Health-related risk factors for falls among early post-menopausal women.

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1 Introduction

By 2014, the world population has reached about 7 billion (Census Bureau). Estimation by World Health Organization reported that between 2000 and 2050, the proportion of the world’s population over 60 years will double from 11% to 22% (WHO; 2014). This demographic pressure is driving different health care needs, such as increased number of falls (WHO; 2014).

Older adults become more susceptible to falls for many reasons, such as age-related physical changes and co-morbidities. Due to physiological change in cardiovascular reflexes, there is orthostatic hypotension in the elderly. Visual and vestibular impairments result in further loss of postural control and increased dizziness symptoms and the situation is aggravated due to decreased proprioceptive sensitivity. In addition to these age-related changes, co-morbidities such as arthritis, stroke, diabetes, hypertension, heart diseases, or dementia and Parkinson disease in the elderly also add an additional burden through disease-specific impairments which all together impact on an older adult’s ability to perform activities of daily living (Boss, Seegmiller 1981).

Though estimation of fall rates varies widely and is related to several factors, about 30% of the women aged 65 and older, and 50% of those aged 85 and older, will fall each year (Lamb, Jørstad-Stein et al. 2005, Tinetti, Speechley et al. 1988). Approximately, 20% of old people’s falls require medical attention and 6-23% of those falling will suffer serious injuries and only about half of the old people, who fall and require hospitalization, will be alive a year later (Rubenstein 2006). Thus, fall is a major public health problem in the rapidly aging global population, and constitutes the leading cause of injury in Finland (Honkanen 1990) limiting temporarily or permanently functional ability of the victim with eventual health and socioeconomic consequences (Rhalimi, Helou et al. 2009). Consequences of falling include fear of falling, loss of confidence as to mobility and the ability to live independently and eventual institutional relocation (Bueno-Cavanillas, Padilla-Ruiz et al. 2000). There can also be equally devastating emotional and psychological effects for the individual who fell and for his or her family members (Huang, Mallet et al. 2012). Indeed, high incidence rate of falls also indicates high health care costs. For example; the fractures produced by falls in the elderly cost about 10 billion dollars a year in US alone (Rubenstein 2006).
In Finland, as in many other developed countries, aging population is continuously creating increasing demands on the health care system and falls are the number one cause of injury deaths (Causes of Death, 2007). The number of deaths due to falls increased from 162 to 627 in older Finnish men and from 279 to 499 in older Finnish women between the years 1971-2009. The prediction about the growing fall death figures is likely to emphasize the increasing fall burden so that by the year 2030, the number of fall induced deaths may double among older Finns. To meet this huge burden, research related to risk factors for falls and fall related injuries is very important (Korhonen, Kannus et al. 2013).

To reduce the incidence and burden of falls, several studies have been conducted to see the common risk factors for falls. Most of these risk factor studies have been small cross-sectional studies with unrepresentative samples which are methodologically weaker than population-based prospective studies. As causes of falls in the elderly are multifactorial, it is relevant to analyze risk factors with large study populations and long follow-up periods. Numbers of conducted prospective studies are comparatively smaller than other studies (Barrett-Connor, Weiss et al. 2009). Again, most of those prospective cohort studies have assessed the one or few risk factors for falling in older adults. With the individual risk factors for falls, it could be a new area of thinking how two or more risk factors jointly affect falling risk in postmenopausal women before old age and if these effects are similar on falls due to slipping as on falls due to other mechanisms (Cesari, Landi et al. 2002).

This thesis is a part of the OSTPRE study (Kuopio Osteoporosis Risk Factors and Prevention Study), which is a longitudinal prospective cohort study with 25-year follow-up and 90% high response rates from repeated follow-up inquiries and had a large baseline target population of 14,220 peri and post-menopausal women in 1989. This cohort is suitable enough for the assessment of roles of health-related risk factors in causation of falls in postmenopausal women before old age (BCRU/OSTPRE).

2 Literature Review

2.1 Definition of fall

According to WHO, a fall is defined as an event which results in a person coming to rest inadvertently on the ground or floor or other lower level (ICD 10 Edition). Former researchers have defined fall also in different ways; for example, an unintentional change in position to a lower level
without an overwhelming hazard (Tinetti, Speechley et al. 1988), as unintentional descent to the floor or ground in a conscious patient (Morse, Tylko et al. 1987) or as loss of balance such that hands, arms, knees, bottom, or body touch or hit the ground or floor (Horbrook, Stevens et al. 1994). Recurrent falls have been defined as at least two falls taking place during one year or as at least falls during a period of six months by (Tinetti 1987) and (Lord, Ward et al. 1994).

2.2 Incidence of falls

About one third of persons aged 65 years or more experience one or more falls annually. However, the incidence of falling events may be about 1500 events/1000 person years, especially among the elderly living in the institutions. The proportion of falls is increasing with age. Falls are reported more frequently in women than men (Campbell, Reinken et al. 1981, Gryfe, Amies et al. 1977, Tinetti, Speechley et al. 1988, O’Loughlin, Robitaille et al. 1993).

2.3 Causes of falls

Numerous studies have analyzed fall events in several ways and have identified various potential causal factors for falls. Some studies classified these factors into extrinsic (modifiable) and intrinsic (non-modifiable) factors. The extrinsic factors include factors which are associated with environment like, poor foot wear, unsafe foot wear as well as unsafe environment whereas the intrinsic causal category includes age related causes and co-morbidity such as decreased functional skills, weakness of lower extremity, neurological conditions, diminished cognitive function, reduced vision and hearing, low blood pressure, acute illness and medication use (Huang, Mallet et al. 2012). Metabolic disorders, anemia, dehydration, cardiopulmonary disorders may also contribute to the increased risk of falls (Akyol 2007). Both extrinsic and intrinsic factors may be permanent or temporary. The role of temporary factors such as disease attack, alcohol intoxication, medication, tiredness, sporting or slippery weather condition as a causative factor for falls is more difficult estimate than the role of permanent factors (Stenhagen, Ekström et al. 2013). Some other study summarized all the factors and classified these into 4 groups: socio-demographic factors, factors related to age, environmental factors and factors related to behaviors (Rhalimi, Helou et al. 2009).
2.4 Risk factors for falls

2.4.1 Health disorders

Association between falls and chronic diseases has been investigated in several studies. The prevalence of falls increases with increasing number of chronic diseases and chronic diseases are important predictors of falling in elderly population, especially in women (Lawlor 2003). Falls are more frequent among patients with neurological impairments with or without connection to gait and balance. The etiology of falls in neurological diseases is multifactorial; there may be a connection between falls and disturbances of sensorimotor system in elderly patients with neurological diseases (Homann 2013).

The risk of falling is increased in many diseases; Parkinsonism is one of the best examples as falling and its consequences are magnified due to strong association between falling and disease severity (Ashburn, Stack et al. 2001). Reasons for falling in Parkinson disease are postural instability, changing posture, involuntary movements, orthostatic hypotension, postprandial hypotension etc. There could be a role for the autonomic nervous system in the genesis of falls in patients with Parkinsonism (Martignoni 2006). Falls are also common in Alzheimer patients; risk of falls was twice as high as in normal age-matched population in a study conducted by Horikawa, Matsui et al (2005). According to their study, a provable reason for falls in Alzheimer disease was periventricular white matter lesions (Horikawa, Matsui et al. 2005).

