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Obesity is Not Protective Against Fracture in Postmenopausal Women: GLOW

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Abstract

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Contributors: JEC drafted the manuscript. JF analyzed the data. NBW, RC, CC, SB, SG, JP, SS, ADP, RL, KGS, JCN, JDA, SA, AZL, CR, and PS were responsible for the acquisition of the data. All authors conceived and designed the study, critically revised the draft for important intellectual content, and gave final approval of the version to be published. JEC is a guarantor for the study. All authors had full access to all of the data (including statistical reports and tables) in the study and can take responsibility for the integrity of the data and the accuracy of the data analysis. Sophie Rushton-Smith coordinated revisions and provided editorial assistance including editing, checking content and language, formatting and referencing.

OBJECTIVE—To investigate the prevalence and incidence of clinical fractures in obese, postmenopausal women enrolled in the Global Longitudinal study of Osteoporosis in Women (GLOW).

METHODS—This was a multinational, prospective, observational, population-based study carried out by 723 physician practices at 17 sites in 10 countries. A total of 60,393 women aged ≥55 years were included. Data were collected using self-administered questionnaires that covered domains that included patient characteristics, fracture history, risk factors for fracture, and anti-osteoporosis medications.

RESULTS—Body mass index (BMI) and fracture history were available at baseline, 1 and 2 years in 44,534 women, 23.4% of whom were obese (BMI ≥30 kg/m^2). Fracture prevalence in obese women at baseline was 222 per 1,000 and incidence at 2 years was 61.7 per 1,000, similar to rates in non-obese women (227 and 66.0 per 1,000, respectively). Fractures in obese women accounted for 23% and 22% of all previous and incident fractures, respectively. The risk of incident ankle and upper leg fractures was significantly higher in obese than in non-obese women whilst the risk of wrist fracture was significantly lower. Obese women with fracture were more likely to have experienced early menopause and to report two or more falls in the past year. Self-reported asthma, emphysema, and type 1 diabetes were all significantly more common in obese than non-obese women with incident fracture. At 2 years, 27% of obese women with incident fracture were receiving bone-protective therapy, compared with 41% of non-obese and 57% of underweight women.

CONCLUSIONS—Our results demonstrate that obesity is not protective against fracture in postmenopausal women and is associated with increased risk of ankle and upper leg fractures. These findings have major public health implications in view of the rapidly rising incidence of obesity. Further studies are required to establish the pathogenesis of fractures in the obese population and to develop effective preventive strategies.

Keywords

Fractures; Obesity; Postmenopausal; Osteoporosis

Fractures are a major cause of morbidity and mortality in postmenopausal women, and incur huge economic costs for health services. One in three women aged ≥50 years will sustain ≥1 fracture during her remaining lifetime, with an estimated annual cost of €30 billion in Europe and $17 billion in the USA.[1–3] The social and economic burden resulting from fractures is predicted to increase at least two-fold in the next few decades as a result of demographic changes in the population.[4]

Low body mass index (BMI) is an important risk factor for fractures in postmenopausal women—an effect mediated predominantly, although not exclusively, through low bone mineral density (BMD).[5] In contrast, obesity is widely believed to be protective against fracture because of higher BMD and reduced impact of falls as a result of increased soft-tissue padding.[6, 7] However, in a recent audit of postmenopausal women presenting to a Fracture Liaison Clinic, 27.7% of women presenting with a fracture had a BMI ≥30 kg/m^2.[8] This suggests that fractures in obese women may contribute significantly to the overall fracture burden in the postmenopausal population.

The Global Longitudinal study of Osteoporosis in Women—a prospective, multinational, observational, population-based study of postmenopausal women—provides an ideal setting in which to investigate the epidemiology and pathogenesis of fractures in obese postmenopausal women.[9] The aim of this study was to document the prevalence of clinical fractures in obese women in the GLOW cohort at baseline, and to establish the incidence of fractures in this population after 2 years of follow-up. Further aims were to examine the skeletal sites of fracture and underlying risk factors in obese women, and to compare these with corresponding data in non-obese and underweight women with fractures.

