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# Abdominal obesity increases the risk of hip fracture. A population-based study of 43,000 women and men aged 60-79 years followed for 8 years. Cohort of Norway

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# Abstract

**Objectives** 

To investigate the association of waist circumference, hip circumference, waist-hip ratio, and body mass index with incident hip fracture.

<u>Design</u>

Prospective cohort study.

Setting

Cohort of Norway (CONOR), a population-based cohort established during 1994-2003. <u>Subjects</u>

19,918 women and 23,061 men aged 60-79 years at baseline, followed for a median of 8 years.

**Exposures** 

Body mass index, waist and hip circumference, and waist-hip ratio.

Main outcome measures

Hip fractures (n=1,498 in women, n=889 in men) identified from electronic discharge registers from all general hospitals in Norway between 1994 and 2008. Height, weight, waist, and hip circumferences were measured at baseline using standard procedures. Information on covariates was collected by questionnaires.

**Results** 

The risk of hip fracture decreased with increasing body mass index, plateauing in obese men. However, higher waist circumference and higher waist-hip ratio were associated with an increased risk of hip fracture after adjustment for body mass index and other potential confounders. Women in the highest tertile of waist circumference had an 86% (95% CI: 51-129%) higher risk of hip fracture compared to the lowest, with a corresponding increased risk in men of 100% (95% CI 53-161%). Lower body mass index combined with abdominal obesity increased the risk of hip fracture considerably, particularly in men. Conclusion

Abdominal obesity was associated with an increased risk of hip fracture when body mass index was taken into account. In view of the increasing prevalence of obesity and the number of older people suffering osteoporotic fractures in Western societies, our findings have important clinical and public health implications.

Key words: Hip Fractures, Abdominal Obesity, Body Mass Index, Waist-Hip Ratio, Waist Circumference

Running head: Obesity and hip fracture

# Abbreviations:

BMI=Body Mass Index WHR=Waist-Hip Ratio WC=Waist Circumference HC=Hip Circumference Fx=Fracture CI=Confidence Interval CONOR=Cohort of Norway NOREPOS=Norwegian Epidemiologic Osteoporosis Studies NORHip=Hip Fracture Database administered by NOREPOS

#### Introduction

Osteoporotic fractures and obesity are highly prevalent among older people in Western societies [1, 2] and are associated with increased morbidity and mortality [2-8]. Both conditions are therefore a major public health concern.

Low body mass index (BMI) is an established risk factor for hip fracture as shown in reviews and meta-analyses [3, 9-13]. Further, several studies have found an inverse association between body size/body fat mass and osteoporotic fractures [14-17]. However, the view that being overweight and obesity are associated with a reduced risk of hip fracture has recently been challenged [18-21]. It has been proposed that adipose tissue may produce harmful effects that counteract the protective effects of weight-bearing on bone [21-23]. Measures of obesity have usually included BMI, percentage of total body fat, or skinfold thickness. However, visceral abdominal fat, in contrast to subcutaneous fat, may negatively impact bone structure and strength [24].

A few prospective studies have investigated the relationship between anthropometric measurements of overall and abdominal obesity and the risk of hip fracture, with inconsistent results [4, 25-27]. Some studies had limited statistical power, whereas others only discussed self-reported information on exposure and/or hip fracture. Thus, the question as to whether abdominal obesity has an adverse effect on hip fracture remains unanswered. The purpose of this study is to examine, in a population-based cohort of 43,000 women and men aged 60-79 years, the relationship between waist circumference (WC), hip circumference (HC), waist-hip ratio (WHR), and BMI to incident hip fracture.

#### **Materials and Methods**

#### **Cohort of Norway**

The Cohort of Norway (CONOR) is a collaboration between epidemiological centers at the four Norwegian University Medical Faculties and the Norwegian Institute of Public Health [28]. Data from 10 regional cohort studies are compiled in a national database. Different age groups were invited to participate in the different studies. The first CONOR study did not measure waist and hip circumference and is therefore not included. Among the remainder, 76,400 individuals in the age 60-79 range were invited, of whom 57% participated. In all CONOR studies the data collection followed standard procedures and measurements were carried out by trained personnel according to a common protocol [28]. All studies used 50 common questions regarding lifestyle and socioeconomic factors, as well as comorbid conditions. At the survey stations, anthropometric variables were measured (www.fhi.no/conor - http://www.fhi.no/dokumenter/7f4211f9df.doc).

