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FRACTURES IN OLDER PEOPLE

– incidence, predictors and consequences

by

Maarit Piirtola

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From the Institute of Clinical Medicine, Family Medicine, University of Turku, Turku, Finland; the Unit of Family Medicine, Turku University Hospital, Turku, Finland; The Satakunta Central Hospital, Pori, Finland; the Härkätie Health Centre; Lieto, Finland; and the Turku City Hospital, Turku, Finland.

Supervisors

Professor Sirkka-Liisa Kivelä (MD, PhD, Chief Physician)
University of Turku, Institute of Clinical Medicine, Family Medicine, Turku, Finland
Satakunta Central Hospital, Pori, Finland
Turku University Hospital, Unit of Family Medicine, Turku, Finland

Professor Raimo Isoaho (MD, PhD, Chief Physician)
University of Turku, Institute of Clinical Medicine, Family Medicine,
Turku, Finland
Malax-Korsnäs Health Centre, Malax, Finland
Nordic School of Public Health, Gothenburg, Sweden

Professor Ismo Räihä (MD, PhD, Chief Physician)
University of Turku, Institute of Clinical Medicine, Family Medicine, Turku, Finland
Turku University Hospital, Unit of Family Medicine, Turku, Finland
Department of Internal Medicine, Turku City Hospital, Turku, Finland

Reviewed by

Adjunct professor Ilona Nurmi-Lüthje (PhD, Head of the Centre)
University of Helsinki, Hjelt Institute, Department of Public Health, Helsinki, Finland
Centre for Injury and Violence Prevention (Start), Kouvola, Finland

and

Adjunct professor Risto Honkanen (MD, PhD)
University of Eastern Finland, Department of Public Health, Finland
University of Eastern Finland, Bone and Cartilage Research Unit, Clinical Research Center,
Kuopio Campus, Kuopio, Finland

Opponent

Professor Jaakko Valvanne (MD, PhD)
University of Tampere, Tampere, Finland

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To my dearest family

ABSTRACT

Maarit Piirtola

FRACTURES IN OLDER PEOPLE
- incidence, predictors and consequences

The Institute of Clinical Medicine, Department of Family Medicine, University of Turku, Finland. Annales Universitatis Turkuensis, Medica – Odontologica Series D.

In older populations, fractures are common and the consequences of fractures may be serious both for an individual and for society. However, information is scarce about the incidence, predictors and consequences of fractures in population-based unselected cohorts including both men and women and a long follow-up.

The objective of this study was to analyse the incidence and predictors of fractures as well as functional decline and excess mortality due to fractures, among 482 men and 695 women aged 65 or older in the municipality of Lieto, Finland from 1991 until 2002. In analyses, Poisson's, Cox proportional Hazards and Cumulative Logistic regression models were used for the control of several confounding variables.

During the 12-year follow-up with a total of 10 040 person-years (PY), 307 (26%) persons sustained altogether 425 fractures of which 77% were sustained by women. The total incidence of fractures was 53.4 per 1000 PY (95% confidence intervals [95% CI]: 47.9 - 59.5) in women and 24.9 per 1000 PY (95% CI: 20.4 - 30.4) in men. The incidence rates of fractures at any sites and hip fractures were associated with increasing age. No significant changes in the age-adjusted incidence rates of fractures were found in either gender during the 12-year follow-up.

The predictors of fractures varied by gender. In multivariate analyses, reduced handgrip strength and body mass index (BMI) lower than 30 in women and a large number of depressive symptoms in men were independent predictors of fractures. A compression fracture in one or more thoracic or upper lumbar vertebras on chest radiography at baseline was associated with subsequent fractures in both genders.

Lower body fractures independently predicted both short- (0-2 years) and long-term (up to 8 years) functional decline in mobility and activities of daily living (ADL) performance during the 8-year follow-up. Upper body fractures predicted decline in ADL performance during long-term follow-up.

In the 12-year follow-up, hip fractures in men (Hazard Ratio [HR] 8.1, 95% CI: 4.4-14.9) and in women (HR 3.0, 95% CI: 1.9-4.9), and fractures at the proximal humerus in men (HR 5.4, 95% CI: 1.6-17.7) were independently associated with excess mortality. In addition, leisure time inactivity in physical exercise predicted independently both functional decline and excess mortality.

Fractures are common among older people posing serious individual consequences. Further studies about the effectiveness of preventing falls and fractures as well as improving care and rehabilitation after fractures are needed.

Keywords: Aged, activities of daily living, consequence, follow-up, fractures, functional decline, elderly, incidence, mobility, mortality, older people, physical exercise, population-based, predictors, risk factors.

TIIVISTELMÄ

Maarit Piirtola

IKÄÄNTYVIEN JA IÄKKÄIDEN HENKILÖIDEN MURTUMAT
- ilmaantuvuus, ennustavat tekijät ja seuraukset

Lääketieteellinen tiedekunta, kliininen laitos, yleislääketiede, Turun yliopisto. Annales Universitatis Turkuensis, Medica – Odontologica Series D.

Murtumat ovat iäkkäillä henkilöillä yleisiä ja niiden seuraukset voivat olla sekä yksilölle että yhteiskunnalle vakavia. Murtumien ilmaantuvuudesta, vaaratekijöistä ja seurauksista on kuitenkin olemassa vain vähän edustaviin väestöaineistoihin perustuvia kohorttitutkimuksia, joissa sekä miehiä että naisia on seurattu pitkään.

Liedon Iäkkäät - tutkimuksen tavoitteina oli analysoida murtumien ilmaantuvuutta, vaaratekijöitä sekä murtumien yhteyttä ennenaikaisen toimintakyvyn heikkenemisen ja kuoleman vaaraan 65 vuotta täyttäneillä henkilöillä. Kahdentoista vuoden seurantatutkimukseen (1991–2002) osallistui 482 lietolaista miestä ja 695 naista (n=1177), ja heistä 616 henkilöä kuului toimintakyvyn muutosta kuvaavaan kahdeksan vuoden (1991-1999) seurantaan. Tutkimuksen analysoinneissa käytettiin Poissonin, Coxin ja kumulatiivisia logistisia regressiomalleja. Luunmurtumien ilmaantuvuus, vaaratekijät ja yhteys ennenaikaisen kuoleman vaaraan analysoitiin erikseen miehillä ja naisilla.

Seuranta-aikana (10 040 henkilövuotta [HV]), 307 (26 %) henkilöä sai yhteensä 425 murtumaa. Murtumista 77 % sattui naisille. Minkä tahansa murtuman ilmaantuvuus oli naisilla 53.4 / 1000 HV (95 %:n luottamusväli [95 % CI]: 47.9 – 59.5) ja miehillä 24.9 / 1000 HV (95 % CI: 20.4 – 30.4). Kaikkien murtumien ja lonkkamurtumien ilmaantuvuus kasvoi iän myötä, mutta rannemurtumien ilmaantuvuus ei ollut yhteydessä ikään. Kahdentoista seurantavuoden aikana ei havaittu tilastollisesti merkitsevää muutosta murtumien ikävakioidussa vuosittaisessa ilmaantuvuudessa.

Murtumien vaaratekijät liittyvät kaatumisiin sekä luun haurastumiseen liittyviin tekijöihin, ja niissä oli eroja miesten ja naisten välillä: naisilla käden heikko puristusvoima ja normaali tai alhainen kehon painoindeksi (BMI) sekä miehillä depressiivisten oireiden suuri määrä. Kompressiomurtuma yhdessä tai useammassa rintarangan tai ylemmän lannerangan nikamassa ennusti itsenäisesti tulevia luunmurtumia sekä miehillä että naisilla.

Kahdeksan vuoden seuranta-aikana alakehon murtumat lisäsivät ongelmia liikkumiskyvyssä ja päivittäisistä toiminnoista selviytymisessä (ADL) sekä lyhyen (0-2 vuotta) että pitkän (2-8 vuotta) seurannan aikana. Yläkehon murtumat ennustivat ongelmia päivittäisistä perustoiminnoista selviytymisessä pitkän seurannan aikana.

