Risk Factors for Postmenopausal Fractures – What We Have Learned from The OSTPRE study

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Kuopio Bone Symposium lecture, 11th June 2015
• Why do we need to assess fracture risk?
• How can we predict fractures?
  – Non-skeletal risk factors
  – Bone densitometric methods
  – Other methods
• OSTPRE experience
Musculoskeletal diseases - major health burden and future challenge -

In developed countries, musculoskeletal diseases account for half of all chronic conditions in people over 50 years of age

- osteoarthritis (OA), osteoporosis (OP) and back pain and spine disorders are the major health burdens in the modern societies

- **Osteoporosis** is the most common metabolic bone disease, affecting over 200 million people worldwide

- Hip, spine and forearm **fractures** are its main consequences, which increase the morbidity and mortality of elderly people.
  - Provided that no successful preventive programs are started, the number of hip fractures will rise from about 1.7 million in 1990 to 6.3 million by 2050
Age-specific and sex-specific incidence of osteoporotic fractures

Consequences of hip fracture

One year after hip fracture

Patients (%)

Death within one year: 20%
Permanent disability: 30%
Unable to walk independently: 40%
Unable to carry out at least one independent activity of daily living: 80%
Consequences of vertebral fractures

- Kyphosis
- Loss of height
- Bulging abdomen
- Acute and chronic back pain
- Breathing difficulties
- Depression
- Reflux and other GI symptoms
- Difficulty with activity of daily living (bending, rising, dressing, climbing stairs)
- Need to use a walking aid

REDUCED INDEPENDENCE AND QUALITY OF LIFE
Similar mortality in patients with vertebral fractures and in those with hip fractures

Adapted from Bliuc D et al. (2009) JAMA 301(5): 513
Consequences of distal radius fractures

• The most common fracture in women at middle age
  – Incidence increases just after menopause
• The most common fracture in men below 70 years
• Only 50% report good functional outcome at 6 months
• Up to 30% of individuals suffer long-term complications
Risk Factors for Osteoporosis and Fractures

- Risk factors impact on
  - Bone mineral density (BMD)
  - Fracture risk
  - Both

- Risk factors fall into the categories of
  - Physical characteristics
  - Lifestyle factors
  - Endogenous factors
  - Diseases and medications

  - Fall related risk factors for fractures – Risk factors for falls
Fracture risk – multifactorial

The relative importance of risk factors
Bone density is not the only factor of fracture risk …

Neuromuscular function
  Environmental risks
  Age

Type of fall
  Energy reduction
  External protection

Bone mass
  Bone structure
  Bone quality

Fall Risk

Impact of fall

Skeletal strength

Fracture risk

- Magnus Karlsson’s talk
- Toni Rikkonen’s talk (OSTPRE-IFP)
- Nadia Afrin’s poster
Health 2000 Survey Finland

Table 15. Prevalence (%) of self-reported falls within the previous 12 months in the Health 2000 Survey.

Table 16. Prevalence (%) of self-reported fractures (broken bones) in the Health 2000 Survey.

Out of a nationally representative sample of 8,028 persons aged 30 years and over, 80% participated in a comprehensive health examination which included a standard clinical examination by a physician. Using standard criteria based on medical history, symptom history and physical status, chronic low-back syndrome.
**KUOPIO OSTEOPOROSIS STUDY (OSTPRE)**

**STUDY DESIGN**

Kuopio Province women aged 47-56 years (N=14,220)

Baseline postal enquiry 1989


Random stratified sample of 3222 women

Bone densitometry I 1990-1991
Bone densitometry II 1995-1997
Bone densitometry III 1999-2002
Bone densitometry IV 2004-2007
Bone densitometry V 2009-2011
Bone densitometry VI (25 yr) 2014-2016

OSTPRE-FPS
Ca+Vit-D trial 2003-2007 N=3000

OSTPRE-IFP
Fall risk prevention 2016-2018 N=1100

**Methods**
- DXA
- Ultrasound
- Fractures
- Biochemistry
- Functional tests
- Falls
- Genetics

**20 yr work packages**
- I Fractures
- II Sarcopenia
- III Bone-Brain-Atherosclerosis (BBA)
- IV National Registers

**HRT trials**
Results – 20 yr follow-up

• The 20-year follow-up showed that 9090/11420 (79.6 %) questionnaires were returned and 1559/2224 (70.1 %) women had undergone bone densitometry and special studies

