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# Should risk of bone fragility restrict weight control for other health reasons in postmenopausal women? – A ten year prospective study

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ABSTRACT

*Background:* The aim of the present study was to investigate the health risks of excess body weight in the light of its protective effects on bone fragility.
*Methods:* Femoral neck and lumbar spine dual X-ray absorptiometry was performed for 1970 Finnish women with a mean baseline age of 58.8 years (range 53.1–65.7 years) in 1994 and 2004. Women were categorized according to baseline BMI into normal <25 kg/m2, overweight 25–29.9 kg/m$^2$ and obese ≥30 kg/m$^2$. Weight change (kg) was categorized into tertiles. Co-morbidities, not allowed to be present at baseline, was based on self-reports. Osteoporosis was defined as femoral neck or spinal (L2–L4) *T*-score <−2.5 SD at 10-year follow-up or <−2.0 SD + low trauma energy follow-up fracture. Uni- and multivariate logistic regression models were used to estimate the 10-year risk of incident health disorders. Adjustment for age, number of diseases, alcohol intake and smoking was used in the multivariate models.
*Results:* Obesity (Ob) and overweight (Ow) were related with higher 10-year risk of hypertension (OR = 2.6 (Ob)/OR = 1.7 (Ow), $p < 0.001$), coronary artery disease (OR = 1.6, $p < 0.05$/OR = 1.2, $p$ = NS), diabetes (OR = 11.7/OR = 5.3, $p < 0.001$), osteoarthritis (OR = 1.4, $p < 0.05$/OR = 1.1, $p$ = NS), chronic back pain (OR = 1.6, $p = 0.007$/OR = 1.2, $p$ = NS) and poor self-rated health (OR = 2.4, $p < 0.05$/OR = 1.5, $p$ = NS) and lower risk of osteoporosis (OR = 0.13/OR = 0.28, $p < 0.001$). Weight change of less than +1 kg was associated 1.8 and 2.6 times lower 10-year risk of having hypertension and breast cancer than weight change over 6.2 kg. Among obese women the absolute risk increase of hypertension was 17%, of diabetes 12%, and absolute risk reduction of osteoporosis 14% in comparison to BMI <25 kg/m$^2$.
*Conclusions:* Health related risks of high BMI outweigh its protective effects on bone. Weight gain increases the risk hypertension and breast cancer.



## 1. Introduction

Among the elderly population there are sex dependent differences in morbidity and disability which become more evident with age [1,2]. Among middle-aged women menopausal transition, caused by physiological exhaustion of ovarian function [3,4], evokes an increase in musculoskeletal, cardiovascular and mental impairments and cancer [5–7]. This, together with predominance of female elderly population, makes these health disorders an important target for research and preventive health care measures [6].

Obesity and overweight are important risk factors for several co-morbidities [8–11] which cause substantial costs [12]. Several recent studies have suggested that obesity and overweight are significant risk factors for diabetes [13], cardiovascular diseases [8,11,14], breast and gastrointestinal cancer [15–17], osteoarthritis [18], depression [19] and poor self-rated health [20]. In contrast, obesity and overweight may be protective against osteoporosis [21–23]. Consequently, there is an apparent dilemma from the view of preventive medicine considering the effects of overweight and obesity on postmenopausal co-morbidity.

Despite several reports on obesity related co-morbidity there are no studies available that would have compared the risks and benefits of obesity within the same cohort. Moreover, meta-analyses and systematic reviews may give misleading risk estimates due to heterogeneity of the included populations. Consequently, the aim of the present study was to investigate the risk of co-morbidities in relation to body weight in a homogenous cohort of postmenopausal Finnish women.

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## 2. Materials and methods

### 2.1. Study population

The study population was based on the prospective Kuopio Osteoporosis Risk Factor and Prevention (OSTPRE) study cohort (http://www.uku.fi/~due2/indexeng.htm). The OSTPRE cohort was established in 1989 by selecting all women born in 1932–1941 and resident in the region of Kuopio, Finland ($n$ = 14,220). The baseline postal inquiry included questions about health-related factors, co-morbidity, medications and anthropometric information and was sent to participants in 1989. The follow-up questionnaires were sent to the 13,100 women who responded at baseline at five year intervals in 1994, 1999 and 2004 and responses were received from 11 954, 11 537, and 10 926 women, respectively. The study protocol has been approved by the ethics committee of University of Kuopio and Kuopio University Hospital. Informed written consent from the participants was collected with the postal inquiries.

The selection of the present study population and follow-up drop outs are outlined in Fig. 1. Of the 13,100 respondents in 1989, 11,055 (84.4%) were willing to undergo DXA bone densitometry. A stratified random sample from this cohort ($n$ = 3686, 33.3%) was selected and invited to attend bone density measurements. Of these women, 3222 (87.4%) underwent DXA in 1989. Valid femoral neck (FN) and lumbar spine (LS) measurements were performed for 2950 women in 1989, 2940 women in 1994 and 2028 women in 2004. Because the first (1989) postal inquiry did not include sufficient information on the co-morbidities necessary for the present study, the 1994 follow-up was set, and referred hereafter, as the baseline for the present study. The mean age of the study population was 58.8 years (SD 2.8) at baseline (in 1994).