METHODS

GLOW is a prospective cohort study involving 723 physician practices at 17 sites in 10 countries (Australia, Belgium, Canada, France, Germany, Italy, Netherlands, Spain, UK, and USA). The study methods have been described previously.[9] In brief, practices typical of each region were recruited through primary care networks organized for administrative, research, or educational purposes, or by identifying all physicians in a geographic area. Each site obtained local ethics committee approval to participate in the study. The practices provided the names of women aged ≥55 years who had been seen by their physician in the past 24 months. Approximately 3,000 women were sought at each site. Self-administered questionnaires (baseline surveys) were mailed to 140,416 subjects between October 2006 and February 2008, with a 2:1 over-sampling of women aged ≥65 years. Non-responders were followed up with a series of postcard reminders, a second questionnaire, and telephone interviews. After appropriate exclusions, 60,393 women agreed to participate in the study. Follow-up questionnaires were mailed 1 and 2 years later to women who had participated in the baseline survey. Women without both 1 and 2 years of follow-up (lost to follow-up or died) and women with incomplete BMI data were excluded from the analysis.

Data Collection

Questionnaires were designed to be self administered and covered domains that included: patient characteristics and risk factors; fracture history; current medication use; and other medical diagnoses. Data on height and weight were collected to allow calculation of BMI. Women were defined as obese if BMI was ≥30 kg/m^2, non-obese if BMI was 18.5–29.9 kg/m^2, and underweight if BMI was <18.5 kg/m^2.

Information was gathered on previous fractures (fractures that had occurred since the age of 45 years) during the baseline survey, and on incident fractures during the 1- and 2-year follow-up surveys. All surveys included report of fracture location, including spine, hip, wrist, and other non-vertebral sites (clavicle, upper arm, rib, pelvis, ankle, upper leg, lower leg, foot, hand, shoulder, knee, and elbow), and occurrence of single or multiple fractures. Self reports of personal risk factors included: history of parental hip fracture; premature menopause (age ≤45 years); number of falls in the past 12 months; use of arms to assist standing from a sitting position; current use of cortisone; fair or poor general health; current cigarette smoking; and consumption of ≥3 units of alcohol daily. Subjects were considered to be taking anti-osteoporosis medication if they reported current use of alendronate, calcitonin, estrogen, etidronate, ibandronate, pamidronate, recombinant human parathyroid

hormone (1–84), raloxifene, risedronate, strontium ranelate, teriparatide, tibolone, or zoledronate. Information was also obtained about other diagnoses, including asthma, emphysema, osteoarthritis, rheumatoid arthritis, colitis, stroke, Parkinson's disease, multiple sclerosis, cancer, and Type I diabetes.

Statistical Analysis

Age was compared across BMI groups using the Kruskal-Wallis test for continuous variables. Fracture rates are reported as rates per thousand women. Only women with complete baseline, 1- and 2-year follow-up surveys were included. We used the Fisher's exact test to make pairwise comparisons of outcomes between BMI categories. To control for multiple pairwise comparisons among the three BMI groups, a statistically significant difference between groups was noted when the p-value from the Fisher's exact test was <0.017. Analyses of characteristics of women by BMI group were limited to those with previous and incident fractures. Logistic regression was used to predict any type of incident fracture and the 10 individual types of incident fracture, in both unadjusted and adjusted models. We adjusted for variables that were significantly associated with the fracture outcomes and which in our opinion were not a part of BMI itself: maternal hip fracture, current estrogen use, current cortisone use, current smoker, fair/poor health, age, osteoarthritis, and Parkinson's disease. All analyses were performed using SAS 9.2 (SAS Institute Inc, Cary, North Carolina).