Several studies reported increased incidence of falls among elderly individuals with mental health condition such as dementia or Alzheimer disease (Finkelstein 2007). Ballard (1999) investigated the potential association of falls in elderly dementia patients; multiple falls were reported by patients with Levy body dementia and Alzheimer disease (LBD) (Ballard 1999). Increased occurrence of falls was also reported among dementia patients with sleep disturbance (Eshkoor 2013). In cerebral ataxia patient, gait variability has been found to be a good predictor for falls in elderly population with neurodegenerative disorders (Schniepp 2014).

One study investigated the relationship between disease-related factors and balance and a history of falls in patients with chronic obstructive pulmonary disease (COPD). According to their results, in COPD patients, hypoxia, dyspnea and fatigue were diseases-related factors which are associated with balance impairments, eventually resulting in falls (Ozalevli 2011). Slowing of gait speed due to altered cerebral blood flow was found to be associated with the development of falls (Sorond,
Impaired vision, poor walking condition were also reported as independent risk factors for falls in another study (Hiura 2012). Chronic musculoskeletal pain contributes to functional decline and muscle weakness that could result in a greater risk of falls in older adults (Leveille, Jones et al. 2009).

Peripheral vestibular disorders have been found to be important predictors for falls in older adults due to their association with an increased number of falls (Liston 2014). A history of cognitive impairment can be a strong risk factor for recurrent falls particularly affecting the short term memory, recall and visuospatial perception which may lead to an increased risk of recurrent falls (Chen 2011).

2.4.2 Medications

Medication use remains another important factor for falling in the elderly. Pharmacokinetic and pharmaco-dynamic properties of drugs change with aging. There is an increase in total body fat of 18-36% in older adults which results in increased half-life of some medications (long-acting benzodiazepines, antipsychotic and antidepressants) and prolonged time to exert their effects and potential adverse effects. The proportion of TBW (total body water) shrinks by 10-15% which can affect the apparent volume of distribution for some drugs (digoxin, lithium and diuretics). There is also 15-20% reduction of serum albumin concentration, especially in malnourished elderly individuals. Drugs (phenytoin, valproic acid and flurazepam), which are highly protein-bound can potentially exert their side effects more frequently in elderly patients with low serum albumin (Rhalimi, Helou et al. 2009).

In older patients, the risk related to the use of medication is important to investigate because of the morbid consequences and adverse drug effects like, postural hypotension, cognitive changes, dizziness etc. Also, a drug’s action is rarely limited to effects on targeted endpoint and systemic side effects are common. Especially in the elderly, medication effects need to be considered from a broader perspective than merely from the benefits and harms of an individual medication for an individual disease. So, it is important to understand how drug uses affect symptoms (dizziness, postural hypotension and psychomotor performance) resulting in an adverse outcome such as falls (Agostini, Tinetti 2002).
2.4.2.1 Type of medications

Several studies identified a common set of medications that are associated with falls. The term “fall-risk increasing drug” (FRIDS) has been used by Van der Velde et al. and subsequently by K Ragh et al to identify medications that are associated with falls as well fracture in older adults. FRIDS include drugs for cardiovascular diseases; (digoxin, type 1a anti-arrhythmic and diuretics) benzodiazepines, antidepressant, anti-epileptic, anti-parkinsonism drugs, opioids and urological spasmolytic drugs (Huang, Mallet et al. 2012). Uses of FRIDS increase the falling risks in older population (Rhalimi, Helou et al. 2009).

Among FRIDS, antidepressants show a constant association with fall. Use of antidepressant has an increased risk of outdoor falls due to several adverse effects like orthostatic hypotension, blurred vision, dizziness, constipation, urinary retention, confusion and cardiovascular problems among older adults (Quach 2013). Again, psychiatric medications are associated with the risk of hyponatremia, resulting from inappropriate secretion of antidiuretic hormone which may cause chronic hyponatremia contributing to an increased risk of falls by impairment of attention, posture and gate mechanisms (Siegel 2008).

Use of psychotropic medication with previous falling history and chronic health disorders such as peripheral sensory deficit may be important predictors of recurrent falls (Luukinen, Koski et al. 1995).

2.4.2.2 Poly-pharmacy (use of more than three medications)

Older adults use more medications because of the co-existence of multiple diseases. Poly-pharmacy is regarded as an important risk factor for falling because prevalence of falls is strongly associated with increasing age and number of drugs used per day (Linjakumpu, Hartikainen et al. 2002). Increase in number of medications (poly pharmacy) and fall-risk increasing drugs (FRIDS) increase the falling risks (Ziere, Dieleman et al. 2006) and poly-pharmacy is reported more 0in women than men (Linjakumpu, Hartikainen et al. 2002).

2.4.3 Anthropometry
Women after menopause have an increased tendency to gain weight. There is evidence that obesity plays a role in falls in old age. Obesity has also been found to be related to certain types of fractures such as ankle fracture (Valtola, Honkanen et al. 2002). Abnormal distribution of the body fat in the abdominal fat may be a higher risk of falls in obese population (Corbeil, Simoneau et al. 2001). Obesity may result in lower levels of physical activity, greater levels of pain, leading to postural balance problems, higher parathyroid hormones in individuals with diabetes mellitus and vitamin D deficiency (Himes 2012). Obesity can lead to higher risk of depression; lower health related quality of life and is therefore associated with an increased incidence of falls (Fjeldstad, Fjeldstad et al. 2008).

2.4.4 Falling and fracture history

Individual risk of falling can be increased with history of previous falls and fracture (Schwartz 2013). The risk of multiple non-syncopal falls have been reported among older persons with a history of a previous fall (Nevitt, Cummings et al. 1989, Nitz 2013)

2.4.5 Health behavior and life style

2.4.5.1 Dietary Calcium Intake

Inadequate nutritional intake is common in the elderly which results in malnutrition and often remains unrecognized. Several nutrients and nutritional indicators (low dietary intake of vitamins and minerals) have been associated with impaired muscle mass and function. Malnutrition has been found to be a risk factor for falls in the elderly aged 65 and older with impaired daily activity (Neyens, Halfens et al. 2012).

Many studies suggested that dietary calcium deficiency may be associated with reduced ability to maintain balance and falls. Dharmarajan (2005) has found a relation of calcium and vitamin D deficiency to falls in older adults. The research study was prospective where community dwelling adults aged <60 years with vitamin deficiency, gait imbalance, history of previous falls, musculoskeletal pain were enrolled for physical examination including blood samples for vitamin D assay. Vitamin D deficiency was observed in adults with gait imbalance and falls. Their results also indicate that vitamin D deficiency is associated with substantial disability and calcium and vitamin D supplements are effective to restore the optimal vitamin D level to reduce number of falls in the elderly (Dharmarajan 2005).
A prospective cohort study involving several elderly women discovered that vitamin D deficiency is an independent predictor of falls in residential care (Flicker 2003). It is hypothesized that change in vitamin D may play a role in decreased physical performance and falls (Buitrago, Vazquez et al. 2000). Vitamin D deficiency is very common in women due to decreased dietary intake, diminished sunlight exposure, reduced skin thickness and impaired intestinal absorption. Deficiency of vitamin D may cause muscle weakness resulting in falls of the elderly, while supplementation can preserve muscle strength and functional ability (Janssen, Samson et al. 2002).