The study population included in this paper was restricted to women and men aged 60-79 years with complete information on height, weight, waist and hip circumferences, marital status, degree of urbanization, study region, and daily smoking, i.e. a total of 19,918 women and 23,061 men. Only 1.4% had missing information on these variables. The mean age at study enrolment was 69.5 years (Table 1).

Data on weight and height from tuberculosis screenings carried out in Norway during 1963-1989 [29] were available in 14,903 of women and 17,960 of men participating in the CONOR studies (60-79 years). The mean (+/- standard deviation) period between the two examinations was 29.3 ( $\pm$ 2.7) years. For additional analyses, these measurements were included in order to assess the possible confounding effect of height loss on the association between abdominal obesity and hip fracture.

#### *Exposure variables*

WC and HC (both in cm) and WHR were all used as continuous variables and divided in gender specific tertiles.

BMI was defined as weight (kg) divided by height (m<sup>2</sup>) and was used both as a continuous variable and divided among the four groups (<22, 22-24, 25-29, 30+) within each gender. A BMI cutoff of less than 22 was chosen because there were few individuals with a BMI of less than 18.5.

## Covariates

Potential confounding factors were: *age* (years), *height* (cm), *smoking* (current daily vs. former/never), *physical activity* (based on two questions regarding number of hours with light and vigorous physical activity during an average week (four categories each, from 0 hours to 3 or more hours per week) summarized (range 1-8), used as a continuous variable and dichotomized into no or little physical activity (score 1-2) vs. more, *consumption of alcohol* (grouped in four (from 1=never to 4=two times a week or more often), used as a continuous variable and dichotomized into drinking two times a week or more vs. less frequently), *length of education* (years), *marital status* (married vs. all others), and use of *post-menopausal hormone therapy* in women (current vs. former/never). In addition we included *place of residence* (divided according to degree of urbanization) and *study region* [28].

In addition, the following questions were used in sensitivity analyses: 1) have you ever broken (fractured) your 1) hip or 2) wrist/forearm (yes/no). If yes, indicate the age at the last occasion. 2) Do you have/have you had osteoporosis (yes/no). Respondents were asked to report the names of all prescribed medications used, and names were coded according to the Anatomical Therapeutic Chemical Classification (ATC) system [30]. Information about use of glucocorticosteroids and medications for osteoporosis were employed in sensitivity analyses.

Based on information from previous tuberculosis screenings, the variable *height loss* was constructed for those individuals with two height measurements. We also used an alternative BMI variable based on weights measured in CONOR and old height measures from tuberculosis screening (n=32,863).

Dates of death, emigration, age, gender, place of residence, marital status, and country of birth were obtained from the National Population Register. Less than 0.5% of participants, of whom two suffered an incident hip fracture during follow-up, were born in Non-Western countries. Thus, country of birth was not accounted for in the analyses.

#### Outcomes

The NORHip database (NOREPOS Hip Fracture Database, administered by the Norwegian Epidemiologic Osteoporosis Studies) contains data on all hip fractures treated in Norwegian hospitals between 1994 and 2008, retrieved from electronic discharge registers [31]. Fractures were identified according to the International Classification of Diseases, Ninth (ICD-9): 820-820.9 and Tenth (ICD-10) Revisions: S72.0-S72.2 including cervical, trochanteric, and sub-trochanteric hip fractures. The validity of the NORHip database was assessed by comparisons to validated hip fracture registries in the cities of Oslo and Tromsø (combined Cohen's kappa 0.95)[31]. These registries have been validated against patient records and X-rays. A detailed description of the quality assurance, classification, and validation of NORHip, is published on: www.norepos.no/research/documentation. In the current study, the first hip fracture diagnosed after participation in the regional CONOR study was used.