Miesten (Hazard Ratio [HR] 8.1, 95 % CI: 4.4-14.9) ja naisten (HR 3.0, 95 % CI: 1.9-4.9) lonkkamurtumat sekä miesten olkavarren yläosan murtumat (HR 5.4 95 % CI: 1.6-17.7) lisäsivät ennenaikaisen kuoleman vaaraa. Vapaa-ajan fyysisessä harjoittelun vähäisyys ennusti itsenäisesti sekä ennenaikaista toimintakyvyn heikkenemistä että kuolemaa.

Murtumat ovat iäkkäillä henkilöillä yleisiä ja niillä on vakavia seurauksia. Tarvitaan lisää tutkittua tietoa tehokkaista kaatumisten ja murtumien ehkäisymenetelmistä. Myös murtumapotilaiden hoitoa ja kuntoutusta tulee kehittää.

Avainsanat: Ikääntyvät ja iäkkäät henkilöt, ilmaantuvuus, fyysinen harjoittelu, kuolleisuus, liikkumiskyky, murtumat, päivittäiset toiminnot, seuraukset, seurantatutkimus, toimintakyvyn lasku, vaaratekijät, väestötutkimus.

CONTENTS

ABBREVIATIONS

ADL	Activities of daily living
ASA	American Society of Anesthesiologists
BMD	Bone Mineral Density
BMI	Body Mass Index
COR	Cumulative Odds Ratio
DXA	Dual-energy X-ray Absorptiometry
GEE	Generalised estimation equations
HR	Hazard Ratio
HV	Henkilövuosi
ICD-9	International Classification of Diseases version 9
ICD-10	International Classification of Diseases version 10
IADL	Instrumental activities of daily living
kPa	KiloPascal
MMSE	Mini- Mental State Examination
ns	Statistically non significant
OR	Odds Ratio
PY	Person year
RR	Risk Ratio
SD	Standard Deviation
ZSDS	Zung Self-rating Depression Scale
WHO	The World Health Organization
95%CI	95% Confidence Interval

LIST OF ORIGINAL PUBLICATIONS

I Piirtola M, Vahlberg T, Isoaho R, Aarnio P, Kivelä S-L. Incidence of fractures and changes over time among the aged in a Finnish municipality: a population-based 12-year follow-up. Aging Clinical and Experimental Research 2007;19(4):269-276.

II Piirtola M, Vahlberg T, Isoaho R, Aarnio P, Kivelä S-L. Predictors of fractures among the aged - a population-based study with 12-year follow-up in a Finnish municipality. Aging Clinical and Experimental Research 2008;20(3):242-52.

III Piirtola M, Löppönen M, Vahlberg T, Isoaho R, Kivelä S-L, Räihä I. Fractures as independent predictors of functional decline in older people - a population-based study with an 8-year follow-up. Submitted.

IV Piirtola M, Vahlberg T, Löppönen M, Räihä I, Isoaho R, Kivelä S-L. Fractures as predictors of excess mortality in the aged - a population-based study with a 12-year follow-up. European Journal of Epidemiology 2008;23(11):747-55.

These articles are referred to in the text by Roman numerals I-IV.

1. INTRODUCTION

Falls and fall-related injuries are common among older persons all over the world (Kannus et al. 2005a; Stevens et al. 2006). Out of all fall-related injuries needing medical attention in older people, every second injury is reported to be a fracture (Johansson 1998). In 2000, the worldwide occurrence of fragility fractures in adults aged 50 years or older was estimated as 9 million (Johnell & Kanis 2006). In Finland, the annual number of hip fractures has been around 7000 in people aged 50 years or older during the years 2000 and 2006 (Kannus et al. 2006; Sund 2006). Because the number of old people is increasing, the number of fractures has been estimated to double (Piirtola et al. 2001) and the number of hip fractures to double or even triple by the year 2030 (Kannus et al. 2006).

The costs of fracture care are high (Piirtola et al. 2002; Nurmi et al. 2003; Borgström et al. 2006). In Finland, the average total cost of one hip fracture patient during the first post-operative year was 14 410 euros in 2003 (Nurmi et al. 2003) and 19 150 euros in 2010, but as much as 47 100 euros if a previously home-dwelling person is placed into a nursing home (Nurmi-Lüthje 2011 unpublished data). Of the fracture costs, 88% are due to fractures in women (Piirtola et al. 2002). Also in the US, the medical expenditures have been reported to be 2-3 times higher for women than for men (Stevens et al. 2006). In the future, however, the number (Piirtola et al. 2001) and the costs of fall-related injuries will rise more rapidly in older men than women (Piirtola et al. 2002).

The impact of fractures on functional performance can be serious (Nurmi et al. 2004; Johnell & Kanis 2006) and lead also to excess mortality (Bliuc et al. 2009). In addition to physical performance and management in activities of daily living (ADL) tasks, hip fractures may seriously affect health-related quality of life (Willig et al. 2001; Borgström et al. 2006). Thus, fracture prevention is an important public health issue.

Falls and fractures can be prevented (Gillespie et al. 2009; Karinkanta et al. 2010). There has, however, been inconsistency regarding the role of fall-related factors and bone fragility in sustaining fractures (Kanis et al. 2005a; Kannus et al. 2005b). Furthermore, it has been reported that factors associated with an increased risk of falls differ between men and women (Campbell et al. 1989). Thus, more detailed information about the gender-specific predictors of fractures is needed in order to make prevention of fractures more effective. Furthermore, more information about the independent impact of fractures on functional decline and excess mortality is needed for planning health and social care services for the aged fracture patients both in acute and long-term care. Lastly, information on gender- and age-specific incidences of fracture as well as secular change of incidence over time and distribution of fractures by type of fracture is also needed to follow the effect of preventive actions.

2. BONE PHYSIOLOGY AND PATHOLOGY

2.1 Bones

There are over 200 bones in a human skeleton (Bjålie et al. 2008). They provide protection for vital organs and form a rigid framework, the skeleton, both for standing and locomotion (Morgan et al. 2008). Bone marrow is the source for blood cells (hematopoiesis) and there is interplay between the bone organ system and the immune system. In addition, bones are involved in metabolic pathways associated with mineral homeostasis of calcium, phosphorus and magnesium. (Morgan et al. 2008).

Bone tissue is not only strong and stiff but also living and dynamic (Morgan et al. 2008). Bone consists of an organic component mainly composed of collagen, bone cells and noncollagenous proteins (20-30% by weight) together with an inorganic component formed by calcium and phosphate (60-70% by weight) and 8-10% water. It is constantly undergoing change: small amounts of bone tissue are continuously being broken down and rebuilt in co-operation between bone resorbing cells (osteoclasts) and bone forming cells (osteoblasts). This is called the remodelling process. In normal states, remodelling serves to balance the load especially in areas where the loading demands are repeatedly high. (Morgan et al. 2008). Two types of bone can be identified according to the pattern of collagen forming the osteoid ("bone unit"): woven bone and lamellar bone (Khan et al. 2001). Woven bone is produced in newborns and in adults after fracture. It is later replaced by stronger lamellar bone.

The skeleton is composed of two parts: the axial skeleton including the head and the trunk, and the appendicular skeleton including bones of the limbs (extremities) and the pelvic girdle (Morgan et al. 2008). Bones can be classified according to their shapes into four types: long, short, flat, or irregular (Bjålie et al. 2008). Long bones include the arm and leg bones; short bones include the bones of the wrist and the ankle; flat bones include ribs, sternum, pelvic, and most of the bones in the skull; and the irregular bones include vertebras along our spine and some small cranial bones.

Long bones, as the tibia, femur, and humerus, can be divided into three parts: the epiphysis, metaphysis, and diaphysis (Morgan et al. 2008). The hard outer layer of bones is composed of compact bone tissue (cortical bone). The interior of the bone epiphysis and metaphysis is filled with trabecular bone tissue, which composes a network for rod- and plate-like elements that make the overall organ lighter and allow room for blood vessels. Trabecular bone accounts only for 20% of the total bone mass but has nearly ten times the surface area of compact bone (Morgan et al. 2008). The proportion of trabecular bone is highest in vertebra (up to 80%) (Ferrari & Ringe 2010) and in the intertrochanteric region of proximal femur (50%), whereas in the middle of radius the proportion of it is only 1% (Khan et al. 2001). The inner and outer surfaces of cortical bones are covered by membranes: endosteum (inner surface) and periosteum (outer side of bone), each playing an important role in bone modelling and remodelling, as well as in the process of healing after fractures (Morgan et al. 2008).