2.4.5.2 Alcohol

Honkanen et al found in a matched case-control study that blood alcohol concentration of above 0.5 g/l was strongly related to falling risk, which increased linearly with increasing blood alcohol level (Honkanen, Ertama et al. 1983). Self-report of alcohol drinking and its possible association with falls has been investigated in several studies. Sorok et al (2006) performed a case-control study using 1735 cases that died of falls and representative control sample (n=13,381) of the U.S. population aged 55 years or older from the 1992 National Longitudinal Alcohol Epidemiologic Survey. After adjustment for age, gender, education and marital status, the study found that drinking history was associated with increased risk of fatal injury from falls in elderly population (Sorock 2006). Several studies considered increased alcohol consumption as a potential cause of falls and fall related injuries (Malmivaara, Heliovaara et al. 1993) whereas other studies found the magnitude of risk of alcohol use for falls or falls-related injuries uncertain (Reid 2002). At the same time, self-reported alcohol consumption has not been found not to be related to an increased risk for falling in several studies. (ILIFFE, HAINES et al. 1991).

2.4.5.3 Smoking

The health consequences of smoking are several. Some cross-sectional studies suggested that smoking is a risk factor for decreased muscle strength leading to a decrease of physical performance in elderly postmenopausal women (Rapuri, Gallagher et al. 2007) and muscle weakness especially in lower extremity is a risk factor for falls (Moreland, Richardson et al. 2004).

The vitamin D-parathyroid hormone system plays an important part in calcium homeostasis and bone mineralization. It has been found that higher serum vitamin D concentration is associated with lower risk of falls in older women (Faulkner, Cauley et al. 2006) and smoking may alter hepatic
metabolism of vitamin D which can adversely affect this vitamin D-parathyroid hormone system and increase falling risk (Yoon, Maalouf et al. 2012). Smoking has significant association with increased fracture risk in postmenopausal women (Kanis, Johnell et al. 2005).

2.4.5.4 Physical Activity

Physical exercise may reduce the risk of falling. Any kind of exercise, even light exercise seems beneficial by improving quality of life and decreasing the risk of falling in elderly (Ekwall 2009). Gait improvement and confidence in walking can be observed in individuals with physical activity (Julius 2012). Regular physical activity has been found to be effective to gain strength, balance, and proprioception and gait improvement (Gillespie, Robertson, 2009). Improvement of the motor and cognitive function of the elderly with Alzheimer diseases (AD) has also been reported by some studies which can play a role in reducing falls in AD patients (Pedroso 2012).

2.4.6 Psychological factors

There are several psychological factors which may contribute to the increased risk of falls.

2.4.6.1 Fear of falling

Fear of falling is a very common serious phenomenon in older individuals (Tischler, Hobson 2005). Falls may cause fear of falling, fear of falling may cause falls and the two outcomes may be related to shared risk factors (Friedman, Munoz et al. 2002). It is hypothesized that higher degree of fear of falling results to poorer balance (de Guzman 2013). Impaired balance has been reported to play an important role in causing falls in the elderly (Binda, Culham et al. 2003). Fear of falling is also associated with decreased functional ability and quality of life in older adults. Older individuals with moderate health and wellbeing, depression and mobility restriction report high occurrence of falls. Fear of falling with reduced physical condition and loss of muscle strength may also result in increased falling risk (VELLAS, WAYNE et al. 1997). Association of fear of falling with mobility,
self-rated health, depression and well-being, poor balance, loss of balance confidence may increase falls in older population (Tiernan, 2014).

2.4.6.2 Life satisfaction

Subjective well-being measured with life satisfaction seems to be strongly related to health status, and also so that dissatisfaction predicts morbidity and mortality (Koivumaa-Honkanen H, 2000). So, as a whole subjective well-being may be a major factor in falls. Indeed, our preliminary report suggests also that life dissatisfaction predicts falls (Honkanen R, Koivumaa-Honkanen H et al 2007) whereas some other study suggests that falls predict a long-term reduction in health-related quality of life (HRQoL) and life satisfaction (LS) in general elderly population (Stenhagen, Ekström et al. 2014).

The relationship between falls and well-being among older adults has been well studied and its significance has been evaluated (Berglund, Ericsson 2003). Well-being is associated with balance score, muscle strength as well as functional mobility and increase in well-being is related with decreased falling risk (Ozcan, Donat et al. 2005). As a fall can cause fear of falling, loss of self-confidence and activity avoidance result in self-imposed functional limitation, which is related to lower subjective well-being and increased falling risk which may decrease quality of life (Cumming, Salkeld et al. 2000).

2.4.6.3 Depression

Depression is associated with falls in the elderly and there are several ways how depression and falls may be related. Depression may precede a fall or falls often bring depression and fear of falling (Tinetti, Speechley et al. 1988). There may be some common sets of risk factors that predict both falls and depression; poor self-rated health, poor cognitive function, impaired ADL (Activities of Daily living), two or more clinic visits in the past month and slow walking speed (Biderman, Cwikel et al. 2002). A patient with CSDS (Clinically significant depression symptoms) shows increased risk of both indoor and outdoor falls (Quach 2013). Among the institutionalized elderly, there is a very high risk of falling in the depressed elderly with clinical conditions and multiple medications (Wang 2012). A significant relationship of depression with fear of falling, anxiety, activity restriction may lead to increased falling risk (Painter 2012). Depression is a common condition in older people with health impairment and remains often undiagnosed and untreated
Higher depression level results in both increased fear of falling and risk of falling (Ni Mhaolain 2012).

2.4.7 Functional ability

Aging is characterized by gradual declines in physical and cognitive functions. There is a decline in muscle mass and muscle strength starting in middle age which ultimately results in functional disability and diminished physical performance. Diminished physical performance can result in falls and subsequent fractures, loss of independence with an increased mortality rate. At the early post-menopausal age, it is important to maintain functional ability (Shin, 2014).

2.4.8 Muscle strength

Falls are frequently occurring during daily activities. Individuals aged 80 years and older have a death rate from falls six times as high as that of younger adults due to several physiological changes that lead to physical weakness (Nelson, Rejeski et al. 2007). A major percentage of physical weakness associated with falls could be prevented by physical activity as multi-component and moderate intensity physical activity maintains greater strength, endurance, postural stability and functional capacity than sedentary life in older adults (Lobo 2012).

2.5 Preventive factors for falls

2.5.1 Intervention programs

Several intervention programs showed positive effects on falling and physical performance. Fall preventive moderate intensity exercise programs can decrease falling risk (Faber 2006). Falls among institutional care individuals can be reduced by exercise programs emphasizing physical fitness (DeSure 2013). Four and eight weeks of intensive Tai Chi training in the elderly has been
found to be effective in improving balance performance due to better vestibular ratio (Tsang, Hui-Chan 2004), whereas other studies found no effective value of tai chi training to reduce high prevalence of falls in elderly living at home (Logghe 2009). Community-based multifactorial falls prevention programs have significant effect in improving functional balance, muscle strength, mobility, as well as physical performance and reduced disability (Mitros 2011). There can be a relationship between increased knowledge of risk factors and increased confidence of performing activities of daily living, greater lower extremity strength and lower fall risk (Burk-Doe 2008).

