC were examined in quartiles of absolute and relative change, with the second quartile (moderate gain) as the reference.

Results

There was a higher risk of death in the first quartile of relative ΔBMI: HR 1.28(1.04-1.56). Absolute ΔBMI suggested the same pattern, but the result was non-significant. ΔWC was not associated with mortality. In cause-specific analyses, the association remained significant for cancer-mortality only. In sensitivity analyses excluding the first 5 years of follow-up, the association was, however, attenuated.

Conclusion

The present study found a higher risk of death among women in the first quartile of relative ΔBMI compared to the second. It was driven by cancer mortality, but may be ascribed to reverse causality. ΔWC was not associated with mortality.

Introduction

Numerous epidemiological studies, as well as meta-analyses, have shown that obesity is a strong and independent risk factor for several cancers, cardiovascular disease, and all-cause mortality (1-4). The association between Body Mass Index (BMI) and all-cause mortality is J-shaped (5) or U-shaped (5-7) with both obesity and underweight being associated with higher mortality. However, nearly all these reports used a single point-in-time measurement of BMI, and they may therefore not be useful in predicting the effect of weight change on future health events. Moreover, existing studies assessing the effect of weight change on mortality have primarily focused on young adult populations (8, 9) or the elderly (10, 11). Few prospective cohort studies have reported the association between weight change and all-cause mortality in adult women in European countries.

It has been suggested, that the association between fat tissue and mortality is modified by the location of body fat (12, 13): Waist Circumference (WC) (an anthropometric measure of abdominal fatness) appears to be more strongly associated with the risk of type 2 diabetes, cardiovascular disease and mortality than BMI (an anthropometric measure of general fatness) (13). Thus, it is important to clarify the association between changes in these anthropometric measures over the life-course, and subsequent risk of mortality, in prospective cohort studies.

To this end, we investigated the association between absolute and relative changes in BMI and WC over a 12-year period, and subsequent all-cause mortality in adult, Swedish women. Furthermore, we investigate the association with the main causes of death in the cohort: Cancer, cardiovascular disease, and other causes, as well as effect-modification by age, smoking, and baseline anthropometric measures.

Methods

Study population

The study cohort and data collection have been described in detail previously (14). In brief, the source population comprised women aged 29-49 years, who resided in the Uppsala Health Care Region in Sweden between 1991 and 1992. A random sample of 96,000 women were asked to fill in a mailed baseline questionnaire, which included queries on anthropometric characteristics, diet, lifestyle and socioeconomic factors. In 2003, a follow-up questionnaire was sent to all women to update information on anthropometric characteristics as well as lifestyle changes. Of those invited, 49,259 (51%) returned the first questionnaire (1991-1992) and of these women, 34,402 (69.8%) also responded to the second questionnaire (2003). We excluded 42 women who died or emigrated before the second questionnaire, and 2,655 and 10,419 women with missing values on included variables in the datasets of BMI and WC change, respectively. Furthermore, we excluded women who reported to have lost or gained BMI or WC outside of the 1st and 99th percentiles for each analytical cohort: 552 women in the dataset on absolute BMI [-4, 9 kg/m^2], 456 in the dataset on absolute WC [-13, 30 cm], 641 in the dataset on relative BMI [-14%, 38%], and 474 women in the dataset on relative WC [-15%, 40%], . The remaining 31,107 (absolute BMI change), 23,272 (absolute WC change), 31,018 (relative BMI change), 23,254 women (relative WC change) were included in the final analyses. The study was approved by the regional Ethical Committee at Uppsala University, and the Ethical Committee at Karolinska Institutet, Stockholm, Sweden.