The mechanical, biological and biochemical demands as well as the microstructure of the bones varies across anatomic sites (Currey 2003; Morgan & Bouxsein 2008). Because bones adapt to the loads imposed on them (Currey 2003; Morgan & Bouxsein 2008), the elastic properties of the bone (collagen fibrae) orient themselves according to the load (Bouxsein 2008). Thus bone is generally strongest in the primary loading direction and, for example, cortical bone in the femoral diaphysis has a high modulus when loaded in the longitudinal direction and trabecular bone in the vertebra body is stronger in the vertical direction compared with transverse direction (Bouxsein 2008). This is why different bone sites bear load (stress) differently and are more easily broken if stress comes from an unusual loading direction (Currey 2003; Morgan & Bouxsein 2008).

2.1.1 Age-related changes

Bones change with development and aging (Boskey & Coleman 2010). The length and diameter of bone increase with age, ending at early adulthood when peak bone mass is attained (Morgan et al. 2008; Seeman 2008). Males generally exhibit a longer growth period, resulting in bones of greater size, mass and overall bone strength. After the age of around 20 years, the adaptive modelling and remodelling capacity of bone diminishes which results to a negative balance: each time slightly less bone is deposited than has been resorbed. In males after the age of 20, bone resorption becomes predominant, and bone mineral content declines about 4% per decade. Females tend to maintain peak mineral content until menopause, after which it declines about 15% per decade and the remodelling process is accelerated. With increasing age, areal and volumetric bone mineral densities decline both in cortical and trabecular bone (Beck et al. 2000). In addition to the age-related increased mineralisation of the matrix, these material changes lead to stiffer but more brittle bones (Bouxsein 2008). However, it is noticeable that not all individuals' bones age similarly (Boskey & Coleman 2010).

There are also structural changes in bone: the thickness of the cortex decreases but the diameter of the bone increases (Morgan & Bouxsein 2008; Aro & Kettunen 2010). More likely, this change in bone geometry allows the bone to resist bending and torsional loads better (Beck et al. 2000; Aro & Kettunen 2010). Changes occur also in the microarchitecture of trabecular bone and vertebra; for example, it becomes more vulnerable in twisting movements of the body (Bouxsein 2008).

With all age-related changes together, bones' mechanical properties, as ability for deformation and absorption of energy while loaded (stressed), decrease and bones become more brittle and less tough. These changes lead to fragility of bone, e.g. presence of osteopenia and osteoporosis (Seeman 2008). However, even a fragile bone copes well with normal living and will break only by external force (Currey 2003).

2.1.2 Osteoporosis

Osteoporosis is an extremely "aging" condition of bones (Boskey & Coleman 2010) and is defined as "a systemic skeletal disease characterised by low bone mass and microarchitectural deterioration of bone tissue with a consequent increase in bone fragility and susceptibility to fractures" (Consensus development conference: diagnosis, prophylaxis, and treatment of osteoporosis 1993; The WHO Study Group 1994). Dual-energy X-ray Absorptiometry (DXA) with the cut-off values set by the working group of the World Health Organization (WHO) is used as the gold-standard for diagnosing osteoporosis and monitoring changes in bone mineral density (BMD) over time. BMD is commonly expressed as a T-score, the standard deviation variance of the patient's BMD compared to a young normal reference population (Miller 2006a; Kanis et al. 2008a). Osteoporosis is defined with as a BMD that lies 2.5 standard deviations (SD) or more below the average for young healthy women (a T-score of <-2.5 SD) (Kanis et al. 1994).

The prevalence of osteoporosis increases with age after the age of 50 years, more rapidly in females than in males (Kanis et al. 1994). In older age, osteoporosis is three times more common in women than in men, partly because women have a lower peak bone mass and partly because of the hormonal changes that occur after the menopause (Miller 2006a; Kanis et al. 2008a). It has been estimated that altogether 30% of the fractures in men, 66% in women and altogether 70% of all inpatient fractures are potentially "osteoporotic" (Court-Brown & Caesar 2006). In 2000, the worldwide estimation of fragile fractures was 9 million in the population of 50 years old or older (Johnell & Kanis 2006).

2.2 Fractures

Fracture is a break or crack in bone. Typical types of fractures are greenstick, spiral, comminuted, transverse, compound and compression fractures (Aro & Kettunen 2010). Fractures occur when an area of bone cannot withstand the force exerted on it (Kannus et al. 2005b; Aro & Kettunen 2010). A normal and healthy bone does not break without external force (injury). However, a fracture might occur more easily due to minimal trauma by an acquired disease of bone such as osteoporosis, osteomalasia, or by abnormal formation of bone in a disease such as osteogenesis imperfecta ("brittle bone disease"), fatigue breakage (a stress fracture) because of repeated micro-trauma, or tumours (Aro & Kettunen 2010). Therefore, there are two critical factors in determining why a fracture occurs: the strength of the bone and the energy of the event (Kannus et al. 2005b; Bouxsein 2008; Aro & Kettunen 2010).

2.2.1 Diagnosis

A diagnosis of a fracture is based on the history and circumstances of an injury, and the physical signs and symptoms. Often a fracture is easy to detect because there is obvious deformity, swelling and local tenderness. Usually, the patient cannot bear weight or pressure on the injured area and may be unable to move the injured limb without severe pain. In lower extremities, even a slightly broken bone is tender to pressure and thus fracture patients complain pain in standing and walking. (Aro & Kettunen 2010).

A fracture can be displaced or non-displaced. If the skin over the fracture is lacerated or torn, the term “open fracture” is used. An X-ray is taken to confirm the diagnosis and to clarify the type of fracture in order to define the treatment method. (Aro & Kettunen 2010). However, a normal X-ray does not necessarily exclude a probability of a fracture, and for example in hip fracture patients, initial X-ray images have appeared to be completely normal for 1% of the patients (The British Orhopaedic Association 2007; Scottish Intercollegiate Guidelines Network 2009). Besides, approximately 15% of hip fractures are non-displaced, and therefore produce no shortening or external rotation of the limb (The British Orhopaedic Association 2007). Where there is doubt about the diagnosis, other diagnostic imaging tests, such as computed tomography and magnetic resonance should be used (Vandevenne et al. 2000; Scottish Intercollegiate Guidelines Network 2009). These methods are also used to rule out other causes of pain, such as pathologic fractures (Vandevenne et al. 2000).

2.2.2 Classification and coding

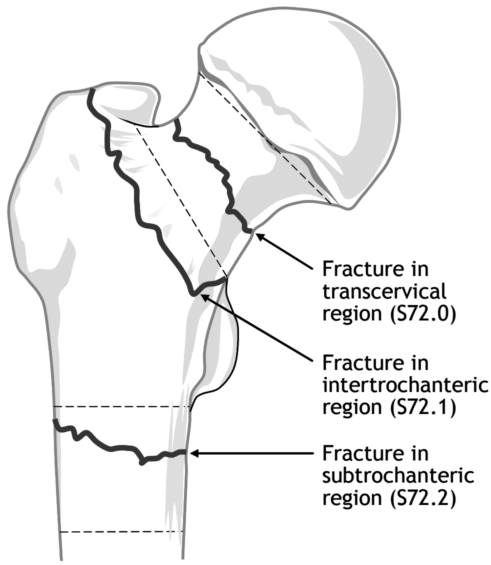
The main issue in classification of fractures is the location: a bone and a region of the bone that need to be identified (The WHO 1995; Marsh et al. 2007). Also classification about the severity of a fracture for the purpose of clinical treatments has been developed (Neer 1970; Marsh et al. 2007). For clinical purposes, fractures are classified according to their location, character and severity (AO Foundation 2009).

The International Classification of Diseases (ICD) has been used in coding and recording diseases and injuries as fractures (The WHO 2009). In Finland, the ICD -9 set of codes has been used during the years 1990-1995. From the year 2005 onwards the version number 10 has been used (The WHO 1995). In ICD-10, fractures are coded in chapter XIX section S.