2.5.2 Use of hormone replacement therapy

Women after menopause often experience several body composition changes such as decrease of lean body mass, increase in body fat mass or bone loss. These changes are believed to be caused by sudden decline in endogenous estrogen production at the time of menopause. It has been reported that decreased lean body mass with aging may contribute to falls and fractures. One third of postmenopausal women experience a fall annually. Among several consequences, 5-10% of falls result in a fracture and 80% of all non-spinal fractures in the elderly are due to a fall. Therefore, it has been hypothesized that menopausal hormone replacement therapy (HRT) may help to alter the body composition among postmenopausal women (Bea 2011).

Several studies have shown that HRT prevents early postmenopausal bone loss as well as has a beneficial effect on balance maintenance in the elderly whereas some study reported a negative effect. To determine the effects of postmenopausal estrogen use on the risk of falling along with muscle strength and neuromuscular function, the study of Osteoporotic Fractures examined 9704 participants aged 65 years or more with the measurements like gait speed, balance, self-reported functional disability etc. After adjusted for age, medications, medical history and personal habits, there was no significant difference in the incidence of falls between current HRT (Hormone replacement therapy) user and never users (Seeley, Cauley et al. 1995).

Randell et al conducted a study with 9792 younger postmenopausal women to see the association between HRT and falling risk. Data were collected from the OSTPRE (Kuopio Osteoporosis Risk Factors and Prevention Study) cohort, Finland. This study found current continuous HRT use as a protective factor only for early (i.e. menopause within less than 5 years) postmenopausal non-slip falls (Randell, Honkanen et al. 2001).

To understand the beneficial effect of HRT on postmenopausal body composition changes which may have association with fall and fracture, many studies have been conducted. Among them, the
WHI (Women Health Initiative) with ET (Estrogen Therapy) and EPT (Estrogen plus progesterone therapy) groups was the largest and longest lasting randomized trial. This double blinded, placebo-control trial was conducted at 40 WHI clinical centers in USA with active HRT and placebo groups of postmenopausal women between 50-79 years old. The study found no significant difference between active HRT and placebo group in either trial for change in lean body mass; and the relationship between HRT and fall risk was not altered by change in lean body mass. HRT showed an early benefit of preserved lean body mass but not in longer term and there was no significant relationship of HRT with decrease falling risk (Bea 2011).

### 2.5.3 Calcium and vitamin D

Several studies have demonstrated a strong relationship between calcium intake, bone mineral density and falls. (Dukas 2004) studied the effect of calcium supplements on fall risk in community dwelling elderly men and women with a randomized, double blinded, placebo-controlled intervention trial, in Switzerland. Dietary calcium intake was assessed at baseline and serum vitamin d and parathyroid hormone were assessed using radioimmunoassay among three hundred seventy-eight community dwelling elderly. Their results indicate that total calcium intake significantly reduces PTH and number of fallers (Dukas 2004). In malnourished older adults, short term nutritional intervention with calcium and vitamin D supplementation has been found to be effective in reducing falls (Neelemaat 2012). Supplementation with calcium has also been found to be a preventive factor for any kind of fractures (vertebral, non-vertebral) among elderly women (Johnston 1993).

### 3Aim of the study

Aim of this thesis was to investigate the health-related risk factors for falls in early postmenopausal women. More specifically, the aims were:

1. To investigate the association between chronic health disorders and risk factors for falls.
2. To study the association between use of medication and risk of falling.
3. To address several health behaviors as risk or preventive factors for falls in postmenopausal women.
4 Subjects and methods

4.1 Study population

The population (n=11495) for this longitudinal study was selected from the Kuopio Osteoporosis Risk Factor and Prevention (OSTPRE) study cohort.

The OSTPRE is a population-based prospective cohort study begun in 1989 with a target population of all the 14,220 peri- and postmenopausal women born in 1932-41 and resident in Kuopio Province, Eastern Finland. The baseline cohort has been followed with postal enquiries at 5-year intervals and this enquiry data is linked with data from national registries. The participating women have given their informed consent for the use of their health record data and the regional ethics committee has approved the study.

4.2 Study design

A total of 13100/14220 women responded to the baseline postal enquiry in 1989. The baseline enquiry was conducted using a structured questionnaire which included data on health-related factors such as health disorders diagnosed by a physician, prescribed medications, fractures, health behavior and gynecological factors.

At the 5 years follow up enquiry, a total of 11945/13100 women responded in 1994 for another structured questionnaire including data on falls during the preceding 12 months, number of falls and type of falls.

![Figure: The study design.](image)
In this study, follow-up included those who had responded to the baseline and 5-year follow-up enquiries. In total, 11945 women were selected to study the health-related risk factors for falls in early postmenopausal women.

4.3 Methods

In this study, fall has been defined as an unexpected unintentional event in which a person comes from standing to lying position. According to International Classification of Diseases (ICD), transport injuries such as falling with bicycle or falls while skating or skiing do not belong to falls. Falls have been studied in to two ways in this study population. They are frequent falling and nature of falls.

Frequent falling means that women fell at least twice in the preceding 12 months. As anyone can fall once, reported falls have been categorized in two categories: 0= no or one fall, 1= two or more falls. Falling data was obtained from the 5-year follow-up data.

The nature of falls means how women have been falling: slip fall or non-slip fall. Kuopio is situated on the 64 degree Northern latitude in Finland with snow for 5 months a year. Thus, slipping on ice is a common cause of injury in elderly women of Eastern Finland (Honkanen R et al 1983). As there are many falls due to slip falls in Finland, it is wise to compare the role of risk factors in slip falls and non-slip falls.

At the baseline, the participants were asked about their life style; dietary calcium intakes, smoking history, free time physical exercise, hours in physical activity, physical hardness at work and any work disability. Data of contraceptive use, hormone therapy, previous fracture history, number of surgeries, parity, number of miscarriages, number of health disorders and number of medications were also collected. From the 5-year follow-up enquiry, number of falls in the preceding 12 months as outcome variable and number of slip falls and non-slip falls were collected.

From the baseline enquiry, self-reports of chronic health disorders diagnosed by physician were obtained. For statistical analysis, the number of health disorders variable with 5 categories was formed: 0=women with no disease, 1=women with 1 disease, 2=women with 2 diseases, 3=women with 3 diseases and 4=women with 4 or more diseases. Reported diseases were classified according to the ICD -10. Data on the number of prescribed medications were similarly classified into 5 categories (0-4): 0=women with no medication, 1=women with 1 medication, 2=women with 2 medications, 3=women with 3 medications and 4=women with 4 or more medications.
To estimate the relative risk of falling related to selected health-related risk factors, the following covariates were considered: age, height, BMI, smoking history, previous fractures history, history of contraceptive use, hormone therapy use, use of medications, number of health disorders, physical exercise, hours in physical exercise, dietary calcium intake, work disability, physical hardness at work, history of live births and history of miscarriage.

### 4.4 Statistical analysis

Data were analyzed using the Statistical Package for Social Sciences (SPSS) version 19 (SPSS Inc., Chicago, IL, USA).

Frequency distributions have been determined for categorical variables and the mean, standard deviation and percentiles for continuous variables. To access (screen for or find out) the predictors of falls, univariate analyses were first carried out with cross-tabulation and chi square test for categorical data and with T-test for continuous data. Relative risks were estimated as Odds Ratios (OR) with 95% confidence intervals. Lastly, to estimate adjusted relative risks of falling, final multivariate logistic regression models were formed by entering into the model all variables which were statistically significant in univariate analysis.