Exposure assessment

In 1991-1992 and 2003, participants completed a self-administered questionnaire, which included queries on height, body weight, WC, education, smoking, alcohol consumption, physical activity (PA), diet, and other lifestyle factors. BMI was calculated as weight in kilograms divided by squared height in meters. Absolute BMI and WC change were calculated as absolute change between the two surveys: (BMI at second questionnaire – BMI at first questionnaire) and (WC at second questionnaire – WC at first questionnaire). Relative BMI and WC change were calculated as percent change in BMI and WC between the two surveys: (100 × (BMI at second questionnaire − BMI at first questionnaire)/ BMI at first questionnaire) and (100 × (WC at second questionnaire − WC at first questionnaire)/ WC at first questionnaire). We investigated quartiles of absolute and relative ΔBMI and ΔWC, with the reference category being the second quartile (moderate increase in BMI/WC) (Table 1).

Outcome information

We estimated the association with total mortality, as well as cause-specific mortality from cancer, cardiovascular disease, and all other causes of death combined.

Information on date and cause of death was obtained by linking each participant to the Swedish Bureau of Statistics and Cause of Death Registry, using the individually unique national registration number. We used ICD-9 codes to classify cause of death for participants who died before 1997, and ICD-10 codes from 1997 and onwards. We included the following codes: Cancer (ICD-9: 140-208, ICD-10: C00-C98), and cardiovascular disease (ICD-9: 390-459, ICD-10: I00-I99). All other ICD-codes were classified as "Other cause of death".

Participants who emigrated were identified through the Emigration registry, and censored at date of emigration. Participants were followed from inclusion into the study, and until date of death, censoring because of loss to follow-up, or December 31st, 2012, whichever occurred first.

Statistical analyses

We used Cox proportional hazards models to estimate the hazard ratio (HRs) and 95% confidence intervals (CIs) with age as time axis to ensure the best possible adjustment for confounding by age. The HRs of ΔBMI and ΔWC were estimated treating the exposure categorically (quartiles), as there was major deviation from linearity for the association between both BMI and WC change, and mortality.

First, we calculated a crude model with adjustment for age (continuous) only (Model 1), and then a fully adjusted model which also included anthropometric baseline measure (BMI or WC), smoking status (categorical, never/former/current), educational level (categorical, ≤10 years/11-13 years/≥14 years), physical activity (categorical, very low/low/normal/high/very high), and alcohol consumption (gram/day, continuous), and for analyses on WC also height (continuous, cm) (Model 2).

We further performed stratified analyses by age category (above/below median age in 2003: 52 years), baseline BMI (above/below baseline median: 22.5 kg/m^2), baseline WC (above/below baseline median: 75 cm), and smoking status (never, former, and current) to detect potential effect modification of the association between ΔBW and ΔWC with all-cause mortality.

Two-sided 95% CIs for HRs were calculated based on the likelihood ratio test of the Cox regression parameter. The proportional hazards assumption of the Cox models was evaluated by calculating weighted Schoenfeld residuals using the ZPH option in the PROC PHREG procedure. Graphical inspection revealed no violation of the proportional hazards assumption. All statistical tests were made on the 5% level of significance. The procedure PHREG in SAS, version 9.4 on a windows platform was used for all statistical analyses.

Results

During 9 years of follow-up, 762 deaths (515 from cancer, 104 from cardiovascular disease, and 143 from other causes) and 570 deaths (390 from cancer, 79 from cardiovascular disease, and 101 from other causes) occurred among women in the analytical cohorts for relative BMI and WC change, respectively. Table 1 shows the baseline distribution of possible confounders for participants within the relative change categories. Several of the possible confounding factors were unevenly distributed across quartiles of change: Compared to participants in the low quartiles of BMI change, participants in the high quartiles had a shorter education and were less physically active. Participants who gained most weight over follow-up reached a higher BMI and WC in 2003, and were more likely to be former smokers. Age and alcohol consumption of participants were similar across quartiles. The same trends were observed across relative WC change categories.

Table 2 shows the association between absolute and relative BMI and WC change and overall mortality. There was a statistically significant higher risk of death for the first compared to the second quartile of relative ΔBMI, with a multivariate HR of 1.28 (95% CI 1.04-1.56). For absolute ΔBMI there was a similar suggestion for the first quartile, which did, however, not reach statistical significance: HR 1.19 (0.94-1.49). Absolute and relative ΔWC was not associated with overall mortality (Table 2).