RESULTS

Of 60,393 women enrolled at baseline, 46,443 (76.9%) completed both 1- and 2-year surveys. We further excluded one woman with a BMI of 130 kg/m^2 and 1908 women with incomplete BMI or fracture history, leaving 44,534 women for further analysis. Among the 57,556 women enrolled at baseline with BMI data, 23.8% were obese, 74.4% were non-obese, and 1.9% were underweight. Of the 44,534 women analyzed, the corresponding figures were 23.4%, 74.9%, and 1.7%, respectively. Average ages (SDs) and weights (SDs) for obese, non-obese, and underweight women were: 67 years (7.9 years) and 90 kg (15.2 kg), 68 years (8.6 years) and 64 kg (8.8 kg), and 70 years (9.8 years) and 46 kg (6.4 kg).

Fracture prevalence at baseline and incidence within 2 years of baseline in obese, non-obese, and underweight women are shown in Table 1 (rates per 1000 women). Both prevalence and incidence of fractures were highest in the underweight group, with similar rates in obese and non-obese women. These differences in prior fracture rates were both statistically significant ($p<0.017$). Because of the distribution of body weight in the cohort, the number of women with previous or incident fractures was highest in non-obese women (7401 and 2170 respectively), intermediate in obese women (2274 and 633 respectively), and lowest in underweight women (220 and 53 respectively). Incident fracture rates in women with morbid obesity (BMI ≥35 kg/m^2) were similar to those in all obese women (BMI ≥30 kg/m^2; data not shown). Obese women were similar to their non-obese and underweight counterparts in having a 2–3-fold higher risk of incident fracture if they had a previous fracture. Obese women with previous or incident fracture were significantly younger than non-obese and underweight women with fracture. Mean ages (SDs) in obese women with

previous or incident fracture were 70 (8.3) and 69 (8.3) years, respectively, compared with 72 (8.9) and 70 (9.3) years in non-obese women, and 73 (9.8) and 73 (11) years in underweight women ($p<0.001$ for both previous and incident fractures).

Fracture rates per 1000 women by skeletal site are shown in Table 2. Obese women were more likely than others to have experienced previous ankle or lower leg fractures and less likely to have had previous wrist, hip, rib or pelvis fractures, while underweight women were more likely to have had previous hip or pelvis fractures than the others ($p<0.017$ for all BMI category pairwise comparisons, except for lower leg, where the difference was only seen between obese and non-obese women).

Incident fracture rates per 1000 women and unadjusted BMI category comparisons also appear in Table 2. Rates were higher for ankle and lower for wrist fractures among obese versus non-obese women, lower for both pelvis and hip fracture among obese versus underweight women, and higher for rib fractures in non-obese versus underweight women ($p<0.017$). After adjusting for maternal hip fracture, current estrogen use, current cortisone use, current smoking, fair/poor health, age, osteoarthritis, and Parkinson's disease, incident ankle fractures remained more common (adjusted odds ratio [OR] 1.5, 95% confidence interval [CI] 1.2, 1.9) and incident wrist fractures less common in obese than non-obese women (OR 0.8, 95% CI 0.6, 1.0), while incident rib fractures remained more common in non-obese than underweight women (OR 7.1, 95% CI 1.0, 50.9). Upper leg fractures were more common in obese than non-obese women in the adjusted analysis (OR 1.7, 95% CI 1.1, 2.5). Unadjusted rates for incident hip and pelvis fractures were no longer statistically significant after covariate adjustment. Although adjusted and unadjusted results for incident lower leg fracture were not statistically significant, these fractures appeared similar to ankle and upper leg fractures with respect to rates in obese versus non-obese women.

Previous and incident fracture rates per 1000 women by BMI group are shown in Table 3 according to risk factors identified at baseline. Main BMI group differences found were a higher fracture incidence for obese versus non-obese women if a woman experienced early menopause, needed to use her arms to assist in standing from a sitting position (also higher if obese than underweight), reported fair or poor health, or reported ≥2 falls in the past 2 years; and a lower incident fracture rate for non-obese versus underweight women with a prior fracture. Table 4 reports rates of various co-morbidities among women with a previous fracture and with an incident fracture within 2 years of baseline, by BMI category. Obese women who fractured tended to have higher rates of co-morbidities than others (especially self-reported asthma), but Parkinson's disease was more common in underweight women who fractured.