The results were reported using odds ratio (OR) with 95% confidence intervals (95% CLs) and P value. The level of statistical significance was defined as p=0.05.
5 Results

5.1 Description of study population

The characteristics of study population (n= 11495) are shown in Table 1. At the baseline, the average age of the study population was 52.3 (range= 47-56 years, SD=2.9) years and 52.2% women were postmenopausal.

Table 1 Baseline Characteristics of 11495 women, in 1989. SD= Standard Deviation

<table>
<thead>
<tr>
<th>Baseline Characteristic</th>
<th>No or one falls, Mean (SD)</th>
<th>Two or more falls, Mean (SD)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Height, cm</td>
<td>161.3 (5.3)</td>
<td>161.2 (5.2)</td>
</tr>
<tr>
<td>Weight, kg</td>
<td>67.9 (11.6)</td>
<td>68.7 (11.9)</td>
</tr>
<tr>
<td>BMI, kg/m</td>
<td>26.1 (4.2)</td>
<td>26.4 (4.4)</td>
</tr>
<tr>
<td>Dietary Calcium intake, mg/d</td>
<td>821.1(394.5)</td>
<td>804.2 (406.3)</td>
</tr>
<tr>
<td>Contraceptive use, years</td>
<td>1.1 (2.6)</td>
<td>1.2 (2.7)</td>
</tr>
<tr>
<td>Hormone Therapy, up to 1994, years</td>
<td>2.4 (3.6)</td>
<td>2.4 (3.6)</td>
</tr>
<tr>
<td>Hormone Therapy, 1989–94, years</td>
<td>1.3 (1.9)</td>
<td>1.3 (1.9)</td>
</tr>
<tr>
<td>Free time exercise, hours/week</td>
<td>4.8 (3.3)</td>
<td>4.8 (3.3)</td>
</tr>
<tr>
<td>Year of last menstruation in 1994</td>
<td>86.9 (5.6)</td>
<td>86.8 (5.6)</td>
</tr>
<tr>
<td>Number of surgeries</td>
<td>0.6 (0.9)</td>
<td>0.7 (0.9)</td>
</tr>
<tr>
<td>Number of pregnancies</td>
<td>2.9 (1.8)</td>
<td>2.9 (2.0)</td>
</tr>
<tr>
<td>Number of miscarriages</td>
<td>1.0 (0.8)</td>
<td>1.1 (1.0)</td>
</tr>
<tr>
<td>Number of medications</td>
<td>1.0 (1.3)</td>
<td>1.2 (1.5)</td>
</tr>
<tr>
<td>Number of diseases, %</td>
<td></td>
<td></td>
</tr>
<tr>
<td>none</td>
<td>37.80 %</td>
<td>29.50 %</td>
</tr>
<tr>
<td>one</td>
<td>32.20 %</td>
<td>32.30 %</td>
</tr>
<tr>
<td>two</td>
<td>17.30 %</td>
<td>2.70 %</td>
</tr>
<tr>
<td>three</td>
<td>8.10 %</td>
<td>9.30 %</td>
</tr>
<tr>
<td>4+</td>
<td>4.50 %</td>
<td>7.10 %</td>
</tr>
</tbody>
</table>
5.2 Number and proportion of women with falls in preceding 12 months

The number and proportion of no fall, one fall, two or more falls in preceding 12 months are presented in Table 2 and for slip falls and non-slip falls are presented in Table 3.

**Table 2 Number (N) and proportion (%) of women with falls in 1994**

<table>
<thead>
<tr>
<th></th>
<th>N, (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>No fall</td>
<td>6761 (63.8 %)</td>
</tr>
<tr>
<td>One fall</td>
<td>1758 (16.6 %)</td>
</tr>
<tr>
<td>Two or more falls</td>
<td>2075 (19.6 %)</td>
</tr>
<tr>
<td>Total</td>
<td>10594 (100 %)</td>
</tr>
</tbody>
</table>

Missing information 1351/11945 (11.3%)

**Table 3 Number (N) and proportion (%) of women with falls according to nature of falls in 1994**

<table>
<thead>
<tr>
<th></th>
<th>N, (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Slip falls</td>
<td>2123 (19.6 %)</td>
</tr>
<tr>
<td>Non Slip falls</td>
<td>1383 (12.7 %)</td>
</tr>
</tbody>
</table>

5.3 Chronic health disorders and falls

5.3.1 Number of Diseases and falls
Altogether, there were 80.4% (n=8519) women who had **no or one fall** whereas 19.6% (n=2075) women had **two or more falls**. The association of number of chronic health disorders and number of falls was studied by cross-tabulation. After comparison with the healthy, it was found that the risk of falling (**two or more falls vs. no or one fall**) increased linearly when the number of health disorders increased (Table 4).

### Table 4 Number of chronic health disorders predicts falls

<table>
<thead>
<tr>
<th>Health Disorders</th>
<th>No or 1 fall (n, %)</th>
<th>2 or more falls (n, %)</th>
<th>(OR)</th>
<th>95 % CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No disease</td>
<td>3224 (84 %)</td>
<td>613 (16 %)</td>
<td>1,0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>With 1 disease</td>
<td>2745 (80,49 %)</td>
<td>670 (19,6 %)</td>
<td>1,28</td>
<td>1,1–1,4</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>With 2 diseases</td>
<td>1475 (76,6 %)</td>
<td>451 (23,4 %)</td>
<td>1,6</td>
<td>1,4–1,8</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>With 3 diseases</td>
<td>694 (78,2 %)</td>
<td>193 (21,8 %)</td>
<td>1,46</td>
<td>1,2–1,7</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>With 4 or more diseases</td>
<td>381 (72,0 %)</td>
<td>148 (28,0 %)</td>
<td>2,04</td>
<td>1,6–2,5</td>
<td>&lt;0,001</td>
</tr>
</tbody>
</table>

**Figure 1** Risk of falling (**odds ratio=OR**) related to the number of chronic health disorders

At the 5 years follow up enquiry, reported **slip falls** were more frequent than **non-slip falls** (Table 3). In cross tabulation analysis, **slip falls** showed a gradually decreasing trend with increasing number of diseases after comparing with the healthy group; risk of **slip falls** was less in women with 4 or more diseases (OR= 1,13) than in women with 1 disease (OR= 1,22) but the differences
are not statistically significant. The association of *slip falls* and number of chronic health disorders are presented in Table 5 as odd ratios (ORs) with 95% CI= 95% confidence intervals and p value.

Table 5 Association between number of chronic health disorders and *slip falls*

<table>
<thead>
<tr>
<th></th>
<th>No Slip falls (N, %)</th>
<th>Slip falls (N, %)</th>
<th>(OR)</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No disease</td>
<td>3204 (82.2 %)</td>
<td>692 (17.8 %)</td>
<td>1.0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>With 1 disease</td>
<td>2781 (79.1 %)</td>
<td>733 (20.9 %)</td>
<td>1.22</td>
<td>1.1-1.4</td>
<td>0.001</td>
</tr>
<tr>
<td>With 2 diseases</td>
<td>1583 (79.5 %)</td>
<td>409 (20.5 %)</td>
<td>1.19</td>
<td>1.0-1.4</td>
<td>0.01</td>
</tr>
<tr>
<td>With 3 diseases</td>
<td>721 (79.8 %)</td>
<td>183 (20.2 %)</td>
<td>1.17</td>
<td>1.0-1.4</td>
<td>0.08</td>
</tr>
<tr>
<td>With 4+ diseases</td>
<td>436 (80.4 %)</td>
<td>106 (19.6 %)</td>
<td>1.13</td>
<td>0.9-1.4</td>
<td>0.31</td>
</tr>
</tbody>
</table>

**Figure 2** Risk (OR) of *slip falls* related to number of chronic health disorders as compared to the risk (OR=1.0) in women without health disorders.