• A total of 3554 women experienced 4748 fractures during the 20 year follow up (1989-2009).
  – 1471 wrist fractures, 303 vertebral fractures, 282 hip fractures, 233 proximal humerus fractures,
Risk factors for Fractures

**Physical Characteristics**

- **Age** – fracture incidence increases with age
- **Gender** – women at higher risk for fx
  - Men have greater body size, higher aBMD, larger bone size (CSA), thicker cortices etc.
- **Height**
  - Women with hip fx are taller *(Cummings et al. NEJM 1995)*
- **Weight and BMI**
The crude incidence of all osteoporotic fractures in 2005-2006 in the population over 50 yrs was 694/100,000 person years for men and 1718/100,000 person years for women.
Table 1. Baseline characteristics of the study population \((n = 11,798)\) according to the distal forearm fracture status: the Kuopio Osteoporosis Risk Factor and Prevention (OSTPRE) Study

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Fracture ((n = 368))</th>
<th>No fracture ((n = 11,430))</th>
<th>Total ((n = 11,798))</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mean age, years</td>
<td>53.2 (2.9)***</td>
<td>52.3 (2.9)</td>
<td>52.3 (2.9)</td>
</tr>
<tr>
<td>Mean height, mm</td>
<td>1610 (54)</td>
<td>1612 (53)</td>
<td>1612 (53)</td>
</tr>
<tr>
<td>Mean weight, kg</td>
<td>66.3 (11.2)**</td>
<td>68.3 (11.7)</td>
<td>68.2 (11.7)</td>
</tr>
<tr>
<td>Mean BMI, kg/m²</td>
<td>25.6 (3.9)**</td>
<td>26.3 (4.3)</td>
<td>26.2 (4.3)</td>
</tr>
<tr>
<td>Mean dairy calcium intake, mg/day</td>
<td>750 (359)**</td>
<td>833 (397)</td>
<td>830 (396)</td>
</tr>
<tr>
<td>Postmenopausal (%)</td>
<td>80.7***</td>
<td>67.5</td>
<td>68.0</td>
</tr>
<tr>
<td>Nulliparous (%)</td>
<td>16.2**</td>
<td>10.9</td>
<td>11.1</td>
</tr>
<tr>
<td>Bilateral oophorectomy (%)</td>
<td>3.9</td>
<td>5.8</td>
<td>5.7</td>
</tr>
<tr>
<td>Hysterectomy (%)</td>
<td>10.9</td>
<td>10.9</td>
<td>10.9</td>
</tr>
<tr>
<td>HRT</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>By baseline (%)</td>
<td>33.2</td>
<td>33.0</td>
<td>33.0</td>
</tr>
<tr>
<td>At baseline (%)</td>
<td>14.0**</td>
<td>21.1</td>
<td>20.9</td>
</tr>
<tr>
<td>During follow-up (%)</td>
<td>30.0***</td>
<td>41.4</td>
<td>41.0</td>
</tr>
<tr>
<td>Smoking (%)</td>
<td>9.5</td>
<td>11.1</td>
<td>11.0</td>
</tr>
<tr>
<td>Physical activity, regular leisure-time (%)</td>
<td>56.4</td>
<td>51.8</td>
<td>52.0</td>
</tr>
<tr>
<td>No. of health disorders, 2+ (%)</td>
<td>38.0**</td>
<td>31.3</td>
<td>31.5</td>
</tr>
<tr>
<td>Long-term work disability (%)</td>
<td>20.4</td>
<td>17.8</td>
<td>17.9</td>
</tr>
<tr>
<td>Fracture history</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Any (%)</td>
<td>26.9***</td>
<td>16.7</td>
<td>17.1</td>
</tr>
<tr>
<td>Wrist (%)</td>
<td>13.0***</td>
<td>4.8</td>
<td>5.1</td>
</tr>
<tr>
<td>Nonwrist (%)</td>
<td>13.9</td>
<td>11.9</td>
<td>12.0</td>
</tr>
</tbody>
</table>

Difference between fracture versus nonfracture cases: *p<0.05; **p<0.01; ***p<0.001.

a Without bilateral oophorectomy.
• Dramatic increase in obesity due to reduced physical activity, increased caloric intake and poor food choices

• Increase in various comorbidities (DM type II, hypertension, hyperlipidemia, breast cancer…)