## Statistical analyses

Comparisons between background characteristics across tertiles of WHR were done by chi-squared tests for categorical and F-tests for continuous variables. Age-adjusted partial correlation analyses of BMI to WHR and WC were performed. Time from participation to the first hip fracture or censoring (emigration, death, or end of follow up December 31, 2008), was computed. Cox proportional hazards regression with restricted cubic splines of WHR and WC were performed to examine hip fracture hazard ratios (HR) across their distributions, with five knots. HRs with 95% confidence intervals (CI) for hip fracture were also estimated in tertiles of WHR, WC, and HC, and with WHR (per 0.1 units), and WC or HC (per 10 cm) entered as continuous variables. Adjustments were made for age, marital status, height, smoking, degree of urbanization, and study region. Marital status was included because it was associated with hip fracture, BMI, WHR, and waist circumference (p<0.01). Adjustment for BMI was included as restricted cubic splines with five knots due to the non-linear association with hip fracture.

HRs for hip fracture at combined levels of WHR and BMI were *estimated* from ageadjusted Cox proportional regression models where BMI was entered as restricted cubic splines and WHR as a continuous variable.

Interaction terms were entered to test whether WHR and WC interacted with BMI, age, and gender on hip fracture risk. BMI was entered as restricted cubic splines, and other variables as continuous or dichotomous variables.

For some participants, data were incomplete for education, physical activity, alcohol consumption, and post-menopausal hormone therapy. The influence of these covariates were analysed separately in additional complete-case analyses.

Sensitivity analyses included: a) adjustment for weight as a continuous variable instead of BMI, b) adjustment for height loss and a recalculated BMI based on height measured at an earlier (tuberculosis screening) visit, and c) excluding participants who reported previous hip or forearm fracture at age 50 or later, those who reported osteoporosis, and those using anti-osteoporosis drugs or corticosteroids.

To evaluate possible co-linearity between WHR, WC, and BMI, we used linear regression analyses and calculated the variance inflation factors (VIF) for the predictors suspected to cause co-linearity (VIF= $1/(1-R^2)$ ).

Log minus log curves confirmed that the assumption of proportionality in the Cox model was present for WHR, HC, and WC.

Data were analysed using Stata version 11.1 and SPSS version 17.0 statistical software. A p-value of less than 0.05 was considered statistically significant.

## **Ethical considerations**

The Cohort of Norway and the linkage between various data sources were approved by the Regional Committee for Medical and Health Research Ethics (South-East) and the Norwegian Data Protection Authority. All participants gave their written informed consent. This study was conducted in full accordance with the Declaration of Helsinki of the World Medical Association.

## Results

During a median follow-up period of 8.1 (range 0-13.4) years, 1,498 women and 889 men suffered a hip fracture. In both genders, an inverse association was found between education and WHR, while the percentage with no/little physical activity increased with increasing WHR (table 1). All tests for differences across WHR tertiles were statistically

significant, except for the association between WHR and daily smoking in women, and WHR and alcohol consumption in men.

## BMI and hip fracture risk

In women, there was an inverse linear association between BMI and risk of hip fracture across the whole distribution of BMI, whereas the hip fracture risk levelled off in men with a BMI just below 30. Compared to women with a BMI of less than 22 kg/m<sup>2</sup>, the HR for hip fracture was 0.76 (95% CI 0.65 to 0.89) in women with a BMI between 22 and 24.9 kg/m<sup>2</sup>, 0.56 (95% CI 0.48 to 0.65) in women with a BMI between 25 and 29 kg/m<sup>2</sup>, and 0.42 (95% CI 0.35 to 0.51) in women with a BMI greater than or equal to 30 kg/m<sup>2</sup>, adjusted for age, height, smoking, marital status, urbanization, and study region. In men, the corresponding HRs for hip fracture were 0.62 (95% CI 0.50 to 0.77), 0.49 (95% CI 0.40 to 0.60), and 0.49 (95% CI 0.37 to 0.63), respectively. The prevalence of obesity (BMI  $\geq$  30) was 24.9% and 16.1% in women and men, respectively.