When examining the association in relation to cause-specific mortality, the association with relative ΔBMI was statistically significantly for cancer mortality only: HR 1.30 (95% CI 1.02-1.66) for the first vs. second quartile, in the multivariate analyses. Again, there was a similar, but non-significant, tendency for absolute ΔBMI: HR 1.20 (95% CI 0.90-1.59) in the multivariate analyses.

We investigated effect modification by smoking, baseline BMI, baseline WC, and age, and found no interaction between change categories and these variables (results not shown). When we further adjusted for total energy intake, the results were similar to those shown in Model 2 (results not shown).

Sensitivity analyses were conducted by excluding the first 2 and 5 years of follow-up, respectively, from the second questionnaire, to avoid that pre-clinical disease may have affected weight change as well as risk of mortality. In these analyses, the association between relative BMI change and mortality in quartile 1 was attenuated: It was significant still, when excluding two years of follow-up: HR 1.26 (95% CI 1.01-1.57), but became non-significant when excluding the first 5 years of follow-up: HR 1.24 (95% CI: 0.95-1.61). We also conducted separate sensitivity analyses in which we excluded women who had a diagnosis of cancer, cardiovascular disease or diabetes, as well as women who were pregnant during the two surveys, respectively, as this may affect their weight change as well as their survival chance. These analyses generated results similar to the main analyses (results not shown).

Discussion

In this prospective study among Swedish women, we found a significantly higher risk of concurrent mortality among women in the first quartile of relative BMI change, compared to women in the second quartile of relative BMI change. Absolute BMI change showed a similar, but non-significant tendency, whereas WC change was not associated with concurrent mortality. When examining cause-specific mortality, the association with relative BMI change, was primarily driven by cancer mortality.

The strengths of the present study includes the population-based design, and the measurement of anthropometric features at both baseline and 12-year follow-up, which is the premise for investigating anthropometric change, as well as the collection of detailed information on potentially confounding variables. Furthermore, the study is based on a large number of incident deaths, and has a virtually complete follow-up of participants through the Swedish Bureau of Statistics and Swedish Cause of Death Registry (14), which is well-validated (15). Finally, a range of sensitivity analyses explores the statistical robustness of our findings.

The limitations of the present study include the fact that the exposure variables and covariates are self-reported, and therefore information bias cannot be ruled out. Furthermore, the participation rate in the original questionnaire was only 51 %, and it was most likely affected by healthy-participant bias. This bias may have been strengthened even further in the follow-up study, where the participation rate was approximately 70% of those returning the first questionnaire. However, one would expect that this should entail a smaller variation in anthropometric change over the study period. As no previous study has compared characteristics of participants and non-participants in the WLH cohort, we can thus only speculate how these groups differ, and how this may affect the results of the present study. Thus, we encourage, that the findings of this study are generalized with caution, as they may not be representative of the general adult women in Sweden.

Our study included no information on whether the participating women changed their weight as a result of bariatric surgery, which may affect the concurrent risk of death in a different matter than a natural weight change. However, we expect that few women in the cohort had surgically induced weight loss, as this procedure is mainly conducted in extremely obese subjects. The 90th percentile for BMI in the present cohort was 30, whereas a Swedish bariatric surgery cohort had a BMI of 38 (-2) in women (16). Furthermore, a surgical intervention would most likely produce such drastic weight loss, that these women would have been excluded from the study when excluding the women outside of the 1st and 99th percentile of weight change.

We included information on weight history at two time-points only, and calculated weight change between these. This is a simplistic approach to the lifetime effect of anthropometry on mortality. For instance, factors such as weight cycling, duration of obesity over a life-course, maximum weight attained at any time, and obesity during childhood and early adulthood (17-19) have been suggested to affect concurrent mortality, and these may thus be potential confounders in the present study, on which we lack information. Furthermore, we also lacked information on whether weight change in the present cohort was intentional or unintentional. Unintentional weight loss and associated generally wasting plays a larger role among the elderly (20-23), and is of less relevance in a primarily healthy, mid-life adult population as the one in the present cohort. We should therefore expect that the bias produced by unintentional, illness-induced weight loss in the present study should affect the results in a relatively minor fashion. However, when conducting sensitivity analyses, in which we exclude the first 2 and 5 years of follow-up, in order to avoid a potential effect of pre-clinical disease, we do see a tendency towards a change in estimates; which become insignificant, when excluding the first five years of follow-up. This may be explained by decreased statistical power in the relatively smaller dataset. However, it could also suggest, that reverse causality plays a role in the results found in the present study.