• Heavier women have:
  – Higher BMD (mechanical loading, estrogen production in adipose tissue), cortical BMD?
  – Lower Fx rates in some skeletal sites (cushioning?)
  – Higher risk of falling
  – More severe fractures

• Weight loss can be harmful for bone

• Among obese women (BMI>30) the absolute 10 year risk increase of hypertension was 17 % and of DM 12 %, whereas absolute risk decrease of osteoporosis was 14 % - Do other health related risks of obesity outweigh its protective effects on bone? (Sirola et al. Maturitas 2012)
Risk Factors for Ankle Fractures
Kuopio Osteoporosis Study

• During the 5 year follow-up, 11,798 women (aged 47-56 years) sustained 194 validated malleolar fractures, giving an incidence of 3.4 fractures/1000 person-years.

• Four independent predictors for malleolar fracture were detected:
  – Fracture history, HR=1.63
  – Obesity (25-30 kg/m² vs. <25 kg/m²), HR=1.69
  – Three or more prescribed drugs, HR=2.03
  – Smoking had a dose-response effect
    • HR=1.73 in those smoking 1-19 cigarettes/day
    • HR=2.94 in those smoking ≥ 20 cigarettes/day

Valtola et al. Bone 2002
Risk Factors for Distal Forearm Fractures
Kuopio Osteoporosis Study

Independent predictors of DFF (Cox model)
(11,798 women aged 47-56yr, 368 DFF in 5 yr fu)

Increase of risk

* Previous wrist fracture 158 %
* Menopause 69 %
* Age (per 1 yr) 6 %

Decrease of risk

* Continuos use of HRT 63 %
* Dairy calcium use 1-1.5 g/d vs. < 0.5 g/d 39 %
* BMI > 25 kg/cm2 36 %
* Parity 29 %

Honkanen et al. Osteoporosis Int 2000
• Different risk profiles for wrist and ankle fractures
  – Ankle fracture = ”Lifestyle fracture ”
  – Wrist fracture = ” Menopausal fracture”
Smoking

• Current smoking is associated with a significantly increased risk of any fracture (RR=1.25) and hip fracture (RR=1.84) compared to non-smokers (Kanis et al. Meta-analysis, Osteoporosis Int 2005 – OSTPRE included)

• Similar gradient of risk has been detected in the OSTPRE study (RR =1.8) (Huopio et al. Osteoporosis Int 2000)
Alcohol

• The amount of weekly alcohol intake was higher in fracture cases than non-fracture cases (OR=1.45)(n=3140) (Tuppurainen et al. Acta Obstet Gyn 1995)

• Physician diagnosed alcoholism increases fracture risk substantially (RR=3.5) (Huopio et al. Osteoporosis Int 2005)

• Low to moderate alcohol intake is associated with better femoral neck (12 %) and spinal (9 %) BMD (Sommer et al. Public Health Nutr 2013)
Fracture history

• Studies of peri- and postmenopausal women with prior fractures had 2.0 times the risk of subsequent fracture compared with women without prior fractures (Klotzbuecher et al. JBMR 2000)

• A previous fracture history was associated with a significantly increased risk of any fracture compared with individuals without a prior fracture (RR = 1.86; 95% CI = 1.75–1.98) (Kanis et al. Bone 2004- OSTPRE included)
  – The risk ratio was similar for the outcome of osteoporotic fracture or for hip fracture.
  – There was no significant difference in risk ratio between men and women.
  – Low BMD explained a minority of the risk for any fracture (8%) and for hip fracture (22%)
Fracture cascade

- **Wrist fracture**: x 2 the risk of
- **Vertebral fracture**: x 5 the risk of
- **Hip fracture***: x 2 the risk of

* In the case of hip fracture, most deaths occur in the first 3-6 months following the event, of which 20-30% are causally related to the fracture event itself.