#### WHR, WC, and HC as predictors of hip fracture risk

No significant association was found between WHR and hip fracture in either gender after adjustments for covariates (Table 2). However, with an additional adjustment for BMI, women in the highest compared to the lowest tertile of WHR had a 49% (95% CI 29% to 72%) increased risk of hip fracture, while the corresponding increase in men was 41% (95% CI 16% to 71%). There was a clear linear increase in the risk of hip fracture with increasing WHR in both genders after adjustment for BMI (Table 2, Figure 1). When studying HC alone as an explanatory variable, the risk of hip fracture decreased with increasing HC in both genders, but the results were not statistically significant after adjustment for BMI. Additional adjustment for waist circumference did not change the results. HRs for hip fractures in the highest compared to the lowest tertile of HC were 0.94 (95% CI 0.76-1.17) in women and 0.97 (95% CI 0.76-1.24) in men, after adjustment for BMI, waist circumference, and other covariates.

WC as an explanatory variable was also inversely related to hip fracture in the initial analysis (Table 3). However, after adjustment for BMI, there was an 86% increased risk of hip fracture in women in the highest compared to the lowest tertile of WC, and a corresponding doubled risk in men. Additional adjustment for hip circumference did not change the results (Table 3, Figure 2).

In the subset with complete information on education, physical activity, alcohol consumption, and use of hormone therapy (n=11,036 women, 19,878 men), additional adjustments for these confounders had minimal impact on the estimates (data not shown).

#### Combined effect of BMI and abdominal obesity on risk of hip fracture

The age-adjusted correlation coefficients between BMI and WHR were 0.44 and 0.57 in women and men, respectively, whereas the corresponding correlation coefficients between BMI and WC were 0.85 and 0.83. Due to the high correlation between WC and BMI, tertiles of WHR were used as the measure of abdominal obesity in this combined analysis. Estimated risks of hip fracture increased by increasing WHR at any level of BMI (Figure 3). However, as expected, fracture risk decreased with increasing BMI in both genders irrespective of level of WHR.

In women variance inflation factors (VIF) for WHR and WC on BMI were 1.24 and 3.57, respectively, whereas the corresponding VIFs in men were 1.45 and 3.13.

No statistically significant interaction was found between WHR and BMI on the risk of hip fracture, nor any significant interaction between WC and BMI. Age did not interact

with WHR or WC. When combining women and men, there was no interaction between gender, WHR, or WC with hip fracture.

### Sensitivity analyses

Replacing BMI with weight produced similar results as those presented in Tables 2 and 3. Further, additional adjustment for height loss or a recalculated BMI value using previous body height did not substantially influence the results. In the analysis excluding participants with a self-reported history of fracture of the forearm or hip after age 50, those who reported having osteoporosis, using glucocorticosteroids or anti-osteoporosis drugs (n=5,508; 22.5% women and 5.7% men), the results were also similar.

## Discussion

Abdominal obesity measured by WHR and WC increased the risk of hip fracture when the effect of BMI was accounted for. Adjustment for multiple confounders did not alter the results. No association was found between HC and fracture when the effect of BMI was taken into account. The risk of hip fracture decreased with increasing BMI, but in men, the decline in hip fracture risk with increasing BMI plateaued in subjects with a BMI just below 30 kg/m<sup>2</sup>. Based on the estimated tertile means of WHR, a greater than two-fold risk of hip fracture was estimated in women and a four-fold risk in men at the combination of high waist-hip ratio and a BMI of 23, compared to a low waist-hip ratio and a BMI of 30.