In the ICD-10 version, the first axis of the numbered code is categorising the site of body and the second axis the type of injury. In fractures, the third digit specifies the bone(s) and the fourth code, 1 or 0, shows if or not there is an open wound related to the fracture. Category S02 includes fractures of the skull and face, S12 fractures of cervical vertebras, S22 fractures of rib(s), sternal bone and thoracic area, S32 fractures of the pelvic, S42 all fractures of collar bone, shoulder blade, humerus fractures and other shoulder fractures, S52 forearm and wrist fractures (radius and ulna), S62 small wrist bones and hand fractures, S72 hip and femur fractures, S82 knee and tibia (tibial, fibular, patella and inner and outer malleolus) fractures and S92 foot fractures. In the subcategories, hip fractures are most typically coded with S72.0, S72.1 and S72.2, Forearm and wrist fractures with S52, tibia and ankle fractures with S82, rib(s) fractures with S22.3 and S22.4, proximal humerus fractures with S42.2, and thoracic and lumbar compression fractures with S22.0 and S32.0. Even though the external causes of injuries may be used in ICD-10 coding, they are rarely used in the Finnish clinical health care system.

Hip fractures (S72.0, S72.1, S72.2)

The term hip fracture refers to a fracture of the upper end of the femur, above a point 5 cm below the distal part of the lesser trochanter (Gillespie 2001). Fractures are categorised according to which part of the bone is involved: femoral neck or cervical fractures (*fractura colli femoris,* S72.0), fractures around the trochanteric region, i.e. inter-/ pertrochanteric fractures (*fractura pertrochanterica, intertrochanterica femoris,* S72.1) and subtrochanteric fractures (*fractura subtrochterica femoris,* S72.2) (Picture 1) (The WHO 1995; Sund et al. 2009). Hip fractures can also be classified into intra-capsular (proximal to the point at which the hip joint capsule is attached to the femur, S72.0) and extra-capsular fractures (distal to the hip joint capsule, S72.1 and S72.2) (Gillespie 2001; Parker 2008; Sund et al. 2009). Intracapsular fractures can be subdivided into displaced and non-displaced fractures, whereas the terms stable and unstable are used in extracapsular trochanteric fractures (Parker 2008). Besides femoral bone, damage or deformity of the acetabulum or injury to the cartilage is connected with hip fractures (Committee of the Institute of Medicine Division of Health Care Services 1990).



Picture 1. Classification of hip fractures.

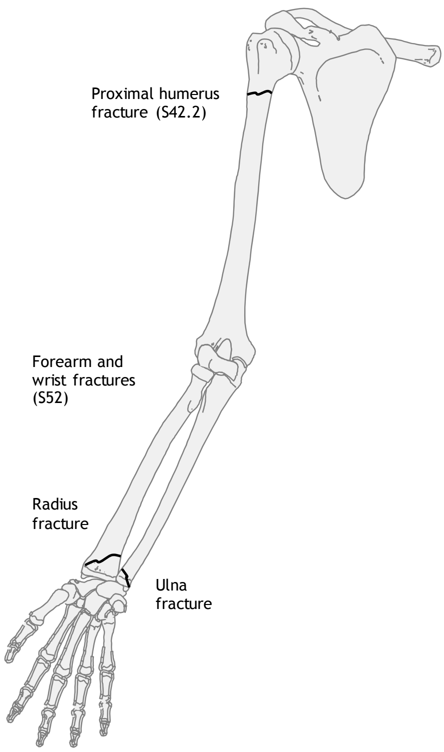
Fractures of the proximal humerus (S42.2)

Fractures of the proximal humerus are called fractures involving the glenohumeral articulation (Picture 2). Most of them (80%) are non-displaced or minimally displaced (Court-Brown et al. 2001).

Fractures of the forearm and wrist (S52)

Wrist fractures can be defined as fractures in the distal part of the radius (Hagino et al. 1999) whereas distal forearm fractures including both radius and ulna (Melton et al. 1998; O'Neill et al. 2001; Thompson et al. 2004; Brogren et al. 2007) (Picture 2).

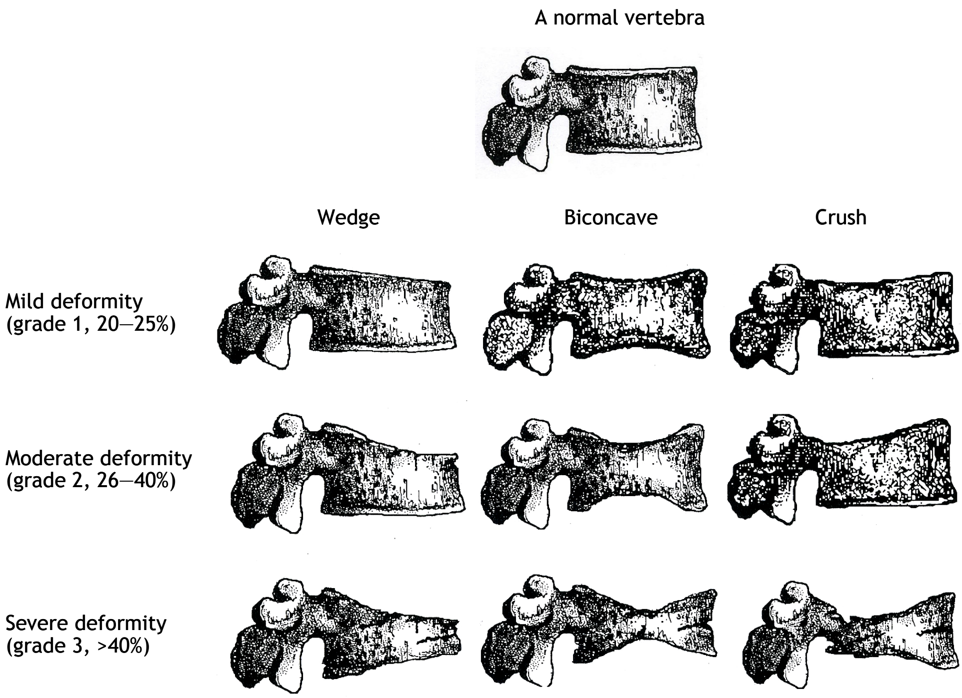
Sometimes, fractures in the scaphoid bone (S62.0), other carpus (S62.1) and even proximal forearm (S52.0-S52.4) have been included in the category of forearm fractures (Thompson et al. 2004). In addition, the code for unspecified parts of wrist and hand fractures has been used (S62.8) (Lofthus et al. 2008). For this reason, the fractures included in forearm and wrist fractures vary widely between the studies.



Picture 2. Fractures of the upper extremity.

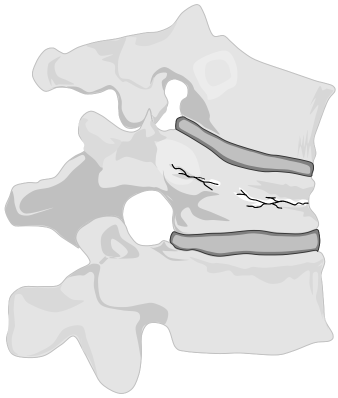
Vertebral compression fractures (S22.0 and S32.0)
Vertebral compression fractures include a wide range of vertebral deformations of cancellous bone (Genant et al. 1993; O'Neill et al. 1996). However, there is no golden standard for the definition of vertebral fractures (Ferrar et al. 2005). Assessment of spine deformity is best accomplished with a lateral view of the thoracic and lumbar spines. One approach is to measure the anterior, middle, and posterior heights of the vertebral body. A fracture can be diagnosed if any single measurement is reduced by 20% or more compared with the other measurements or "normal" vertebra (Genant et al. 1993; Burshell & Victores 2000). The deformities of vertebra can be defined as: a) wedge-shaped b) biconcave or "fish" shaped and c) crushed or collapsed vertebra (Picture 3) (Genant et al. 1993; Tamayo-Orozco et al. 1997; Vandevenne et al. 2000; Haczynski & Jakimiuk 2001).