A study of weight trajectories before death suggested that weight loss began already 9 years before death (23). With a median follow-up time of 9 years in the present study, some women could thus display signs of weight loss associated with preclinical disease already at baseline, or between baseline and follow-up. However, the study also found that for cancer deaths specifically, weight loss accelerated over the last 3 years before death (23). The majority of the deaths in the WLH cohort are cancer-related (67.6%), and cancer usually develops over a long period of time. Also, the study found that the period of weight loss before death increased with age (23). Given that the WLH cohort is relatively young, we should thus expect the deflection point in weight trajectory to occur only a few years before death. We can, thus, neither confirm, nor refute, that the findings of the present study are driven by pre-clinical disease affecting weight change.

Previous studies on weight change and mortality in mid-life adults are few, as most studies have focused on the elderly. The association in this age-group is not directly comparable to that of younger adults (22, 24), as weight generally decreases in the elderly (60+ years) and body fat is redistributed towards a higher proportion of abdominal, particularly visceral, fat (22). Furthermore, a limited body of literature has focused on habitual weight gain over adult life, as does the present study. Most of the existing literature on weight and mortality centres on the effects of weight loss in overweight/obese individuals, which entails different metabolic effects, and thus a different association with concurrent mortality. Interestingly, however, these studies have generally found an increased long-term overall mortality among those losing weight (25), which parallels the findings of the present study.

Given the limited statistical power, especially in the sub-group analyses of cause-specific mortality and in the sensitivity analyses in the present study, more studies in larger cohorts or with a longer follow-up time are required to investigate the association between weight change and concurrent mortality in more detail. Given the suggestion of potential reverse causality in the findings of the present study, this should be taken into account also when designing and modelling future studies in the field.

We found no association between WC and concurrent mortality, but only for BMI, where it was significant for relative BMI change, but suggested the same tendency for absolute BMI change. BMI is usually considered a marker of general fatness, whereas WC is a marker of specific, abdominal fatness, which has been found more strongly associated with cardiovascular mortality (13). Given the demographics of the present cohort, which is female and relatively young, the risk of cardiovascular death is generally relatively low, as also reflected in the small number of events during follow-up (104 in the relative BMI cohort, 79 in the relative WC cohort). Hence, changes in WC could be more relevant in cohorts with a higher risk of cardiovascular death.

Conclusion

In conclusion, the present study in a cohort of adult, Swedish women found a higher risk of death among women in the first quartile of relative BMI change over follow-up, compared to the second quartile. This was primarily driven by cancer mortality, but the results of sensitivity-analyses suggested that it could be a result of reverse causality. We found no association between changes in WC and concurrent mortality. Future studies in the field are warranted, and should carefully take potential reverse causality into account. They would also benefit from including more detailed information on anthropometric change, including whether it is intentional or unintentional, as well as a detailed lifetime history. Generalisations of the findings in the present cohort of relatively young women should be exceeded with extreme caution to other demographic groups.