## Strengths and weaknesses of the study

In this population-based study, the large number of participants and fractures enabled detailed analyses on the association between anthropometric parameters and hip fracture, in addition to sensitivity analyses to verify the findings. In all participants, weight, height, and waist and hip circumference were measured in a standardized way. Waist-hip ratio is associated with the amount of visceral adipose tissue, as measured by computed tomography and magnetic resonance imaging [32], and is a widely used index in epidemiologic studies. Both WHR and WC are considered valid indicators of abdominal adiposity, and they both seem to be equally good or even better predictors of total mortality compared to BMI [4, 8, 33]. BMI is a measure of total body mass, including fat and lean mass (muscle, water, internal organs and bone). Physically fit subjects may have a relatively high BMI, due to a greater muscle mass. Although grouping people by BMI may lead to misclassification of total body fat mass in some individuals, this is unlikely to explain our results in persons aged 60-79 years.

Height loss might influence BMI, WC, and WHR. Thus, height loss could potentially bias our results, as it could be a consequence of vertebral fractures and thus indicate osteoporosis and an increased risk of hip fracture. However, neither adjustments for height loss nor use of a recalculated BMI based on height measured when the subjects were much younger (on average, 29 years earlier) altered the results. Also, excluding participants with self-reported previous hip or forearm fracture, those with self-reported osteoporosis, and those using anti-osteoporosis drugs or corticosteroids, did not change the results.

Our findings are limited to older Caucasian women and men and may not be generalized to populations of other ages or ethnic backgrounds.

#### Strengths and weaknesses in relation to other studies

The inverse relationship between BMI and hip fracture is consistent with conclusions in published reviews and meta-analyses [3, 9-11, 13]. A few investigators have, however, concluded that obesity may not be protective against osteoporotic fractures [18, 19], or that

very high BMI even increases the risk of hip fracture [12, 19]. Evidence of a harmful effect of very high BMI was not found in our study, but the confidence intervals were wide in this BMI range. However, in men in the highest tertile of BMI, there was no further protective effect of increased BMI compared to men in the second tertile. This might be due to the higher WHR in men than in women. After controlling for WHR, there was also a downward trend between BMI and fracture in men (Figure 3).

Because we had information on waist and hip circumferences, we were able to explore whether the protective effect of high BMI could be attributable to a "padding" effect of adipose tissue on the hip, absorbing the energy in a fall. Surprisingly, hip circumference had no independent effect beyond that of BMI. Moreover, waist circumference had the opposite effect after adjustment for BMI (i.e., a higher waist circumference was associated with an increased risk of hip fracture).

Fat in the abdominal region may influence bone independently of the loading effect of BMI [21]. Only a few prospective studies have investigated anthropometric measures of abdominal obesity as a risk factor for hip fracture [4, 25-27]. A prospective study including 56 self-reported hip fractures in men aged 40-75 years showed no statistically significant trend across WHR or WC, but an almost fourfold increased risk of hip fracture in the highest compared to the lowest WHR quintile after adjustment for BMI [25].

In the Iowa Women's Health Study (55-69 years at baseline), all anthropometric measures and fractures were self-reported. Corresponding to our findings, the risk of hip fracture increased with increasing WHR and WC after adjustment for BMI [4, 26]. However, no association was found between WHR and hip fracture after adjustment for BMI in the European multicenter EPIC cohort [27], in which 261 hip fractures were identified during 8 years of follow-up.

Some studies have measured abdominal fat by DXA. In a nested case-control study with 89 hip fractures, no statistically significant association was found between abdominal fat and hip fracture, after adjustment for weight [34].

## Possible explanations, implications and unanswered questions

Inconsistent results between studies of obesity and fractures may be due to differences in study populations, type of fractures studied [3, 18, 35-38], study design, and available covariates. Distribution of body fat, the ratio between fat mass and lean mass, and the way obesity was measured in different studies may also explain some of the divergent results [11, 16].

It has been proposed [39] that a positive association between abdominal obesity and hip fractures could be due to inappropriate statistical handling of highly intercorrelated variables. Since both the correlation coefficients and the VIFs between BMI and WC were higher than the corresponding results for WHR, we used WHR, with acceptable correlation coefficients and VIFs, in the final analyses (Figure 3). However, the results from the Cox regression analyses were only modestly different for WHR and WC (Tables 2 and 3). Thus, co-linearity does not seem to bias our results.