In wedge fractures, the anterior (or posterior) height of vertebra body has been reduced, whereas the central portions of both vertebra body endplates have collapsed in biconcave fractures. In crushed fractures, the whole vertebra is collapsed compared with a "normal" vertebra (Genant et al. 1993; Haczynski & Jakimiuk 2001). In addition to the type of compression, the vertebral fractures can be graded by their severity (mild, moderate, severe); severity of deformity increases as the of height loss increases (Genant et al. 1993; Burshell & Victores 2000).



Picture 3. Genant's classification of vertebral compression fractures by the reduction of vertebra's height (Genant et al. 1993).

Wedge-shaped deformity is most frequent in thoracic vertebra, whereas concave depressed deformities are more common in the lumbar spine (Vandevenne et al. 2000). It is noticeable that a single vertebra may display the characteristics of more than one type of compression. In women, the most frequent types of vertebral fractures have been reported to be: wedge (51%), biconcave (17%), crush (13%), wedge and crush (7%), wedge and biconcave (6%), crush and biconcave, and all three types of deformity (4%) (Ismail et al. 1999). In men, the frequency distribution is alike (Ismail et al. 1999). As a result of several collapsed anterior vertebra, the vertebras fuse together and the spine bends forward causing a kyphotic deformity (Picture 4) (Old & Calvert 2004). Over time, multiple compression fractures may result in significant loss of height (Old & Calvert 2004).



Picture 4. Wedge-shaped deformity of vertebras causing a kyphotic deformity.

In addition to ICD-10 coding, the most commonly used classification of long bone fractures is *AO classification* (AO Foundation 2009). The AO classification is based on the location of the fractures, the presence of impaction, angulation, translation or comminution of the surgical neck and the presence or absence of a dislocation. The Orthopaedic Trauma Association has also launched *OTA classification*, developed on the basis of the AO classification (Marsh et al. 2007). In addition, several other fracture-based classifications are used. For example, proximal humerus fractures can also be classified according to the *Neer classification* (Neer 1970). The Neer classification system is based on the location and displacement of the fracture, the number of fracture fragments and the presence or absence of a dislocation (Neer 1970) and it is simpler compared with the AO classification.

Severity of an injury

The terminology and classification of the type of injuries behind any accidental event varies. In using the word trauma or accident (external force) in categorisation, it is common to group accidents at least to "severe" and "moderate" (Johansen et al. 2000; Olsson et al. 2004). Usually severe accidents include accidents that could conceivably lead to a fracture in anyone (as traffic accidents, falling objects and falls from higher level), whereas moderate accidents usually include falls from standing or lower heights (Johansen et al. 2000). Another method in categorisation is to use energy related to the event when terms "high-", "moderate-" and "low-" energy falls/injuries have been used (Kannus et al. 2005b; Bergström et al. 2008). Low-energy falls have been rated either falls from standing or lower heights (Kannus et al. 2005b) or falls from a lower level than 1 metre (Bergström et al. 2008). In practice, very few fragility-related fractures among older persons are related to severe accidents (Johansen et al. 2000; Bergström et al. 2008; Formiga et al. 2008) and for example, 95% of hip fractures are due to falling from standing height or a lower level (Formiga et al. 2004). However, the direction of a fall, even in a "low-energy" fall-related accident, can create high-impact force towards the site of bone and thus the term “fall-induced high-impact injuries” has been suggested to be used in fractures sustained by older people (Kannus et al. 2005b).

There is evidence that the type of fracture differs by the severity of injury and gender. In women, the majority (73%) of wrist fractures are sustained with an aetiology of moderate injury, whereas in men over 51% of wrist fractures are caused by severe injuries like falling from a high level or by traffic accidents (Brogren et al. 2007).

2.2.3 Treatment and healing process

The treatment and healing of the fracture depends on the severity of the fracture (the condition of the blood and nerve supply), type of the bone (cortical or cancellous bone), condition of the bone (age and the presence of osteoporosis), immobilisation after a fracture, presence of an infection or complications and presence of other injuries (Gruber et al. 2006).

One of the most important factors in the healing process is the amount of damage in blood vessels (Aro & Kettunen 2010). All fractures result in blood vessel disruption and tearing around the broken bone, and the ensuing blood clot fill the fracture site leading to localised hypoxia and acidosis (Gruber et al. 2006). The fractures may damage skin, nerves, blood vessels, ligaments, cartilage and internal organs. Open fractures may result in severe blood loss and infection. The nerve endings that surround bones contain pain fibres becoming irritated when the bone is broken or bruised. In addition, the muscles that surround the injured area may go into spasm when they try to hold the broken bone fragments in place, and these spasms cause further pain. Thus, initial treatment for fractures of the arms, legs, hands and feet in the field include splinting the extremity in the position it is found, elevation and ice. Immobilisation is essential as well as control of bleeding and pain. (Aro & Kettunen 2010).

The aim of the medical treatment of fractures is to reposition the fragments correctly. The location of the fracture, as well as its severity, influences the choice of treatment (Committee of the Institute of Medicine Division of Health Care Services 1990; Parker 2008). The most common conservative treatment of fractures is reposition and immobilisation of the body part (usually a plaster/cast, brace, splint, or sling in distal parts of limbs) (Handoll et al. 2007; Aro & Kettunen 2010). More serious and displaced fractures need to be placed under local or general anaesthesia. Operative reduction may be considered for the most seriously displaced fractures as hip fractures (Parker 2008; Aro & Kettunen 2010).

At the beginning of the healing process, blood clots are formed on the broken ends of bone. Over three to 12 weeks, the two bone portions are fused together with a combination of fibrous cells and cartilage (callus). This bridge is temporary and not as strong as real bone (Gruber et al. 2006; Aro & Kettunen 2010). Over the next months, the temporary bone (woven bone) is gradually replaced with real bone (lamellar bone) (Gruber et al. 2006). The process is described as "bony substitution" (Khan et al. 2001). The healing process after a fracture takes on average 48 weeks to complete (Aro

& Kettunen 2010). The process is longer in lower extremities compared with upper extremities. Unlike skin, broken bones heal without forming scar tissue. Clinically a fracture is healed when the broken area is firm. During a fracture, the muscle strength and power in addition to range of motion tend to decrease in immobilised extremities.

3. REVIEW OF THE LITERATURE

3.1 Incidence of fractures

Fractures are common all over the world (Johnell & Kanis 2004a; 2006) but especially high incidence rates of fractures have been shown in Scandinavia (Gullberg et al. 1997; Ismail et al. 2002). In Asian and African populations, the incidence of fractures has been lower compared with the white population living in North America or northern Europe (Hagino et al. 1999; Zebaze & Seeman 2003). Similarly, the fracture incidence rates are higher for white than for black population in the US (Baron et al. 1996).

At younger ages, males have a higher incidence of fractures compared with females, but after the age of 45-54 years the incidence of fractures in women overtakes that of men (Johansen et al. 1997; van Staa et al. 2001; Bergström et al. 2008; Ahmed et al. 2009). The rates start to rise especially at the age of 60 years (Baron et al. 1996; Melton et al. 1999b; Kanis et al. 2000; Ismail et al. 2002), after which the number and incidence of fractures are shown to increase with age all over the world (Jones et al. 1994; Baron et al. 1996; Gullberg et al. 1997; Ismail et al. 2002).

The incidences of “osteoporotic fractures” or “fragilily fractures” such as hip, spine, wrist, pelvic and upper humeral fractures, increase after the age of 50 years (Jones et al. 1994; Kannus et al. 1999; Rogmark et al. 1999; Sanders et al. 1999; Kanis et al. 2000; Lofthus et al. 2001; Chang et al. 2004). However, in the population under 70 years of age upper extremity fractures are dominating, whereas in the population 70 years and older hip and vertebral fractures become more predominant (Bergström et al. 2008) and fractures are located more centrally to the body (proximal fractures) (Baron et al. 1996; Sakuma et al. 2008). Advanced age and age-related factors also increase the severity of injuries after a fall (Sterling et al. 2001; Bouxsein 2008).

In Europe, the age-standardised incidence of any limb fractures in the population aged 50 to 79 years is reported to be 7.3 per 1000 PY (95% CI: 6.1 to 8.5) in men and 19.0 per 1000 PY (95% CI: 17.1 to 20.8) in women (Ismail et al. 2002). The incidence rate of foot or ankle fractures seems to be unrelated to age (Seeley et al. 1996; Johansen et al. 1997).