The use of anti-osteoporosis medication was significantly lower in obese women with fracture than in non-obese or underweight women with fracture. Among women with a previous fracture, 21% of obese, 35% of non-obese, and 54% of underweight women received anti-osteoporosis medication at baseline; in the same groups who experienced an incident fracture, rates of baseline anti-osteoporosis medication were 27% of obese, 41% of non-obese, and 57% of underweight ($p<0.001$ for all pairwise comparisons, except for incident fractures, non-obese versus underweight women).

DISCUSSION

Our results challenge the widespread belief that obesity is protective against fracture, and indeed suggest that obesity is a risk factor for certain fractures, particularly those of the ankle and upper leg. In this large, population-based cohort of postmenopausal women, the rates of both previous and incident fracture in obese women were similar to those observed in non-obese women. Although the highest fracture rates occurred in underweight women, the small proportion of women in the underweight group meant that the actual number of fractures in this population was low, and accounted for only 2.2% and 1.9% of the total number of past and incident fractures, respectively. In contrast, fractures in obese women accounted for 23% and 22% of all previous and incident fractures, respectively, in the GLOW population.

An association between BMI and fracture site was demonstrated, the risk of incident ankle and upper leg fractures being higher in obese versus non-obese women, and of incident fractures of the wrist being lower. Relative protection against hip and pelvis fractures in obese women, as noted for previous fractures, may result from the protective effects of abdominal fat tissue on the impact of falls,[10] while the lower rate of wrist fractures might reflect the direction of falls (possibly more likely to be sideways or backwards as opposed to forwards) in obese individuals. Because of reduced physical mobility, obese women are more likely to fall during activities with little forward momentum, thus protecting the wrist from impact, while the absence of soft tissue padding in the ankle and leg, together with the high impact of the fall, make these sites more vulnerable.

In other studies, varying associations between obesity and fracture site have been reported. Gnudi et al found that, in 2,235 postmenopausal women with fracture, increased BMI was associated with a significantly higher risk of humerus fracture and a lower risk of hip fracture, but no relationship was seen between BMI and either wrist or ankle fractures.[11] In a study of men and women aged 20–80 years, Bergkvist et al reported that ankle fracture was significantly related to obesity.[12] Finally, Nielson et al have recently reported that obesity was associated with an increased risk of non-spine fractures in men aged ≥65 years, although there was insufficient power to examine the association between BMI and all individual fracture sites. Interestingly, in this study, the risk of hip fracture was also higher in obese men, an effect that was independent of BMD.[13] Data on vertebral fracture in obese individuals are sparse, although in one study in postmenopausal women, obesity appeared to be associated with increased risk.[14]

Risk factors for fracture also differed according to BMI in our study. Early menopause was significantly associated with high BMI, rates of 19–20% being recorded in obese women with either previous or incident fracture, as opposed to rates of 10–14% in non-obese and underweight women. Whether obesity predisposes to, or is a consequence of, early menopause is unclear. In a recent study, surgical menopause, early hormone replacement therapy, higher serum androgen levels, and lower levels of sex-hormone-binding globulin predicted incident obesity, suggesting that the latter is the case.[15] In the present study, current estrogen use was not more common in obese than in non-obese or underweight women, but past use of estrogen was not documented.

Obese women with fracture also reported a higher frequency of falls, fair or poor general health, and use of arms to assist standing from a sitting position, suggesting that an increased risk of falls and possibly also impaired protective responses to falling may be important risk factors for fracture associated with obesity. Increased risk of falls and reduced physical function have previously been demonstrated in obese women and men.[16–19] We also found that higher BMI was significantly associated with a number of co-morbidities, including asthma, emphysema, and type 1 diabetes. These conditions are all associated with obesity and have adverse effects on bone health through a variety of mechanisms, including reduced physical activity, co-medications, and increased risk of falls.[20–31] Obese women with fracture thus had several markers of frailty, possibly explaining the significantly younger age at which incident fracture occurred, compared with non-obese or underweight women.