References:

Family History of Fracture

• A family history of hip fracture in parents was associated with a significant risk both of all osteoporotic fracture (RR 1.54) and of hip fracture (RR = 2.27) The risk was not significantly changed when BMD was added to the model (Kanis et al. Meta-analysis, Bone 2004)

• Sister’s fracture history indicates higher fracture risk compared to fractures of other first degree relatives (Sirola et al. Osteoporosis Int 2009)
Table 5 Clinical risk factors used for the assessment of fracture probability ([8] with permission from the WHO Collaborating Centre, University of Sheffield, UK)

<table>
<thead>
<tr>
<th>Risk Factor</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age</td>
</tr>
<tr>
<td>Sex</td>
</tr>
<tr>
<td>Low body mass index</td>
</tr>
<tr>
<td>Previous fragility fracture, particularly of the hip, wrist and spine,</td>
</tr>
<tr>
<td>including morphometric vertebral fracture in adult life</td>
</tr>
<tr>
<td>Parental history of hip fracture</td>
</tr>
<tr>
<td>Glucocorticoid treatment (≥5 mg prednisolone daily or equivalent for 3 months or more)</td>
</tr>
<tr>
<td>Current smoking</td>
</tr>
<tr>
<td>Alcohol intake 3 or more units daily</td>
</tr>
</tbody>
</table>

Causes of secondary osteoporosis

- Rheumatoid arthritis
- Untreated hypogonadism in men and women, e.g. premature menopause, bilateral oophorectomy or orchidectomy, anorexia nervosa, chemotherapy for breast cancer, hypopituitarism, androgen deprivation therapy in men with prostate cancer
- Inflammatory bowel disease, e.g. Crohn's disease and ulcerative colitis. It should be noted that the risk is in part dependent on the use of glucocorticoids, but an independent risk remains after adjustment for glucocorticoid exposure.
- Prolonged immobility, e.g. spinal cord injury, Parkinson's disease, stroke, muscular dystrophy, ankylosing spondylitis
- Organ transplantation
- Type 1 and type 2 diabetes
- Thyroid disorders, e.g. untreated hyperthyroidism, thyroid hormone suppressive therapy
- Chronic obstructive pulmonary disease
Glucocorticoids, RA, Asthma

Chronic Health Disorders

- 3078 women aged 47-56 years, follow-up 3.6 years, 276 fractures, physician diagnosed chronic diseases, drug reimbursement register

- **Adjusted HR for fracture**
  - Hypertension, HR 1.4 (1.1-1.9)
  - Hypertension + obesity, HR 2.0 (1.4-3.0)
  - Coronary heart disease, HR 1.8 (1.1-2.8)
  - Hyperthyroidism, HR 1.7 (1.0-2.9)
  - Epilepsy, HR 2.0 (1.1-3.6)
  - Alcoholism, HR 3.5 (1.3-9.5)
  - Chronic hepatic disease, HR 5.2 (1.7-16.4)

_Huopio et al. Osteoporosis Int 2005_
Hormone Related Risk Factors for Fractures

- Menopause increases fracture risk (Tuppurainen et al. Maturitas 1993)

- Non-use/Use of hormone therapy
  - In early postmenopausal women, HRT use > 6 months during a 5-yr follow-up decreased the fracture risk significantly (HR 0.49-0.74)(n=7217) (Randell et al. JBMR 2002)
  - 5-year HRT prevents non-vertebral fractures in non-osteoporotic postmenopausal women in comparison with placebo (RR 0.29)(n=464) (Komulainen et al. Maturitas 1998)
  - Estrogen receptor alpha genotype modulates the protective effect of HRT on fracture risk (Salmen et al. JBMR 2000)
Bone Mineral Density

• Before 1995 there was a lack of prospective studies on the usefulness of BMD at the time of menopause
• A total of 3222 women (mean age 53.4, 47-59) were followed for fractures over a period of 2 years (mean 2.4 years)
• 183 fractures occurred in 168 women (wrist 47, ankle 31, rib 28..)
• RR for suffering from any fx per 1 SD decrease in spine BMD was 1.5 and in femoral neck 1.4
• DXA at the time of menopause predicts fracture risk
• Our subsequent studies have confirmed this finding

Kröger et al. JBMR 1995
Bone Ultrasound

• Several studies have shown that peripheral bone ultrasound measurement predicts fractures in elderly women

• 420 women (mean age 59.6) underwent calcaneal US measurement and were followed for a mean of 2.6 years; 32 fractures were detected

• US predicted fracture even after adjustment of BMD (HRs for 1 SD decrease of SOS and BUA were 1.8 and 1.4, respectively)

• Recent meta-analysis reported similar HRs (McCloskey et al. Osteopor Int 2015)