3.1.1 Hip

The age-standardised incidence of hip fractures in the population aged 50 to 79 years in Europe is reported to be 0.8 per 1000 PY (95% CI: 0.4 to 1.0) in men and 1.3 per 1000 PY (95% CI: 0.8 to 1.7) in women (Ismail et al. 2002).

The incidence of hip fractures increases with age both in men and women all over the world (Sanders et al. 1999; Ismail et al. 2002; Moayyeri et al. 2006) (Figure 1). The female/male ratio varies in different populations from 0.9 to 2.9 (Moayyeri et al. 2006).

However, in the majority of studies covering data from the last two decades, the female/male ratio in sustaining hip fractures has been reported to be around 2.5 (Moayyeri et al. 2006). In the Finnish PERFECT data in the years 2005, 2006 and 2007, the ratios reported are 2.4, 2.3 and 2.1, respectively (Sund et al. 2008).

The site of hip fractures is distributed rather equally both to left and right sides (Endres et al. 2006; Melton et al. 2009). Among Finnish patients at 50 years or over, approximately 61-63% of the hip fractures have been reported to be cervical, i.e. intracapsular fractures (S72.0), and 37-39% trochanteric, i.e. extracapsular fractures (S72.1 or S72.2) (Lönnroos et al. 2006; Sund et al. 2009). The amount of cervical fractures is reported to be higher compared with trochanteric fractures also in some other studies (Lofthus et al. 2001; Endres et al. 2006; Melton et al. 2009).

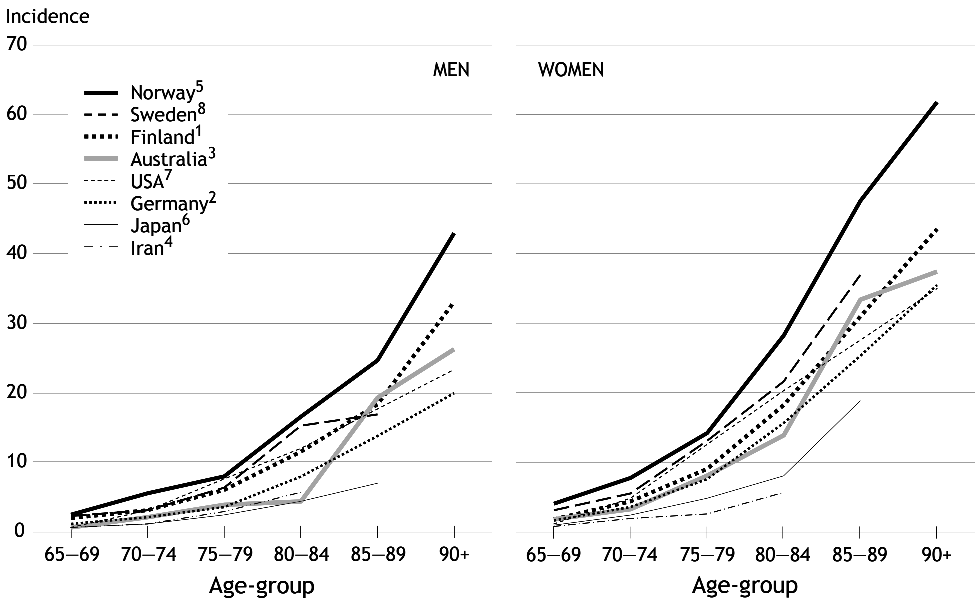


Figure 1. Age- and gender-specific incidence rates of hip fractures per 1000 person years. References: 1) (Kannus et al. 2006); 2) (Icks et al. 2008); 3) (Sanders et al. 1999); 4) (Moayyeri et al. 2006); 5) (Lofthus et al. 2001); 6) (Hagino et al. 1999); 7) (Melton et al. 2009); 8) (Kanis et al. 2000).

3.1.2 Forearm and wrist

Forearm and wrist fractures belong to the most common fractures in people 65 years or over (Hagino et al. 1999; Ismail et al. 2002; Thompson et al. 2004). The incidence of upper limb fractures is higher in Scandinavia compared with other European countries but wrist fractures are reported to be at least as common in Eastern Europe as in Scandinavia (Ismail et al. 2002). In Africa, the incidence of wrist fractures is reported to be very low (Zebaze & Seeman 2003). Among the persons aged 50 to 79 years recruited from population-based registers in 31 European centres and standardised to the European population at the same age, the incidence of forearm fractures is reported to be 1.7 per 1000 PY (95% CI: 1.1 to 2.3) in men and 7.3 per 1000 PY (95% CI: 6.2 to 8.5) in women (Ismail et al. 2002).

Forearm and wrist fractures are especially common in older women (Kaukonen 1985; O'Neill et al. 2001; Ismail et al. 2002; Flinkkilä et al. 2010). Overall, distal forearm fractures are reported to be three to four times more common in women compared with men (Kaukonen 1985; Melton et al. 1998; Thompson et al. 2004; Flinkkilä et al. 2010). The site of distal forearm fractures is distributed rather equally both to left (52-59%) and right (41-48%) sides (Melton et al. 1998; Hagino et al. 1999; O'Neill et al. 2001; Endres et al. 2006; Brogren et al. 2007).

The incidence of distal forearm fractures is reported to increase with age both in men and women after the age of 65 years, especially in older women (Melton et al. 1998; O'Neill et al. 2001; Thompson et al. 2004) (Figure 2). However, an age-related increase in the incidence has not been reported in all countries (Seeley et al. 1996; Johansen et al. 1997) and the incidence of wrist fractures in aged men has remained low and plateau in England (O'Neill et al. 2001) and in Sweden (Brogren et al. 2007). Similarly, no increase in the incidence has been found in Japan (Hagino et al. 1999).

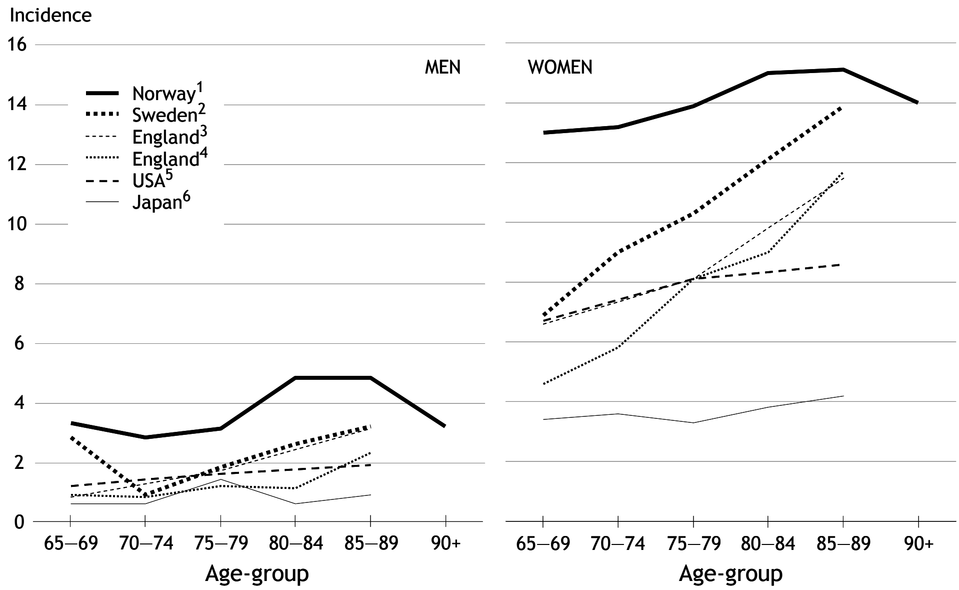


Figure 2. Age- and gender-specific incidence rates of forearm and wrist fractures per 1000 person years. References: 1) (Lofthus et al. 2008); 2) (Kanis et al. 2000); 3) (Thompson et al. 2004); 4) (O'Neill et al. 2001); 5) (Melton et al. 1998); 6) (Hagino et al. 1999).