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Table 1: Characteristics of participants in the WLH cohort at time of follow-up, per quartiles of relative Body Mass Index and waist circumference change, respectively

	All (N=31,018)		BMI change (Q1: ≤2.2%) (N=7,179)		BMI change (Q2:2.2-7.4%) (N=8,425)		BMI change (Q3:7.4-13.6%) (N=7,689)		BMI change (Q4: >13.6%) (N=7,725)	
Characteristics	Median	P10-P90	Median	P10-P90	Median	P10-P90	Median	P10-P90	Median	P10-P90
Deceased, N	762		216		189		163		194	
Cancer deaths (%)	67.6		63.4		70.4		67.5		69.6	
CVD deaths (%)	13.7		16.7		13.2		9.2		14.4	
Other causes of death (%)	18.8		19.9		16.4		23.3		16.0	
Age at follow-up	52	43-59	52	44-60	52	44-59	51	44-59	51	43-59
BMI (kg/m^2) at baseline	22.5	20-27.5	23.5	20.5-28.5	22	19.5-27	22.5	19.5-27	22.5	19.5-27.5
WC at baseline	75	67-88	76	68-90	74	67-86	75	67-87	75	67-88
BMI (kg/m^2) at follow-up	24	21-30	23	20-28	23	21-28	25	21-30	27	23-33
WC (cm) at follow-up	83	72-98	80	70-95	80	71-93	84	73-98	89	78-104
BMI change in percent	7.4	-2.2-20.0	-2.0	-8.0-2.0	4.8	2.3-7.0	10.2	8.1-12.8	18.4	14.3-28.6
WC change in percent	9.1	-1.2-2.2	2.9	-5.6-12.0	7.1	0-15.6	10.7	2.6-20.0	16.9	6.8-29.0
Absolute BMI change	1.5	-0.5-4.5	0	-2-0.5	1	0.5-1.5	2.5	2-3	4	3-6.5

Absolute WC change	7	-1-16	3	-4-9	5	0-12	8	2-15	13	5-22
Education (%)										
≤ 10	26.5		28.5		24.3		26.0		27.6	
11-13	39.6		37.8		38.9		38.5		43.0	
≥ 14	33.9		33.7		36.8		35.5		29.4	
Alcohol drinking	5.3	1.6-15.2	5.2	1.5-15.3	5.4	1.6-14.9	5.3	1.6-15.4	5.2	1.5-15.0
Smoking status (%)										
Never	46.8		45.0		49.2		49.2		43.5	
Former	32.7		30.0		31.5		32.2		37.0	
Current	20.5		25.1		19.3		18.6		19.6	
Physical activity (%)										
Very low	2.9		2.8		2.0		2.2		4.8	
Low	13.4		10.5		10.4		13.3		19.7	
Normal	46.6		43.8		45.0		48.1		49.6	
High	27.1		29.3		31.0		27.7		20.0	
Very high	10.0		13.7		11.7		8.7		5.9	
	All (N=23,254)		WC change (Q1: ≤3.8%) (N=5,741)		WC change (Q2:3.8-9.1%) (N=5,787)		WC change (Q3:9.1-15.2%) (N=6,089)		WC change (Q4: >15.2%) (N=5,637)	
Deceased, N (%)	570		130		136		158		146	
Cancer deaths	68.4		65.4		69.9		67.1		71.2	
CVD deaths	13.9		17.7		14.7		14.6		8.9	
Other causes of death	17.7		16.9		15.4		18.4		19.9	

2 (4)

Age at follow-up	52	44-59	52	43-59	52	44-59	52	44-59	52	43-59
BMI (kg/m^2) at baseline	22.5	19.5-27.5	22.5	19.5-28	22.5	19.5-27	22.5	19.5-27	23	20-28
WC at baseline	75	68-88	78	69-92	75	68-87	75	67-86	74	67-86
BMI (kg/m^2) at follow-up	24	21-30	23	20-28	24	21-29	25	21-30	27	23-33
WC (cm) at follow-up	82	72-98	77	68-91	80	72-92	84	75-96	90	80-105
BMI change in percent	7.3	-2.3-20.0	2.0	-7.7-10.5	5.0	-2.0-13.2	9.4	2.0-18.2	15.6	4.8-28.6
WC change in percent	9.1	-1.0-21.4	0	-6.8-2.9	6.6	4.3-8.6	11.8	9.6-14.5	20.0	16.2-30.1
Absolute BMI change	1.5	-0.5-4.5	0.5	-2-2.5	1	-0.5-3	2	0.5-4	3.5	1-6.5
Absolute WC change	7	-1-16	0	-6-2	5	3-7	9	7-11	15	12-23
Education (%)										
≤ 10	25.5		25.5		24.0		25.4		27.2	
11-13	39.6		38.5		38.7		39.1		42.0	
≥ 14	34.9		36.0		37.3		35.5		30.8	
Alcohol drinking	5.3	1.6-15.2	5.1	1.5-14.7	5.4	1.6-15.2	5.4	1.6-15.0	5.1	1.6-15.9
Smoking status (%)										
Never	48.3		48.7		52.1		48.6		43.9	
Former	32.3		29.7		30.3		32.7		36.5	
Current	19.4		21.7		17.6		18.8		19.6	