Table 6 and Figure 3 present associations between number of chronic health disorders and *non-slip falls* carried out by cross-tabulation with ORs (95% CI) as estimates of relative risk. Baseline chronic health disorders strongly predicted *non-slip falls*, the prediction increased linearly with increasing number of diseases and the OR was 2.2 for women with 4 or more diseases compared to healthy women (P<0.001).
Table: 6 Association between the number of chronic health disorders and non-slip falls

<table>
<thead>
<tr>
<th></th>
<th>No Non slip fall (N, %)</th>
<th>Non slip falls (N, %)</th>
<th>(OR)</th>
<th>95 % CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>No disease</td>
<td>3501 (89,9 %)</td>
<td>395 (10,1 %)</td>
<td>1,0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>With 1 disease</td>
<td>3064 (87,2 %)</td>
<td>450 (12,8 %)</td>
<td>1,3</td>
<td>1,1-1,5</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>With 2 diseases</td>
<td>1702 (85,4 %)</td>
<td>290 (14,6 %)</td>
<td>1,51</td>
<td>1,3-1,8</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>With 3 diseases</td>
<td>763 (84,5 %)</td>
<td>141 (15,6 %)</td>
<td>1,64</td>
<td>1,3-2,0</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>With 4 or more</td>
<td>435 (80,3 %)</td>
<td>107 (19,7 %)</td>
<td>2,18</td>
<td>1,7-2,8</td>
<td>&lt;0,001</td>
</tr>
</tbody>
</table>

Figure 3 Risk (OR) of non-slip falls related to the number of chronic health disorders (the risk of the healthy is denoted as 1.0)
5.3.2 Risk of falling by type of ICD disease main category

Relationships of individual ICD disease groups with number of reported falls were studied and showed that following diseases were associated with the increased risk of falling as measured with two or more falls during the preceding 12 months: mental disorders, nervous system disorders, endocrine, metabolic and nutrition disorders, cardiovascular disorders, respiratory disorders, digestive disorders, musculoskeletal diseases and other diseases. Results are presented in table 7 with OR= Odds ratio, 95% CI= 95% confidence interval and p value after compared with healthy comparison group.

Table 7 The relationship of ICD main groups of diseases and falling risk (OR)

<table>
<thead>
<tr>
<th>Disease Main Category</th>
<th>N</th>
<th>No fall or one fall %</th>
<th>2 or more falls %</th>
<th>(OR)</th>
<th>95% CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td>3837</td>
<td>84</td>
<td>16</td>
<td>1,0</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infectious Diseases</td>
<td>28</td>
<td>82.1</td>
<td>17,9</td>
<td>1,14</td>
<td>0,4-3,0</td>
<td>0,787</td>
</tr>
<tr>
<td>Neoplasma</td>
<td>312</td>
<td>77,6</td>
<td>22,4</td>
<td>1,19</td>
<td>0,9-1,6</td>
<td>0,198</td>
</tr>
<tr>
<td>Mental Disorders</td>
<td>466</td>
<td>76,6</td>
<td>23,4</td>
<td>1,61</td>
<td>1,3–2,0</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td>423</td>
<td>72,1</td>
<td>27,9</td>
<td>2</td>
<td>1,6–2,5</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>Blood Disorders</td>
<td>58</td>
<td>72,4</td>
<td>27,6</td>
<td>2</td>
<td>1,1–3,6</td>
<td>0,017</td>
</tr>
<tr>
<td>Endocrine, Metabolic &amp; Nutritional Disorders</td>
<td>2340</td>
<td>79,4</td>
<td>20,6</td>
<td>1,36</td>
<td>1,2–1,6</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>Cardiovascular Disorders</td>
<td>3036</td>
<td>78,2</td>
<td>21,8</td>
<td>1,47</td>
<td>1,3–1,7</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>Respiratory Disorders</td>
<td>634</td>
<td>74,4</td>
<td>25,6</td>
<td>1,8</td>
<td>1,5–2,2</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>Digestive Disorders</td>
<td>949</td>
<td>76,2</td>
<td>23,8</td>
<td>1,64</td>
<td>1,4–1,9</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>Genitourinary diseases</td>
<td>207</td>
<td>76,8</td>
<td>23,2</td>
<td>1,59</td>
<td>1,1–2,2</td>
<td>0,006</td>
</tr>
<tr>
<td>Skin Diseases</td>
<td>149</td>
<td>71,8</td>
<td>28,2</td>
<td>2,06</td>
<td>1,4–2,9</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>Musculoskeletal Diseases</td>
<td>2816</td>
<td>77,1</td>
<td>22,9</td>
<td>1,55</td>
<td>1,4–1,8</td>
<td>&lt;0,001</td>
</tr>
<tr>
<td>Other Diseases</td>
<td>529</td>
<td>75,8</td>
<td>24,2</td>
<td>1,68</td>
<td>1,3–2,0</td>
<td>&lt;0,001</td>
</tr>
</tbody>
</table>
Figure 4 Risk (OR) of falling related to diseases classified according to ICD main classes (the risk of the healthy denoted as OR=1)

The same disease groups showed statistically significant relationships with non-slip falls. Table 8 presents the summary of association of different diseases groups and risk of non-slip falls with OR=Odds ratio, 95% CI= 95% confidence intervals and p value. There was no significant relationship between slip falls and classes of chronic health disorders.

Table 8 Risk (OR) of non-slip falls related to diseases classified according to ICD main classes.

<table>
<thead>
<tr>
<th>Disease Group</th>
<th>N</th>
<th>No Non slip falls %</th>
<th>Non slip falls %</th>
<th>(OR)</th>
<th>95 % CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Healthy</td>
<td>3896</td>
<td>90</td>
<td>10</td>
<td>1.0</td>
<td>0.5-4.1</td>
<td>0.516</td>
</tr>
<tr>
<td>Infectious Diseases</td>
<td>29</td>
<td>86.2</td>
<td>13.8</td>
<td>1.41</td>
<td>1.1-2.2</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Neoplasma</td>
<td>319</td>
<td>85</td>
<td>15</td>
<td>1.57</td>
<td>1.3-2.3</td>
<td>0.006</td>
</tr>
<tr>
<td>Mental Disorders</td>
<td>470</td>
<td>83.4</td>
<td>16.6</td>
<td>1.76</td>
<td>1.3-2.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Nervous System Disorders</td>
<td>432</td>
<td>80.3</td>
<td>19.7</td>
<td>2.2</td>
<td>1.7-2.8</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Blood Disorders</td>
<td>57</td>
<td>78.9</td>
<td>21.1</td>
<td>2.4</td>
<td>1.2-4.5</td>
<td>0.007</td>
</tr>
<tr>
<td>Endocrine, Metabolic &amp; Nutritional</td>
<td>2402</td>
<td>86.7</td>
<td>13.3</td>
<td>1.36</td>
<td>1.2-1.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Disorders</td>
<td>3134</td>
<td>85.4</td>
<td>14.6</td>
<td>1.51</td>
<td>1.3-1.7</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Cardiovascular Disorders</td>
<td>660</td>
<td>82.7</td>
<td>17.3</td>
<td>1.85</td>
<td>1.5-2.3</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Respiratory Disorders</td>
<td>991</td>
<td>84.6</td>
<td>15.4</td>
<td>1.61</td>
<td>1.3-1.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Digestive Disorders</td>
<td>214</td>
<td>84.1</td>
<td>15.9</td>
<td>1.67</td>
<td>1.1-2.4</td>
<td>0.007</td>
</tr>
<tr>
<td>Genitourinary Diseases</td>
<td>153</td>
<td>83</td>
<td>17</td>
<td>1.81</td>
<td>1.2-2.8</td>
<td>0.006</td>
</tr>
<tr>
<td>Skin Diseases</td>
<td>2874</td>
<td>84.3</td>
<td>15.7</td>
<td>1.65</td>
<td>1.4-1.9</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Musculoskeletal Diseases</td>
<td>540</td>
<td>81.5</td>
<td>18.5</td>
<td>2.01</td>
<td>1.6-2.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Other Diseases</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Figure 5 Risk of non-slip falls in women with a chronic health disorder classified according to ICD main classes as compared to the risk of the healthy (OR=1)