3.1.3 Proximal humerus

Fractures of the proximal humerus are shown to be three times (Cooley & Jones 2001; Ismail et al. 2002) or even seven times (Sakuma et al. 2008) more common in older women compared with older men. In the European population aged 50 to 79 years, the age-adjusted incidence of proximal humerus fractures is reported to be 0.7 per 1000 PY (95% CI: 0.4 to 1.1) in men and 2.0 per 1000 PY (95% CI: 1.4 to 2.6) in women (Ismail et al. 2002). In Southern Tasmania, the gender-specific rates have been 0.5 and 1.6, respectively (Cooley & Jones 2001). In European men, the incidence rates are highest in Scandinavia (1.1 per 1000 PY) and Southern Europe (1.2 per 1000 PY) and, in women in Scandinavia (5.2 per 1000 PY) and in Western Europe (1.9 per 1000 PY) (Ismail et al. 2002).

The incidence of proximal humerus fracture increases with age (Kelsey et al. 1992; Baron et al. 1996; Kanis et al. 2000) (Figure 3) especially after the age of 40 (Court-Brown et al. 2001). More than 70% of proximal humerus fracture patients are older than 60 years and the incidence is especially high in women 80 to 89 years of age (Baron et al. 1996; Court-Brown et al. 2001). In Japan, the incidence is reported to rise especially after the age of 89 years (Sakuma et al. 2008) but the same phenomenon has not been seen either in England (Court-Brown et al. 2001) or in Finland (Kannus et al. 2009b).

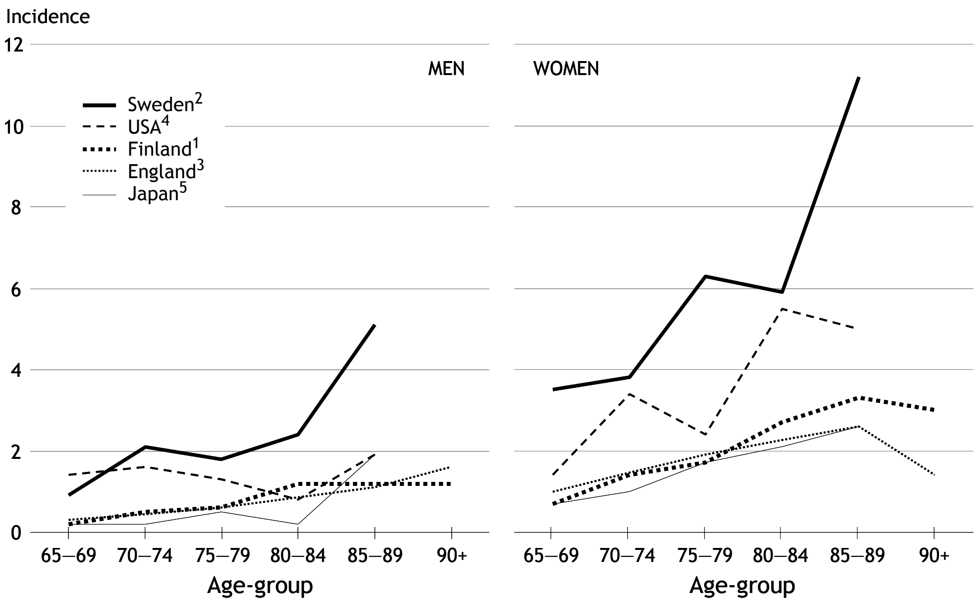


Figure 3. Age- and gender-specific incidence rates of proximal humerus fractures per 1000 person years. References: 1) (Kannus et al. 2009b; Kannus 2010 unpublished data) ; 2) (Kanis et al. 2000); 3) (Court-Brown et al. 2001); 4) (Melton et al. 1999b); 5) (Hagino et al. 1999).

3.1.4 Vertebra

Due to permanent deformities in the vertebral body, the term prevalence, instead of incidence, is commonly used with vertebral fractures. Only 30% of vertebral deformities are clinically diagnosed (Greendale & Barrett-Connor 2008). The prevalence of vertebral fractures varies due to identification criteria of the deformities and due to the population included in the studies. In a population-based sampling obtained from 36 centres in 19 European countries with 15 570 males and females aged 50-79 years, an average prevalence of vertebral deformity was 12% of females and 12% of males (O'Neill et al. 1996). The prevalence increases with age, and the increase is more marked in women (Santavirta et al. 1992; O'Neill et al. 1996; Ismail et al. 1999; Cooley & Jones 2001; Felsenberg et al. 2002). At the age of 75 to 79 years, the prevalence was 29.3 per 1000 PY in women and 13.6 in European men (Felsenberg et al. 2002). A male-to-female ratio in vertebral fractures is reported to vary from 1:1.5 in Tasmania (Cooley & Jones 2001) and 1:2 in Europe (Felsenberg et al. 2002) to 1:3 in Japan (Sakuma et al. 2008). There is some evidence about geographic variation in fracture prevalence: rates have been shown to be higher in Scandinavian countries than elsewhere in Europe (O'Neill et al. 1996; Felsenberg et al. 2002).

3.1.5 Secular change

The number of fractures or even the age-specific incidence rates of different fracture types are anticipated to increase in the future (Kannus et al. 1996a; Gullberg et al. 1997; Melton et al. 1998; Kannus et al. 1999; Lönnroos et al. 2006). Regardless of prognostic studies dealing with the incidence of fractures in the future, there are not many population-based or cohort-based secular trend studies about the change in the incidence of all types of fractures during the past decades.

In Finland, several types of fractures needing hospital care show a stabilised or decreasing trend (Kannus et al. 2006; Kannus et al. 2009a; Kannus et al. 2009b). Although some studies support the increasing trend in age-specific rates of several osteoporosis-related fractures in women 40 to 69 years (Islam et al. 2009), there is also evidence that the prevalence of age-specific osteoporosis has not increased during the last decades, at least in Swedish postmenopausal women (Ahlborg et al. 2010). The rate of low-trauma fractures of the proximal humerus among 80-year-old or older women in Finland has been reported to have stabilised (Kannus et al. 2009b). Therefore, it is most likely that the number of the most common age-related fractures will increase mainly due to demographic changes in the population, i.e. the numerical increase of older persons (Boufous et al. 2004; Kannus et al. 2006). At the same time, there is also some evidence that the number of fall-induced severe cervical spine injuries seems to have risen alarmingly, at a rate that cannot be explained merely by demographic changes (Kannus et al. 2007).

The mean age of patients sustaining hip fractures has increased over time world-wide: it was 73 years in the 1960s and 79 years in the 1990s (Haleem et al. 2008). In Finland, the average age of hip fracture patients was 78.5 years in 2005 (Sund et al. 2008). Even though the mean age of hip fracture patients has increased, there is rather strong evidence suggesting that at least the age-specific incidence of hip fractures has stopped to increase or stabilised (Huusko et al. 1999; Lofthus et al. 2001; Boufous et al. 2004) or even declined (Kannus et al. 2006; Chevalley et al. 2007; Brauer et al. 2009; Leslie et al. 2009; Melton et al. 2009). However, a slight overall increase in the incidence rates has been noticed in Central Finland (Lönnroos et al. 2006) and in Germany (Icks et al. 2008). The results are somewhat controversial in aged men with hip fractures; the incidence rates have either stabilised or even increased (Chevalley et al. 2007; Icks et al. 2008; Fisher et al. 2009; Melton et al. 2009). Since the 1960s, the proportions of males and females sustaining hip fractures has, anyhow, been stable during the last decades (Haleem et al. 2008). However, because the number of old people is increasing, the total number of hip fractures is predicted to increase in the future (Piirtola et al. 2001; Johnell & Kanis 2006; Kannus et al. 2006).

3.2. Predictors for falls and fractures

Every third person aged 65 years or older and living in a community falls annually, but among those living in institutional care at advanced age and/or declined functional level, the rate is much higher (Tinetti et al. 1988; Luukinen et al. 1994). In average, every second fall leads to an injury (Nevitt et al. 1991) and 5-10% cause fractures (Tinetti et al. 1988; Nevitt et al. 1991; Nachreiner et al. 2007). In falling accidents with loss of consciousness, the risk for a severe injury is even higher (Nevitt et al. 1991).