Several studies have explored clinical, epidemiological and pathophysiologic links between obesity and osteoporosis [21, 39-44]. Possible mechanisms include the effect of mechanical loading, the "padding" effect of fat mass, the association of fat mass with the secretion of bone active hormones from pancreatic beta-cells, and the secretion of bone active hormones and pro-inflammatory cytokines from adipocytes [21, 40, 41]. The relationship between fat and bone is complex [16, 21, 39, 40, 44, 45].

Metabolic syndrome and insulin resistance has also been related to bone [46-48] and a recent study suggests that hyperinsulinemia is independently associated with lower bone strength [46].

Our findings suggest that a high BMI is protective, whereas high WHR and WC are harmful, after adjustment for BMI. Perhaps fat mass in different body locations may affect bone differently [24, 49]. Visceral fat has been found to be inversely related to total body and regional BMD in adolescents and adults [50, 51]. In a study of bone structure and strength, subcutaneous fat appeared to be beneficial to bone, whereas visceral fat had the opposite effect [24]. These findings are consistent with those of a Korean study, suggesting a negative correlation between abdominal obesity (measured by WC) and bone mineral content, independent of total fat mass [45]. Findings from other studies also suggest an inverse association between WHR or WC and BMD, particularly when the effect of body weight has been taken into account [21, 22, 47-49].

Another possible explanation for our findings could be that fat mass in general is detrimental to bone [43], but that its unfavorable effect may be counterbalanced by a concomitant increase in mechanical loading due to higher body weight, resulting in the inverse relationship between BMI and hip fracture risk [3, 9, 13]. Based on this hypothesis, the loading effect of BMI and weight would be dominating as predictors of hip fracture, compared to WHR and WC. However, this is not supported by the common finding of a protective effect of high BMI on forearm fracture [3, 18, 35, 37], as the loading effect of body weight on the distal forearm is limited.

A third possible mechanism for an increased fracture risk with increasing WHR and WC after adjusting for BMI might be mechanical instability and impaired balance induced by an increased body size in the abdominal region, leading to a fall [52]. It has been suggested that carrying excess weight on the torso rather than on the hips increases the risk of falls that result in hip fracture, perhaps due to a higher center of gravity [26]. Also the direction and impact of the fall, and factors that attenuate a fall – e.g. the ability to stop oneself with one's hands while falling, could influence the consequences of a fall [53]. Unfortunately, we do not have any information about injury mechanism in the present study.

## Conclusion

In this large prospective study, high BMI was protective of hip fracture. However, at any given BMI, greater abdominal obesity measured by waist circumference or waist-hip ratio increased the risk of hip fracture considerably. Hip circumference did not influence these results. A more than twofold risk of hip fracture was estimated in women and a fourfold risk in men, who had a combination of a high waist-hip ratio and a BMI of 23, compared to the combination of a low waist-hip ratio and a BMI of 30. One simple explanation could be that decreased hip fracture risk with increasing BMI is due to higher mechanical loading and "padding" associated with general adiposity, whereas a high waist circumference might be linked to unfavorable humoral factors. Our findings have potentially important clinical and public health implications in view of the rising prevalence of obesity in many populations around the world.

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# Contributors

AJS: conception and design, analyses and interpretation of data, drafting, critically revising the paper, final approval of the version to be published

KH: conception and design, analyses and interpretation of data, critically revising the paper, final approval of the version to be published

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HEM: conception and design, analyses and interpretation of data, critically revising the paper, final approval of the version to be published

All authors had full access to all data (including statistical reports and tables) in the study and take responsibility for the integrity of the data and the accuracy of the data analysis. AJS is the guarantor.

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# **Disclosure statement**

All authors have completed the ICMJE uniform disclosure form at <u>www.icmje.org/coidisclosure.pdf</u> (available on request from the corresponding author) and declare: no support from any organization for the submitted work; no financial relationships with any organization that might have an interest in the submitted work in the previous three years; no other relationships or activities that could appear to have influenced the submitted work.