Physical activity (%)					
Very low	2.7	2.3	1.6	2.6	4.5
Low	13.4	10.4	10.8	13.9	18.8
Normal	46.8	42.5	46.3	48.6	49.8
High	27.3	31.4	29.8	26.6	21.2
Very high	9.8	13.4	11.6	8.4	5.6

BMI = Body Mass Index
WC = waist circumference
Q1 = first quartile
Q2 = second quartile
Q3 = third quartile
Q4 = fourth quartile

Table 2: Crude and adjusted hazard ratios (HR) (95% confidence intervals) for overall mortality in relation to absolute and relative Body Mass Index and waist circumference changes in the WLH study.

	Deceased/total participants	Model 1[a]	Model 2[b]
Absolute changes			
BMI change			
Q1	197/6,877	1.25 (0.99-1.57)	1.19 (0.94-1.49)
Q2 *(ref)*	115/5,088	1.00	1.00
Q3	128/6,064	0.95 (0.74-1.23)	0.93 (0.72-1.19)
Q4	131/5,166	1.19 (0.92-1.52)	1.03 (0.80-1.33)
WC change			
Q1	121/5,270	0.99 (0.77-1.26)	0.91 (0.71-1.17)
Q2 *(ref)*	137/5,733	1.00	1.00
Q3	128/5,456	0.95 (0.75-1.21)	0.90 (0.70-1.14)
Q4	182/6,651	1.15 (0.92-1.44)	0.98 (0.78-1.23)
Relative changes			
BMI change			
Q1	244/ 8171	1.35 (1.10-1.64)	1.28 (1.04-1.56)
Q2 *(ref)*	161/ 7433	1.00	1.00
Q3	159/ 7601	0.98 (0.79-1.22)	0.96 (0.77-1.19)
Q4	198/ 7813	1.26 (1.02-1.55)	1.12 (0.90-1.38)
WC change			
Q1	131/5823	0.97 (0.76-1.23)	0.90 (0.71-1.15)
Q2 *(ref)*	135/5705	1.00	1.00
Q3	156/5961	1.09 (0.87-1.38)	1.02 (0.81-1.28)
Q4	148/5765	1.11 (0.88-1.40)	0.96 (0.76-1.22)

[a] Adjusted for time-dependent variables (age and time under study)

[b] Adjusted additionally for baseline anthropometric measures (BMI or WC) (continuous), smoking status (categorical), education (categorical), physical activity (categorical), and alcohol drinking (continuous). Analyses on WC are additionally adjusted for height (continuous).

BMI = Body Mass Index, WC = waist circumference, Q1 = first quartile, Q2 = second quartile, Q3 = third quartile, Q4 = fourth quartile

Table 3: Crude and adjusted hazard ratios (HR) (95% confidence intervals) for cause of death in relation to absolute and relative Body Mass Index and waist circumference changes in the WLH study.