While higher BMI is generally associated with higher BMD, there is increasing evidence that the effects of fat on bone mass vary according to its distribution, subcutaneous fat having beneficial effects and visceral fat having adverse effects. This difference may be mediated by the presence of lower levels of leptin and higher levels of adiponectin and pro-inflammatory cytokines in visceral fat.[32, 33] In addition, increased visceral fat is associated with insulin resistance, which may also exert adverse effects on bone.[34, 35] Vitamin D status is inversely related to BMI and to insulin resistance, providing another mechanism by which visceral fat mass might contribute to bone loss.[36, 37] In addition, the higher serum parathyroid hormone levels reported in obese individuals could have adverse effects on cortical bone.[38, 39] The effects of obesity on bone health are therefore complex and require further elucidation.

The use of bone protective medication in women with either a previous or incident fracture decreased significantly with increasing BMI. Among obese women, only 27% of those with an incident fracture were receiving treatment, as opposed to 41% and 57% in the non-obese and underweight groups, respectively. The low treatment rate in obese women may reflect the perception that they are protected by their higher BMD and that fractures in this population are therefore not “fragility” or “osteoporotic” fractures. Furthermore, assessment of fracture risk in obese women using algorithms such as FRAX® will generate lower fracture probabilities than in non-obese or underweight women because of the influence of BMI and/or BMD in these estimations, and fracture probability is less likely to achieve the intervention thresholds set in guidelines.[40–42] However, higher BMD in people with higher BMI may represent appropriate adjustment of the skeleton to increased body weight and may not necessarily confer greater bone strength for that individual.[43–45] In a cohort of postmenopausal women in the Study of Osteoporotic Fractures, obese women with incident, non-vertebral fractures had significantly lower BMD and a significantly greater likelihood of previous fracture history than their obese counterparts without fracture, demonstrating that fractures in obese women share some of the characteristics of fragility fractures.[46]

Even if fractures in obese postmenopausal women are perceived as fragility fractures, the evidence base for bone protective therapy in this population is weak. Only a minority of obese postmenopausal women with fracture have osteoporosis, and a substantial proportion has normal BMD as defined by a T-score ≥−1.[8] In clinical trials of anti-osteoporosis medications, the proportions of obese women have generally been small, and those who

have been included have had low BMD. The anti-fracture efficacy demonstrated in these studies cannot therefore necessarily be extrapolated to obese women with higher BMD, and in one study of the effects of clodronate in postmenopausal women not selected on the basis of low BMD, fracture reduction was lower in women with higher BMI than in those with lower BMI.[47] Further studies are therefore required to establish the anti-fracture efficacy of bone protective interventions in obese women with fracture, including investigation of the possibility that higher doses might be required.

Strengths and Weaknesses

Major strengths include the large sample size and prospective nature of the study, enabling examination of the characteristics of both previous and incident fractures. Limitations include the observational nature of the study, which makes it subject to bias, both in terms of the sampling of physicians and the recruitment of participants. Fractures were self reported and were not confirmed radiologically, and spine fractures were under-represented, as subclinical vertebral deformities were not included. Fractures were not excluded on the basis of how they occurred. While information was collected about activity during fracture, <2% of fractures occurred during a motor vehicle accident. It is possible that some of the fractures may have been pathological in nature, but some clinicians may elect not to treat these fractures. Weight and height, risk factors, medications, and co-morbidities were also self reported; for fractures and medication use there is evidence that self-reports are reasonably reliable,[48–53] and comparison of USA GLOW data with the National Health And Nutrition Examination Survey (NHANES) III cohort showed that the distribution of risk factors among women in GLOW was broadly similar to that among women enrolled in NHANES.[9]

Self-reporting of co-morbidities may be less reliable; in particular, type 1 diabetes, which was specified on the questionnaire, may have been confused with type 2 diabetes. However, there is no reason why inaccuracies in self-reports of co-morbidity or any of the other characteristics included in this study should vary across the BMI groups. Therefore, any such reporting error would tend to underestimate the effect of BMI on fracture risk. Finally, although this study included diverse geographical regions, no Asian or African countries were included and our results may therefore not be generalizable to these populations.