Huopio et al. Osteopor Int 2004
Novel Technologies

- Trabecular bone score from Spinal DXA images (TBS) (Silva et al. JBMR 2013)
- Radiographic texture analysis (Thevenot et al. JBMR 2013)
- Reference point intendation (Diez-Perez et al. 2010)
- Cortical thickness mapping (Poole et al PLoS One 2012)
- 3D-DXA-FEA (Väänänen et al. Biomech Model Mechanobiol 2011)
- Bindex (Karjalainen et al. Osteoporosis Int 2012)
Bindex®

- Measures cortical bone thickness at the tibial and radius shaft and gives an estimate from proximal femur BMD (Density Index, DI)

When used with FRAX, only 30% of subjects will need axial DXA measurement, compared with the standard protocol (69 vs. 244 /448)

Karjalainen et al. Osteoporos Int 2012
Karjalainen et al. Osteoporosis Int (submitted)
Physical activity

- Physical activity is associated with lower femoral bone loss but it may predispose to wrist fractures in elderly women (Rikkonen et al. JBMR 2010)
  - 8560 women (mean age 52.2) 15 yr follow-up
  - 2641 follow-up fractures
  - HR for wrist fracture 1-2-1.4 in active quartiles
  - 2.1 x higher rate of wrist fx in winter months (Nov-Apr)

- Postural balance predicts falls and fractures (Salonen et al. manuscript)
Functional tests and Fractures

- A total of 2,928 postmenopausal women took part in the functional capacity and muscle strength tests (5 yr time point). The duration of fracture follow-up varied from 6.43 to 9.86 (mean 8.37) years. A total of 261 end-point fractures occurred.

**Results:**
- Inability to stand-on-one-foot for 10 seconds increased the risk (HR) of hip fracture 9.11-fold (1.98-42.00).
- Decreased grip strength associated with 1.05-fold (1.01-1.09) increased risk of hip fractures.
- Low leg extension strength associated with 1.02-fold (1.00-1.03) higher risk for all fractures.
- The self-assessed ability to walk less than 100 meters at baseline increased the risk of ankle 2.36-fold (1.10-5.08), hip 11.57-fold (2.73-49.15) and clinical vertebral fractures 3.85-fold (1.45-10.22).

- According to these results the standing-on-one-foot less than 10 seconds, grip strength and a question about ability to walk less than 100 meters may help to predict postmenopausal fractures *(Kärkkäinen et al. Osteoporosis Int 2008)*.

- Functional capacity was decreased in women with femoral neck osteoporosis (WHO classification) compared to women with normal or osteopenic BMD: SOOF -39% (p=0.001), GS -18% (p<0.001), leg extension strength -19% (p=0.007) and ability to squat down on the floor -40% (p=0.004) *(Kärkkäinen et al. Bone 2009)*.
RESULTS

- Altogether 56.9% of the women had none of the three risk factors indicating functional decline and were regarded as a reference group.
- All cause mortality was 9.2% (n=258).
- Total number of fractures 578, including 35 hip fractures.
- Mortality (RR 1.4-2.7) and hip fracture incidence (RR 3.3-8.4) were significantly higher in women with any functional decline (n=1204, Blue) than women without decline (n=1587, Green).
BMD and Cumulative Risk Factors

- 3068 perimenopausal women (47-56 yr)
- 295 fractures, mean follow-up 3.6 years
- Independent risk factors for fracture (Adjusted RRs)
  - Low BMD (1 SD), RR 1.3-1.4
  - Fracture history, RR 1.7-1.9
  - Chronic illnesses (>3), RR 1.4-1.6
  - Non use of HT, RR 1.5-2.2
  - Smoking, RR 1.8

Huopio et al. Osteopor Int 2000
Table 1. Characteristics of the total study population (n = 3068) and random sample (n = 1931) at baseline in fracture and nonfracture groups