5.4 Use of medication and falls

Use of prescribed medications was categorized for statistical analysis into 5 groups. The risk of falling (2 or more falls vs. 0-1 fall) increased almost linearly with increasing number of prescribed medications in use at baseline (Table 9 and Figure 6).

Table 9 Association between use of medication and falls

<table>
<thead>
<tr>
<th>Healthy(use of no medication)</th>
<th>N</th>
<th>No fall or one fall, %</th>
<th>Two or more falls, %</th>
<th>OR</th>
<th>CI 95 %</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>With 1 medication</td>
<td>2352</td>
<td>79,1</td>
<td>20,9</td>
<td>1,21</td>
<td>1,0–1,3</td>
<td>0,086</td>
</tr>
<tr>
<td>With 2 medications</td>
<td>1346</td>
<td>80</td>
<td>20</td>
<td>1,14</td>
<td>1,0–1,3</td>
<td>0,086</td>
</tr>
<tr>
<td>With 3 medications</td>
<td>669</td>
<td>77,6</td>
<td>22,4</td>
<td>1,32</td>
<td>1,1–1,6</td>
<td>0,005</td>
</tr>
<tr>
<td>With 4 or more medications</td>
<td>667</td>
<td>73,3</td>
<td>26,7</td>
<td>1,66</td>
<td>1,4–2,0</td>
<td>&lt;0,001</td>
</tr>
</tbody>
</table>
Figure 6 The relationship between the use of medications and falling risk (OR)

Use of medications also showed a significant relation with non-slip falls. There was no statistically significant relation of use of medication with slip falls.

Table 10 Association between use of medication and non-slip falls. OR = odds ratio, 95% CI = 95% confident intervals.

<table>
<thead>
<tr>
<th>Healthy(use of no medication)</th>
<th>N</th>
<th>No Non slip-falls %</th>
<th>Non slip falls %</th>
<th>OR</th>
<th>CI 95</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>With 1 medication</td>
<td>2939</td>
<td>87,4</td>
<td>12,6</td>
<td>1,05</td>
<td>1,0–1,2</td>
<td>0,451</td>
</tr>
<tr>
<td>With 2 medications</td>
<td>1389</td>
<td>87,6</td>
<td>12,4</td>
<td>1,04</td>
<td>0,9–1,2</td>
<td>0,674</td>
</tr>
<tr>
<td>With 3 medications</td>
<td>682</td>
<td>85,5</td>
<td>14,5</td>
<td>1,25</td>
<td>1,0–1,6</td>
<td>0,057</td>
</tr>
<tr>
<td>With 4 or more medications</td>
<td>686</td>
<td>80,2</td>
<td>19,8</td>
<td>1,82</td>
<td>1,5–2,2</td>
<td>&lt;0,001</td>
</tr>
</tbody>
</table>
Previous fracture history was considered as another risk factor for falls in this study population. According to the baseline enquiry, there were about 10.1% women (n= 1210) who had any kind of fracture history. At the 5 years follow up, increased risk of two or more falls were recorded in women with previous fracture history compared to women with no fracture history (P value=0.019, OR= 1.20). There was no significant increase in the risk of slip falls related to fracture history. The risk of non-slip falls was increased in women with previous any fracture history (P=0.014, OR= 1.24).

Table 11 Proportion (%) of falls with previous fracture history

<table>
<thead>
<tr>
<th></th>
<th>Two or more falls %</th>
<th>Slip falls %</th>
<th>Non Slip falls %</th>
</tr>
</thead>
<tbody>
<tr>
<td>No fracture History</td>
<td>19.3</td>
<td>19.4</td>
<td>12.5</td>
</tr>
<tr>
<td>Fracture History</td>
<td>22.3</td>
<td>20.7</td>
<td>15.1</td>
</tr>
</tbody>
</table>

Figure 7 The relation of use of medication with non-slip falls

5.5 Previous fracture history and falls
5.6 Smoking and falls

There were about 9.1 % women (n= 1322) in this study population who reported smoking history. Smoking history was treated as a 2-category variable: nonsmoker and smoker. Smoker category includes women with previous smoking, current smoking, regular smoking, irregular smoking, light smoking and heavy smoking history.

The relationship of smoking with falls was very interesting. Smokers reported falls less frequently than nonsmokers (P<0.000, OR= 0.67). A similar association was also observed for slip falls (P=0.038, OR= 0.84) but non slip falls were not related to smoking. (P= 0.623, OR= 0.95).

Table 12 Proportion (%) of falls with smoking history

<table>
<thead>
<tr>
<th></th>
<th>Two or more falls %</th>
<th>Slip falls %</th>
<th>Non slip falls %</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non smokers</td>
<td>20.2</td>
<td>19.8</td>
<td>12.8</td>
</tr>
<tr>
<td>Smokers</td>
<td>14.6</td>
<td>17.3</td>
<td>12.3</td>
</tr>
</tbody>
</table>
Figure 9 The Comparison of smoking history and occurrence (%) of two or more falls, slip falls and non-slip falls in post-menopausal elderly women

5.7 Risk factors for two or more falls according to the final multiple logistic regression analysis

To see the joint effects of the risk factors for two or more falls, a multivariate model was constructed by including variables which were related to falls in univariate analysis as covariates. The independent predictors for two or more falls were age, number of diseases and smoking which were presented in the Table 13 with OR= odds ratio, 95% CI= 95% confidence interval and p value. So, we found that the medication effect faded away after inclusion of health disorders in the model the same independent variables were used for slip falls and non-slip falls but the results were not statistically significant.