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## **Figure legends**

**Figure 1**. Hazard ratios (solid lines) with 95% confidence intervals (dashed lines) for hip fracture across the distribution of waist-hip ratio (WHR) in women and men aged 60-79 years, adjusted for age and body mass index\* (1-99 percentiles included) \*Body mass index is included as restricted splines. WHR means as reference, women=0.83, men=0.93.

**Figure 2**. Hazard ratios (solid lines) with 95% confidence intervals (dashed lines) for hip fracture across the distribution of waist circumference (WC) in women and men aged 60-79 years, adjusted for age, hip circumference, and body mass index\* (1-99 percentiles included) \* Body mass index is included as restricted splines. WC means as reference, women=85 cm, men=95 cm.

**Figure 3.** *Predicted* hazard ratios for hip fracture in women and men at different levels of body mass index (BMI) and waist-hip ratio (WHR)\*

\*Reference category in women BMI=30 kg/m<sup>2</sup> and WHR 0.76 (tertile mean) and in men BMI=30 kg/m<sup>2</sup> and WHR 0.87 (tertile mean)

Estimated from Cox proportional regression models entering BMI as restricted cubic splines and WHR and age as continuous variables. The WHR values presented are gender specific tertile means.

	WHR Women			WHR Men				
	Low	Middle	High	Total	Low	Middle	High	Total
	<u>&lt;</u> 0.79	>0.79-	>0.85		<u>&lt;</u> 0.90	>0.90-	>0.96	
		0.85				0.96		
Number of participants	6,660	6,626	6,632	19,918	7,615	7,742	7,704	23,061
Age (years)	68.6	69.6	70.0	69.4	69.1	69.5	69.8	69.5
Height (cm)	161.4	160.7	160.2	160.8	174.6	174.9	174.7	174.7
Waist-hip ratio (cm/cm)	0.76	0.82	0.90	0.83	0.87	0.93	1.01	0.93
Body mass index (kg/m <sup>2</sup> )	24.8	27.4	29.6	27.3	24.6	26.7	28.8	26.7
Education (years) <sup>1</sup>	10.3	9.8	9.3	9.8	11.2	10.9	10.5	10.9
Not married $(\%)^2$	41.1	43.1	45.6	43.3	21.5	22.8	26.6	23.6
Living in city ( $\geq$ 20,000	47.8	44.0	49.6	47.1	56.2	58.9	61.1	58.7
inhabitants) (%)								
Daily smoking (%)	20.8	19.3	19.8	20.0	25.5	22.5	23.2	23.7
No/ little physical activity $(\%)^{1}$	10.9	14.1	18.7	14.5	6.9	8.9	12.0	9.3
Alcohol consumption $\geq 2$ times				7.6				
per week $(\%)^1$	9.2	7.0	6.4		20.5	20.7	21.4	20.9
Current use of post-menopausal	20.8	17.1	15.5	17.9				
hormone therapy $(\%)^1$								

Table 1. Baseline characteristics according to tertiles of waist-hip ratio (WHR) in women and men 60-79 years (Cohort of Norway).<sup>1</sup>

<sup>1</sup>Means for continuous variables, proportions for categorical variables. Number of participants with available data: Age, height, waisthip ratio, BMI, degree of urbanization and smoking: 19,918 women, 23,061 men; Education: 18,155 women, 21,650 men; No/little physical activity: 16,640 women, 21,283 men; Alcohol: 18,597 women, 22,010 men; Post-menopausal hormone therapy: 13,591 women.

<sup>2</sup> Not married=single, divorced, separated, widowed

p-value: Test for homogeneity (Pearson 2-sided chi-squared test for categorical variables, F-test (ANOVA) for continuous variables Women: All tests for differences across WHR tertiles had p-values <0.001, except daily smoking (p=0.082)

Men: All tests for differences across WHR tertiles had p-values <0.001, except height (p=0.034) and alcohol consumption (p=0.341).

# Table 2.

Incidence per 10,000 person years and hazard ratio (HR) with 95% confidence interval (CI) of hip fracture in women and men aged 60-79 years according to waist-hip ratio and adjusted for covariates and body mass index (BMI) (Cohort of Norway).