<table>
<thead>
<tr>
<th>Variable</th>
<th>Fracture cases</th>
<th>Nonfracture cases</th>
<th>p value(^a)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Total study population</strong></td>
<td>(n = 257)</td>
<td>(n = 2811)</td>
<td></td>
</tr>
<tr>
<td>Age (years)</td>
<td>53.5 (53.1–53.9)</td>
<td>53.4 (53.3–53.5)</td>
<td>0.532</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>68.1 (66.6–69.5)</td>
<td>69.1 (68.6–69.5)</td>
<td>0.212</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>160.9 (160.3–161.6)</td>
<td>161.2 (161.0–161.4)</td>
<td>0.422</td>
</tr>
<tr>
<td>Menarchal age (years)</td>
<td>13.7 (13.5–13.9)</td>
<td>13.7 (13.7–13.8)</td>
<td>0.742</td>
</tr>
<tr>
<td>Postmenopausal (%)</td>
<td>73.8</td>
<td>69.0</td>
<td>0.121</td>
</tr>
<tr>
<td>Spinal BMD (g/cm(^2))</td>
<td>1.064 (1.045–1.083)</td>
<td>1.135 (1.129–1.141)</td>
<td>0.000</td>
</tr>
<tr>
<td>Femoral neck BMD (g/cm(^2))</td>
<td>0.885 (0.870–0.901)</td>
<td>0.932 (0.927–0.937)</td>
<td>0.000</td>
</tr>
<tr>
<td>HRT use (%)</td>
<td>18.7</td>
<td>26.7</td>
<td>0.006</td>
</tr>
<tr>
<td>HRT duration (years)</td>
<td>2.5 (2.0–3.1)</td>
<td>2.8 (2.7–3.0)</td>
<td>0.281</td>
</tr>
<tr>
<td>Previous fracture history (%)</td>
<td>34.6</td>
<td>21.4</td>
<td>0.000</td>
</tr>
<tr>
<td>Maternal hip fracture (%)</td>
<td>6.3</td>
<td>6.0</td>
<td>0.858</td>
</tr>
<tr>
<td>Dietary calcium intake (g/day)</td>
<td>748 (698–798)</td>
<td>799 (784–813)</td>
<td>0.048</td>
</tr>
<tr>
<td>Alcohol users (%)</td>
<td>40.9</td>
<td>38.6</td>
<td>0.470</td>
</tr>
<tr>
<td>Daily coffee intake (cups)</td>
<td>4.3 (4.0–4.5)</td>
<td>4.3 (4.2–4.3)</td>
<td>0.942</td>
</tr>
<tr>
<td>Regular smokers (%)</td>
<td>15.6</td>
<td>11.1</td>
<td>0.038</td>
</tr>
<tr>
<td>Women with three or more physician-diagnosed chronic illnesses (%)</td>
<td>20.2</td>
<td>15.0</td>
<td>0.027</td>
</tr>
</tbody>
</table>

Table 3. Relative risk estimates (RR) of risk factors at baseline for all follow-up fractures

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Total study population (n = 3068)</th>
<th></th>
<th>Random population (n = 1931)</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Unadjusted RR (95% CI)</td>
<td>Adjusted RR(^a) (95% CI)</td>
<td>Unadjusted RR (95% CI)</td>
<td>Adjusted RR(^a) (95% CI)</td>
</tr>
<tr>
<td>Previous fracture history (yes vs no)</td>
<td>1.89 (1.45–2.45)</td>
<td>1.68 (1.24–2.23)</td>
<td>1.52 (1.06–2.17)</td>
<td>1.33 (0.94–1.88)</td>
</tr>
<tr>
<td>HRT (no vs yes)</td>
<td>1.54 (1.14–2.13)</td>
<td>1.52 (1.06–2.17)</td>
<td>1.59 (1.06–2.37)</td>
<td>1.46 (0.99–2.16)</td>
</tr>
<tr>
<td>Spinal BMD (per 1 SD decrease)</td>
<td>1.51 (1.33–1.71)</td>
<td>1.43 (1.27–1.64)</td>
<td>1.50 (1.27–1.77)</td>
<td>1.46 (1.25–1.71)</td>
</tr>
<tr>
<td>Femoral neck BMD (per 1 SD decrease)</td>
<td>1.45 (1.28–1.65)</td>
<td>1.39 (1.23–1.59)</td>
<td>1.41 (1.20–1.66)</td>
<td>1.50 (1.26–1.79)</td>
</tr>
<tr>
<td>Three or more chronic illnesses (yes vs no)</td>
<td>1.43 (1.06–1.94)</td>
<td>1.37 (1.00–1.87)</td>
<td>1.08 (0.69–1.69)</td>
<td>0.94 (0.60–1.47)</td>
</tr>
<tr>
<td>Smoking at baseline (yes vs no)</td>
<td>1.47 (1.05–2.06)</td>
<td>1.36 (0.97–1.91)</td>
<td>1.18 (0.70–2.00)</td>
<td>1.12 (0.68–1.87)</td>
</tr>
<tr>
<td>Dietary calcium intake (per 1 quartile decrease)</td>
<td>1.16 (1.03–1.30)</td>
<td>1.10 (0.99–1.23)</td>
<td>0.87 (0.75–1.01)</td>
<td>0.89 (0.77–1.02)</td>
</tr>
<tr>
<td>Post- vs premenopausal</td>
<td>1.21 (0.92–1.61)</td>
<td>0.89 (0.65–1.21)</td>
<td>1.41 (0.98–2.01)</td>
<td>1.04 (0.70–1.55)</td>
</tr>
<tr>
<td>Age at baseline</td>
<td>1.02 (0.97–1.07)</td>
<td>1.00 (0.95–1.04)</td>
<td>1.03 (0.97–1.08)</td>
<td>0.99 (0.93–1.04)</td>
</tr>
<tr>
<td>Weight at baseline (per 1 kg increase)</td>
<td>0.99 (0.98–1.00)</td>
<td>1.01 (0.99–1.02)</td>
<td>1.00 (0.99–1.01)</td>
<td>1.02 (1.00–1.03)</td>
</tr>
<tr>
<td>Height at baseline (per 1 cm increase)</td>
<td>0.99 (0.97–1.01)</td>
<td>1.00 (0.98–1.03)</td>
<td>1.00 (0.97–1.03)</td>
<td>1.00 (0.97–1.04)</td>
</tr>
<tr>
<td>Maternal hip fracture (yes vs no)</td>
<td>1.05 (0.63–1.73)</td>
<td>0.91 (0.53–1.57)</td>
<td>1.60 (0.91–2.82)</td>
<td>1.47 (0.86–2.51)</td>
</tr>
</tbody>
</table>