CONCLUSIONS

The finding that obesity is not protective against fracture in postmenopausal women and is associated with increased risk of incident upper leg and ankle fractures has major public health implications. The morbidity and economic costs associated with fractures in the obese population are likely to be higher than in non-obese women because of a greater risk of non-union, post-operative complications, co-morbidities, and slower rehabilitation.[54, 55] Furthermore, in view of the rapidly rising incidence of obesity,[56, 57] the contribution of fractures in obese women to the global fracture burden will increase significantly over the coming years. Understanding the pathogenesis of these fractures and developing effective strategies for their prevention are important areas for future research.

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Table 1

Previous and Incident Fractures among Obese, Nonobese, and Underweight Women With or Without Previous Fracture[*]

	Group 1: Obese (n = 10,441)	Group 2: Nonobese (n = 33,349)	Group 3: Underweight (n = 744)	*P* Value[†]
Previous fracture (n = 9895)	222 (2274)	227 (7401)	300 (220)	1 vs 3, 2 vs 3
Incident fracture[‡] (n = 2856)[§]	61.7 (633)	66.0 (2170)	72.4 (53)	
No history of previous fracture (n = 1679)	46.3 (362)	51.8 (1294)	45.3 (23)	
History of previous fracture (n = 1114)	116.4 (258)	114.1 (826)	140.8 (30)	

[*] n = 44,534; rates per 1000 women (number of fractures).

[†] We performed pairwise comparisons among the 3 groups, and report any results where $P \leq .017$ (for example, 1 vs 2 means the difference between group 1 [obese] and group 2 [nonobese] is statistically significant at alpha = .017 level).

[‡] Within 2 years of baseline a fracture of clavicle, upper arm, wrist, spine, rib, hip, pelvis, ankle, upper leg, lower leg, hand, foot, elbow, knee, or shoulder.

[§] Some of these women were missing history of previous fracture.

Table 2

Frequency of Fractures by Skeletal Location in Obese, Nonobese, and Underweight Women (Rates per 1000 Women)

	Previous Fracture				Incident Fracture (Within 2 Years of Baseline)			
Fracture Site	**Group 1: Obese (n = 10,441)**	**Group 2: Nonobese (n = 33,349)**	**Group 3: Underweight (n = 744)**	***P* Value***	**Group 1: Obese (n= 10,441)**	**Group 2: Nonobese (n = 33,349)**	**Group 3: Underweight (n = 744)**	***P* Value***
Clavicle	11.0	12.5	21.6		2.0	2.3	1.4	
Upper arm	28.9	26.3	39.2		6.1	6.0	6.8	
Wrist	67.0	85.7	108	1 vs 2, 1 vs 3	12.1	15.4	17.6	1 vs 2
Spine	18.6	20.9	33.9	1 vs 3	5.6	7.0	8.1	
Rib	35.6	41.2	58.0	1 vs 2, 1 vs 3	8.1	9.3	1.4	2 vs 3
Hip	11.2	15.9	43.3	1 vs 2, 1 vs 3, 2 vs 3	3.8	4.6	11.0	1 vs 3
Pelvis	6.0	10.6	23.0	1 vs 2, 1 vs 3, 2 vs 3	1.9	2.7	8.1	1 vs 3
Ankle	75.3	55.2	50.0	1 vs 2, 1 vs 3	13.3	8.5	6.9	1 vs 2
Upper leg	9.7	7.5	13.5		3.7	2.5	5.4	
Lower leg	28.9	23.0	27.0	1 vs 2	5.3	3.6	2.7	

*We performed pairwise comparisons among the 3 groups, and report any results where Fisher's exact test P ≤.017 (for example, 1 vs 2 means the difference between group 1 [obese] and group 2 [nonobese] is statistically significant at alpha = .017 level).