	Cancer			Cardiovascular disease			Other cause of death		
	Deceased/ total participants	Model 1_a	Model 2_b	Deceased/ total participants	Model 1_a	Model 2_b	Deceased/ total participants	Model 1_a	Model 2_b
Absolute changes									
BMI change									
Q1	132/6,877	1.25 (0.94-1.65)	1.20 (0.90-1.59)	31/6,877	1.60 (0.85-3.01)	1.47 (0.78-2.77)	34/6,877	1.03 (0.61-1.74)	0.98 (0.58-1.65)
Q2 *(ref)*	77/5,088	1.00	1.00	14/5,088	1.00	1.00	24/5,088	1.00	1.00
Q3	90/6,064	1.00 (0.74-1.36)	0.98 (0.73-1.33)	14/6,064	0.86 (0.41-1.81)	0.82 (0.39-1.72)	24/6,064	0.86 (0.49-1.51)	0.82 (0.46-1.44)
Q4	89/5,166	1.20 (0.89-1.63)	1.10 (0.81-1.50)	21/5,166	1.57 (0.80-3.09)	1.22 (0.62-2.43)	21/5,166	0.92 (0.51-1.64)	0.71 (0.39-1.28)
WC change									
Q1	78/5,270	0.91 (0.67-1.22)	0.86 (0.64-1.16)	20/5,270	1.06 (0.57-1.95)	0.91 (0.49-1.68)	23/5,270	1.29 (0.71-2.35)	1.16 (0.63-2.12)
Q2 *(ref)*	96/5,733	1.00	1.00	21/5,733	1.00	1.00	20/5,733	1.00	1.00
Q3	86/5,456	0.91 (0.68-1.22)	0.88 (0.66-1.18)	21/5,456	1.01 (0.55-1.86)	0.92 (0.50-1.69)	21/5,456	1.07 (0.58-1.98)	0.96 (0.52-1.78)
Q4	127/6,651	1.15 (0.88-1.49)	1.04 (0.79-1.36)	17/6,651	0.70 (0.37-1.32)	0.53 (0.28-1.01)	38/6,651	1.65 (0.96-2.83)	1.24 (0.72-2.16)
Relative changes									
BMI change									
Q1	163/8,171	1.36 (1.06-1.73)	1.30 (1.02-1.66)	37/8,171	1.36 (0.81-2.27)	1.19 (0.70-1.99)	44/8,171	1.30 (0.82-2.07)	1.26 (0.79-2.01)
Q2 *(ref)*	107/7,433	1.00	1.00	24/7,433	1.00	1.00	30/7,433	1.00	1.00
Q3	106/7,601	0.98 (0.75-1.28)	0.97 (0.74-1.27)	15/7,601	0.63 (0.33-1.19)	0.59 (0.31-1.12)	38/7,601	1.26 (0.78-2.04)	1.20 (0.74-1.94)
Q4	139/7,813	1.32 (1.03-1.70)	1.23 (0.96-1.59)	28/7,813	1.22 (0.71-2.11)	0.98 (0.57-1.71)	31/7,813	1.07 (0.65-1.76)	0.85 (0.51-1.41)
WC change									

Q1	86/5,823	0.92 (0.68-1.23)	0.87 (0.65-1.17)	23/5,823	1.15 (0.63-2.09)	1.00 (0.54-1.83)	22/5,823	1.05 (0.58-1.91)	0.93 (0.51-1.71)
Q2 *(ref)*	94/5,705	1.00	1.00	20/5,705	1.00	1.00	21/5,705	1.00	1.00
Q3	105/5,961	1.06 (0.80-1.40)	1.01 (0.76-1.33)	22/5,961	1.04 (0.57-1.91)	0.92 (0.50-1.68)	29/5,961	1.30 (0.74-2.28)	1.15 (0.66-2.02)
Q4	105/5,765	1.13 (0.86-1.50)	1.02 (0.77-1.26)	14/5,765	0.71 (0.36-1.41)	0.56 (0.28-1.11)	29/5,765	1.40 (0.80-2.45)	1.11 (0.63-1.96)

[a] Adjusted for time-dependent variables (age and time under study)

[b] Adjusted additionally for baseline anthropometric measure (BMI or WC) (continuous), smoking status (categorical), education (categorical), physical activity (categorical), and alcohol drinking (continuous). Analyses on waist circumference are additionally adjusted for height (continuous).

BMI = Body Mass Index, WC = waist circumference, Q1 = first quartile, Q2 = second quartile, Q3 = third quartile, Q4 = fourth quartile