\(^a\) Adjusted for age, weight, height, menopausal status, BMD, previous fracture history, maternal hip fracture, use of HRT, smoking, calcium intake and multiple chronic health disorders.
Bone Density and Cumulative Risk Factors
- Kuopio Osteoporosis Study (OSTPRE)-

Huopio et al. Osteopor Int 2000
Calcium and Vitamin D

- Calcium and Vitamin D supplementation prevents recurrent/multiple falls and falls requiring medical attention falls in postmenopausal women
- The supplementation increases total body BMD
- The supplementation did not prevent fractures in home-living Eastern Finland women aged 65-75 years who have good nutritional Ca and moderate nutritional vitD intakes

Kärkkäinen et al. Osteoporosis Int 2010, Maturitas 2010 - Salovaara et al. JBMR 2010
• The OSTPRE –study has contributed in many ways to clinical practice in Finland and internationally
  – Validation and development of FRAX Finland
  – Osteoporosis Guidelines in Finland (2014)
  – Meta-analyses, textbook chapters
Meta-analyses – OSTPRE included

- Kanis JA et al. Smoking and fracture risk: a meta-analysis. Osteoporos Int 2005
- Johnell O et al. Predictive value of BMD for hip and other fractures. J Bone Miner Res 2005
Lake Laatokka, Carelia 2015
KUOPIO OSTEOPOROSIS STUDY (OSTPRE)

Kuopio Province in Eastern Finland
All women aged 47-56 years (N=14,220)
Baseline postal enquiry in 1989

Random stratified sample of 3222 women DXA and functional test follow up in five year intervals 1989-2009

Complete data of 2791 women with 15 year follow-up (1994-2009)
✓ Questionnaires, DXA, functional tests
✓ Fracture and cause of death registries

ADDITIONAL DATA
Fracture validation
Functional tests
Falls

NATIONAL REGISTRIES
- Hip fractures
- Mortality
- ICD outcomes

ASBMR Poster: FR0455
RESULTS

- Altogether 56.9% of the women had none of the three risk factors indicating functional decline and were regarded as a reference group.
- All cause mortality was 9.2% (n=258),
- Total number of fractures 578, including 35 hip fractures.
- Mortality (RR 1.4-2.7) and hip fracture incidence (RR 3.3-8.4) were significantly higher in women with any functional decline (n=1204, Blue) than women without decline (n=1587, Green).

![Graph showing cumulative mortality and hip fracture incidence over follow-up years with Logrank test p-values 0.001 and <0.001 respectively.]