Table 3

Frequency of Risk Factors Identified at Baseline among Women with Previous and Incident* Fractures (Rates per 1000 Women)

	Previous Fracture				Incident Fracture (within 2 Years of Basline)			
Risk Factor	**Group 1: Obese (n = 2274)**	**Group 2: Nonobese (n = 7401)**	**Group 3: Underweight (n = 220)**	***P* Value†**	**Group 1: Obese (n = 633)**	**Group 2: Nonobese (n = 2170)**	**Group 3: Underweight (n = 53)**	***P* Value†**
Previous fracture					416	390	566	2 vs 3
Maternal hip fracture	156	164	162		141	177	159	
Current estrogen use	55.9	73.6	77.6	1 vs 2	57.1	73.4	94.3	
Early menopause	194	127	128	1 vs 2	200	139	98	1 vs 2
Current cortisone use	49.3	38.2	51.2		48.2	49.6	19.2	
Weight loss ≥10 lb	113	103	207	1 vs 3, 2 vs 3	132	117	208	
Current smoker	56.6	79.6	152	1 vs 3, 2 vs 3	86.3	92.3	173	
Alcohol >20 units/week	1.3	5.2	0.0	1 vs 2	3.2	8.3	0.0	
Arms assist	605	359	347	1 vs 2, 1 vs 3	595	348	327	1 vs 2, 1 vs 3
Fair/poor general health	342	240	347	1 vs 2, 2 vs 3	345	257	321	1 vs 2
Falls								
1 in past 2 years	270	265	298		256	259	358	
≥ 2 in past 2 years	242	187	234	1 vs 2	308	211	264	1 vs 2

*Incident fracture is defined as a fracture of at least one of the following bones: clavicle, upper arm, wrist, spine, rib, hip, pelvis, ankle, upper leg, lower leg, hand, foot, elbow, knee, or shoulder.

†We performed pairwise comparisons among the 3 groups, and report any results where Fisher's exact test P ≤.017 (for example. 1 vs 2 means the difference between group 1 [obese] and group 2 [nonobese] is statisticallv significant at alpha = .017 level).

Table 4

Frequency of Comorbidities Identified at Baseline among Women with Previous and Incident* Fractures (Percentage of Women)

	Previous Fracture				Incident Fracture (within 2 Years of Baseline)			
	Group 1: Obese (n = 2274)	**Group 2: Nonobese (n = 7401)**	**Group 3: Underweight (n = 220)**	***P* Value†**	**Group 1: Obese (n = 633)**	**Group 2: Nonobese(n = 2170)**	**Group 3: Underweight (n = 53)**	***P* Value†**
Asthma	20	11	13	1 vs 2	19	12	4	1 vs 2, 1 vs 3
Emphysema	14	10	17	1 vs 2, 2 vs 3	16	10	8	1 vs 2
Osteoarthritis	51	45	44	1 vs 2	51	46	44	
Rheumatoid arthritis	1.3	1.0	2.3		1.3	1.3	1.9	
Colitis	3.5	2.4	1.8	1 vs 2	2.9	2.4	0.0	
Stroke	5.8	4.7	3.7		5.7	4.2	1.9	
Parkinson's disease	0.4	0.8	2.3	1 vs 3	1.3	1.0	3.8	
Multiple sclerosis	1.0	0.8	0.9		1.0	1.3	0.0	
Cancer	18	16	15		18	16	15	
Type 1 diabetes	6.7	2.7	1.4	1 vs 2	10	3.2	1.9	1 vs 2

*Incident fracture is defined as a fracture of at least one of the following bones: clavicle, upper arm, wrist, spine, rib, hip, pelvis, ankle, upper leg, lower leg, hand, foot, elbow, knee, or shoulder.

†We performed pairwise comparisons among the 3 groups, and report any results where Fisher's exact test $P \leq .017$ (for example, 1 vs 2 means the difference between group 1 [obese] and group 2 [nonobese] is statistically significant at alpha = .017 level).