Table 13 Results of the final logistic regression model for the risk factors of two or more falls

<table>
<thead>
<tr>
<th></th>
<th>Two or more falls( OR)</th>
<th>95 % CI</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age, baseline</td>
<td>0.96</td>
<td>0.94–0.98</td>
<td>&lt;0,000</td>
</tr>
<tr>
<td>With 1 disease</td>
<td>1.31</td>
<td>1.2–1.5</td>
<td>&lt;0,000</td>
</tr>
<tr>
<td>With 2 diseases</td>
<td>1.67</td>
<td>1.4–1.9</td>
<td>&lt;0,000</td>
</tr>
<tr>
<td>With 3 diseases</td>
<td>1.54</td>
<td>1.3–1.8</td>
<td>&lt;0,000</td>
</tr>
<tr>
<td>With 4 or more diseases</td>
<td>2.20</td>
<td>1.8–2.7</td>
<td>&lt;0,000</td>
</tr>
<tr>
<td>Smoking</td>
<td>0.66</td>
<td>0.5–0.8</td>
<td>&lt;0,000</td>
</tr>
</tbody>
</table>
There were several other factors which have been considered as risk factors for falls. They were; BMI (Body mass Index), height, dietary calcium intake, free time exercise, hours in physical exercise, physical hardness at work, hormone therapy, contraceptive use, parity, history of miscarriage as a gynecological factor and number of surgeries. The unadjusted relationship of these individual risk factors has been studied for two or more falls, slip falls and non-slip falls by using cross tabulation and univariate logistic regression model. None of the results was significant.

4 Discussion

This is a large population-based cohort study with 11495 participants, and with a postal enquiry repeated after the 5-year follow-up with a 90% response rate. To see how former exposure predicts falls with several assessment methods, this study investigates intrinsic (individual) factors rather than extrinsic (environmental) as possible risk factors for falls, since less association of environmental hazards with falling have been reported in former studies, while both increasing and decreasing trends of falling have been observed according to individual factors (Tinetti, Speechley et al. 1988). Again, extrinsic factors such as poor lighting and slippery road during the winter are
not easily modified by the individuals themselves, while several modifiable intrinsic factors such as chronic health disorders, medication use and certain health behaviors may be more useful predictors to be evaluated within health care as risk factors for falls with the purpose to build up a strategy for fall prevention in elderly people (Huang, Mallet et al. 2012, Tinetti, Baker et al. 1994).

Information on falls and suspected risk factors were collected with postal enquiry. These self-reported falls were not validated. About 11% of the study population did not respond to questions regarding falls. These non-responders were excluded from the analyses. Whether they did not respond due to non-existent falls or for some other reason remained uncertain. However, the proportion of responses to this question (89%) and the response rate to the enquiry (90%) resulted in a combined nonresponse (0.89*0.90=0.80) which still remains reasonable. It is, therefore, unlikely that these nonresponses have severely affected incidence of falls or prevalence of risk factors so that severely distorted risk estimates had been obtained in this study.

Literature suggests that about 30% of the people aged 65 years and over will experience a fall (Tinetti, Speechley et al. 1988). In this study, the mean age of participating women was lower – about 56-57 years. By identifying risk factors for falls in early post-menopausal women, the increasing economic and social burden of falls among older women can be reduced by introducing different fall prevention programs before old age. (Gillespie, Robertson et al. 2009).

In this study population, about 36% of our women reported at least one fall a year and about one-fifth of women reported two or more falls (frequent faller). So our result is less than that for the elderly (Tinetti et al). This small number of frequent falling can be again explained by the age of the participants who were at the age of 52-61 and have relatively low prevalence of falling (Prevention, Panel 2001).

In this study, reported slip falls were more frequent than non-slip falls. One possible explanation for the great number of slip falls could be the location of study, Kuopio, Finland, where slip fall on ice is common in elderly women due to snow and ice for 5 months in a year (Rikkonen, Salovaara et al. 2010). Another reason might be the season (May-June 1994 just after the winter) the enquiry was performed.

As in other studies (Lawlor 2003), the risk of frequent falling rose with number of chronic diseases in this study population. The association was higher (double) with multiple pathology; 4 or more diseases compared to the healthy. There was a dose response relationship between number of falls and number of chronic health disorders. An interesting relationship was observed between nature of
falling and number of chronic disorders. Slip falls showed a decreasing trend with increasing number of chronic disorders, while the risk of nonslip falls increased linearly with increasing number of chronic diseases. This suggests that health disorders do not increase the risk of slip falls. Among chronic health disorders, the study found neurological diseases as predictors of falls due to its positive relationship with frequent falling and nature of falling which supports the findings of other studies. Like previous studies, this study also found several chronic health disorders associated with frequent falling and non-slip fall. They were; mental disorders (Finkelstein 2007, Kao 2012), Cardiovascular disorders (Dharmarajan, Avula et al. 2007), respiratory disorders (Ozalevli 2011), musculoskeletal disorders (Leveille, Jones et al. 2009) and other diseases. The risk of recurrent falls and non-slip falls may increase with the presence and number of chronic health disorders due to direct effects of these diseases on functional ability and therefore, on falling risk or due to several indirect effects such as reduced physical activity, muscle weakness and poor balance.

A significant association was observed in this study population between multiple medications and frequent falls as observed in former studies (Ziere, Dieleman et al. 2006). Higher risk of falling was observed in women with 4 or more medications when compared with the healthy. The possible explanations for the mechanism of action might be adverse side effects of medications such as cognitive changes, dizziness, postural hypotension, etc. (Agostini, Tinetti 2002) due to the underlying disease. In accordance with this hypothesis, we noticed that non-slip falls but not slip falls were related to poly pharmacy in our study.

Among several consequences of falls, fracture is the most important as 5-10% of falls result in a fracture (Nevitt, Cummings et al. 1989). The risks of recurrent falling, slip and nonslip falls were increased in this population who had previous any find of fracture history. Previous fracture history can limit physical activity, impaired balance or fear of further falling may increase the proportion of any kind of falling (Grisso, Kelsey et al. 1991, Li 2003). Kelsey found that women with wrist fracture were healthy and slip falls are a usual cause of wrist fracture. So one might reason and conclude that women with a slip fall - because they often sustain a wrist fracture – may be healthier than other women.

Smoking has been found to be a risk factor for fractures in several studies (Kanis, Johnell et al. 2005). There are limited studies which report the possible association of smoking with falling tendency. From the smoking history of this population, lower numbers of falls were reported by the smokers. Smoking seems to be protective for smokers. The possible explanation might be less
physical activity by smokers than non-smokers (Blair, Jacobs Jr et al. 1985). That is why; *frequent falling* and *slip falls* were reported less often among smokers. This assumption is confirmed (corroborated) by our finding that smoking failed to show any protective effect for *non-slip falls*. There was no effect of smoking on *non-slip falls* among the elderly population. The risks for *non-slip falls* remain similar with or without fracture history.

This study did not find daily calcium intake as a protective factor for falling which contradicts other studies (Dukas, Bischoff et al. 2004). There were no impact of physical exercise (Nelson, Rejeski et al. 2007) and hormone replacement therapy (Randell, Honkanen et al. 2001) on falling tendency either. This study did not investigate how individual medications might possibly increase falling risk which may also be a powerful risk increasing mechanism in addition to poly pharmacy (Tinetti 2003).

**5 Conclusion**

The risk of falling is multifactorial with several modifiable factors. This study found that the number of chronic health disorders is an important predictor for non-slip falls but not for slip falls. In addition we found that increasing number of prescribed drugs in daily use is a risk factor for falls. This result supports the recommendation of the Prevention Panel for the prevention of falls among the elderly, stating that use of medication is a modifiable risk factor for falling (Prevention, Panel 2001). However, we found that the medication effect faded away after inclusion of health disorders in the model. This might mean that health disorders are a more important risk factor for falls than medications.

The result of the study can help to identify post-menopausal women at greater risk for falling so that strategies for prevention can be implemented.
6 References