	Person years pyr)	Crude incidence of hip fracture	Model <sup>1</sup> HR (95% CI)	Model <sup>2</sup> HR (95% CI)	Model <sup>3</sup> HR (95% CI)
		per 10,000 pyr			
Waist-hip ratio <sup>+</sup>					
Women (n=19,918)					
Lowest tertile	59820	78.6	1.0	1.0	1.0
Middle tertile	59062	92.4	1.06 (0.94-1.20)	1.08 (0.95-1.22)	1.34 (1.18-1.53)
Highest tertile	55026	87.6	1.01 (0.89-1.14)	1.03 (0.91-1.17)	1.49 (1.29-1.72)
Per 0.1 unit increase	173908	86.1	0.98 (0.90-1.06)	0.99 (0.92-1.07)	1.25 (1.14-1.36)
<b>Men</b> (n=23,061)					
Lowest tertile	64821	46.3	1.0	1.0	1.0
Middle tertile	64646	48.0	0.98 (0.84-1.15)	0.98 (0.83-1.15)	1.25 (1.06-1.49)
Highest tertile	59486	46.9	0.98 (0.83-1.16)	0.96 (0.81-1.13)	1.41 (1.16-1.71)
Per 0.1 unit increase	188953	47.0	1.03 (0.92-1.14)	1.01 (0.91-1.13)	1.38 (1.22-1.56)

<sup>1</sup> Model adjusted for age
 <sup>2</sup> Model 1 adjusted for marital status, height, smoking, degree of urbanization, study region
 <sup>3</sup> Model 2 adjusted for BMI (entered as cubic splines)
 <sup>4</sup> Tertile limits: Women: 0.79 and 0.85; Men: 0.90 and 0.96

## Table 3

Incidence per 10,000 person years and hazard ratio (HR) with 95% confidence interval (CI) of hip fracture in women and men aged 60-79 years according to waist circumference adjusted for covariates, body mass index (BMI), and hip circumference (Cohort of Norway).

	Person years (pyr)	Crude incidence of hip fracture per 10,000 pyr	Model <sup>1</sup> HR (95% CI)	Model <sup>2</sup> HR (95% CI)	Model <sup>3</sup> HR (95% CI)	Model <sup>4</sup> HR (95% CI)
Waist circumference <sup>5</sup>						
<b>Women</b> ((n=19,918)						
Lowest tertile	64186	94.4	1.0	1.0	1.0	1.0
Middle tertile	58467	83.6	0.79 (0.71-0.89)	0.82 (0.73-0.92)	1.29 (1.11-1.50)	1.28 (1.10-1.49)
Highest tertile	51254	78.6	0.73 (0.64-0.83)	0.77 (0.68-0.88)	1.86 (1.51-2.29)	1.84 (1.49-2.27)
Per 10 cm increase	173908	86.1	0.86 (0.82-0.90)	0.87 (0.83-0.92)	1.32 (1.21-1.45)	1.32 (1.20-1.44)
<b>Men</b> (n=23,061)						
Lowest tertile	65069	50.9	1.0	1.0	1.0	1.0
Middle tertile	66980	43.3	0.81 (0.69-0.95)	0.82 (0.70-0.96)	1.34 (1.10-1.64)	1.32 (1.08-1.62)
Highest tertile	56904	47.1	0.89 (0.76-1.05)	0.87 (0.74-1.03)	2.00 (1.53-2.61)	1.94 (1.48-2.54)
Per 10 cm increase	188953	47.0	0.94 (0.87-1.00)	0.93 (0.87-1.00)	1.57 (1.38-1.80)	1.56 (1.36-1.78)

<sup>1</sup> Model adjusted for age
<sup>2</sup> Model 1 adjusted for marital status, height, smoking, degree of urbanization, study region
<sup>3</sup> Model 2 adjusted for BMI (entered as cubic splines)
<sup>4</sup> Model 3 adjusted for hip circumference
<sup>5</sup> Tertile limits: Women: 80 cm and 90 cm; Men: 90 cm and 99 cm