### 2.2. Co-morbidity

The information on co-morbidities was based on question in postal inquiry: "Please state, if you have any of the following diseases that have been diagnosed by a physician?", followed by a list of selected health disorders and options "Other, specify?" and "No chronic diseases". The end-point co-morbidities for the present study were selected based on public health importance and literature review and were: hypertension requiring medication, chronic heart failure, coronary artery disease, stroke, diabetes (treated with insulin, oral substances or diet), breast cancer, any cancer (including breast, ovarian, uterus, pancreatic, colorectal, kidney and esophageal cancers), osteoarthritis and chronic back pain. Self-rated health, although not considered as a disease, was additionally included.

Osteoporosis was not included in the list of self-reported health disorders but was defined as $T$-score under −2.5 SD of femoral neck (FN) or lumbar spine (LS) based upon the 10-year densitometry [24]. In order to take into account bone fragility, women with FN or LS BMD under −2.0 SD (i.e. severe osteopenia) and any low-trauma energy fracture during the follow-up were also judged to be "osteoporotic". At baseline, non-osteoporotic women had FN and LS $T$-score over −2.5 without history of low trauma energy fracture. Low-trauma energy fractures (due to falling at same level or from less than 1 m height) during the 10-year FU (1994–2005) were recorded based on questions in the FU postal questionnaires. All self-reported fractures were validated from medical reports by the study group physicians. However, rib fractures were accepted also without radiological evidence, based on clinical examination reported in the medical records. The false positive rate in self-reported fractures was 16.5% and the false negative rate was 21.6% [25].

Participants with the co-morbidity under investigation at baseline were excluded. For example, women with hypertension at baseline were excluded when the risk of hypertension was studies and women with osteoporosis at baseline were excluded when the risk of osteoporosis was studied. The number of any health disorder was used as adjusting variable in all analyses.

### 2.3. Other variables of interest

The height and weight of each study subject were measured by a study group nurse with a calibrated weight scale and stadiometer at densitometry. The body mass index (BMI) was calculated as weight/height$^2$ (kg/m$^2$) and categorized according to World Health Organization criterion into (1) normal (under 25 kg/m$^2$) (2) overweight (25–30 kg/m$^2$) and (3) obesity (over 30 kg/m$^2$). Weight change was calculated as [(weight in 2004 (kg)) − (weight in 1994 (kg))] and divided into tertiles. Information on smoking was obtained with the question: "Do you smoke currently?". The use of alcohol was investigated with the question: "What is on average the amount of alcohol beverages you use montly as bottles of beer, glasses of wine and drinks of distilled spirits", and was converted into grams of pure alcohol. The total number of all diseases was calculated as a sum of self-reported diseases (Cf. Section 2.2).

### 2.4. Bone mass measurements

The DXA measurements of LS (L2-L4) and FN were carried out using Lunar DPX scanner (Lunar Co, Madison, WI, USA) at baseline (in 1994) measurement in Kuopio University Hospital by specially trained nurses. Quality standards were tested daily. The reproducibility of this method has been reported previously [26,27]. The Lunar DPX scanner was replaced with the Lunar Prodigy before the 10-year (2004) densitometry. The differences in the BMD results between these scanners were corrected with best fit first order polynomial functions. The FN and LS BMD values were converted into $T$-scores based on reference population of Finnish young women aged 20–40 years [27].

### 2.5. Statistical methods

Statistical analyses were carried out using the Statistical Package for Social Sciences (SPSS ver. 16, SPSS Inc., Chicago, IL, USA) for Windows. Logistic regression models were used to estimate the 10-year risk of co-morbidities according to BMI and weight change and they were adjusted for generally acknowledged risk factors for postmenopausal morbidity: baseline age, alcohol intake, smoking and self-reported number of diseases. In multivariate analysis, all variables were entered simultaneously in to the logistic regression model. The odds ratios were obtained individually for each co-morbidity and the given co-morbidity and was not allowed being present at baseline (in 1994).

## 3. Results

There were 58 women with missing end-point morbidity information (Fig. 1). Table 1 represents the baseline characteristics of the study population that completed the follow-up ($n$ = 1970) as well as the characteristics of the 970 drop-outs. The age range of the present study population was 53.1–65.7 years (mean 58.8 years, SD 2.8 years). Out of the final study population 636 (32.3%) were normal weight, 785 (39.8%) overweight and 549 (27.9%) obese. The tertiles of weight change during the follow-up were (1) under 1 kg, (2) 1–6.2 kg, and (3) over 6.2 kg. The incidence of co-morbidities for the final study population during the follow-up for women *without* the given co-morbidity at baseline was: hypertension 25.7%, chronic heart failure 6.2%, coronary artery disease 10.3%, stroke 5.0%, diabetes 7.3%, osteoarthritis 22.3%, breast cancer 2.8%, any