Risk factors for falls (Tinetti et al. 1988; Campbell et al. 1989; Bergland et al. 2003) and injurious falls (Nevitt et al. 1991; Tinetti et al. 1995; Bergland & Wyller 2004) have been studied widely. Fractures are caused by multiple factors, depending both on the force of a fall and the strength of a bone (Figure 4) (Woolf & Åkesson 2003; Kannus et al. 2005b; Sambrook et al. 2007; Silva 2007; Boonen et al. 2008). It is noticeable that even though only a small percentage of all falls cause fractures, the majority of all fractures occur as a consequence of a fall (Kannus et al. 2005a; Sambrook et al. 2007; Kelsey & Samelson 2009). Thus, the strongest single factor and determinant of a fracture seems to be the actual fall rather than bone fragility (Kannus et al. 2005b; Järvinen et al. 2008; van Helden et al. 2008).

Risk factors can be classified as intrinsic risk factors such as medical conditions, psychological or bone-related factors, and extrinsic hazard related factors such as slippery road conditions (Close 2009). A great number of risk factors, such as advanced age, low body mass index and female gender, are related to both falls (Kannus et al. 2005a; The American Geriatrics Society 2010; Tinetti & Kumar 2010) and reduced bone strength (Nordin 2008; Papaioannou et al. 2009; Sweet et al. 2009; Waugh et al. 2009; Wu et al. 2009). Risk factors may vary and interact individually (Woolf & Åkesson 2003; van Helden et al. 2008; Close 2009) and at least the variables associated with falls differ between the genders (Campbell et al. 1989). The individual probability of falling (Close 2009) and fractures (Tromp et al. 1998) increases as the number of individual risk factors increases. Thus, persons at advanced age with multiple risk factors for falls or low bone strength have an especially high risk for sustaining fractures. Gender-specific predictors of fractures in the prospective cohort studies are shown in table 1.

In addition to age-related biological changes both for fall- (Close 2009) and bone-related factors (Pietschmann et al. 2008), fractures are also associated with the Caucasian race (Kannus et al. 1996b) and lifestyle or behaviour factors (Kannus et al. 1996b; Bergström et al. 2008). For example smoking, low level of physical activity and poor nutrition are associated with both falls and fractures (Kanis et al. 2005c). Because the age- and gender-adjusted incidence of hip fractures seems to be lower in rural populations, there has been some debate about the influence of rural and urban living conditions on the risk of sustaining hip fractures (Kannus et al. 1996b). However, the difference in incidence rates between rural and urban populations has not been reported in all studies (Lüthje et al. 1995c).

Even though a fracture predicts subsequent fractures (Honkanen et al. 1997; Johnell et al. 2004b), the strength of predictors depends on the type and mechanism of fracture (Honkanen et al. 1997). The loading conditions are determined crucially by the type and severity of fall as fall height and energy, fall direction and mechanism, anatomical site of the impact (direction of external force towards a bone), energy absorption capacity, and impact force attenuation of the body-landing surface (Kannus et al. 2005b; Aro & Kettunen 2010). Fall biomechanics and characteristics of the fall have thus an important impact on the occurrence and severity of a fracture (Greenspan et al. 1994; Aro & Kettunen 2010), and the fall height increases the energy in an injury (Aro & Kettunen 2010).

In community-dwelling fallers, the potential energy of the fall (the height of the centre of body's gravity from the ground) has been proven to be a risk factor for sustaining hip fractures (Greenspan et al. 1994). In addition, fall direction (falling to the side) has been shown as an independent risk factor for sustaining hip fractures both in community-dwelling (Greenspan et al. 1994) and frail institutionalised (Greenspan et al. 1998; Parkkari et al. 1999) older people. However, in older individuals, almost all upper extremity fractures occur as a result of a fall, the most typical fall direction being forward and the main impact of the fall straight to the fracture site (Palvanen et al. 2000; Kelsey & Samelson 2009).

3.2.1 Fall-related risk factors

A history of previous falls predicts future falls (Ganz et al. 2007), hip fractures (Cumming & Klineberg 1994) and proximal humerus fractures (Lee et al. 2002). The relationship of previous falls in sustaining fractures has been reported to been stronger among older men than older women (Cumming & Klineberg 1994). It is noticeable that the association between previous falls and future falls is shown to be stronger when the number of previous falls is two or more (Leclerc et al. 2008).

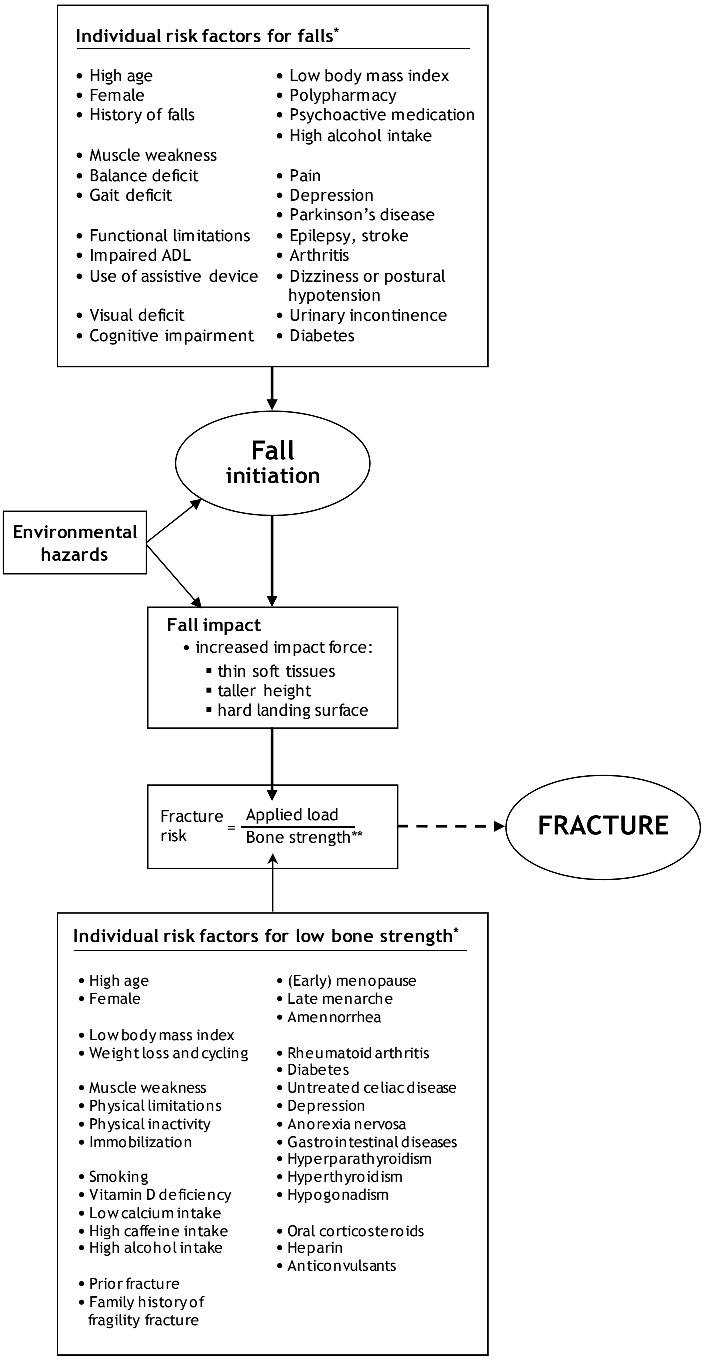


Figure 4. Risk factors for falls and factures.
*Adapted and modified from literature (Kannus et al. 2005a; Nordin 2008; Papaioannou et al. 2009; Sweet et al. 2009; Waugh et al. 2009; Wu et al. 2009; Karinkanta et al. 2010; The American Geriatrics Society 2010; Tinetti & Kumar 2010). ** Bone strength is determined by bone geometry (size and shape) and structure (architecture) and material properties.

Table 1. Predictors of fractures in the prospective cohort studies by gender.

Study	Participants	Follow-up in years	Adjustments *	Independent predictors (protectors) for fractures (p<0.05): Men (Ratio: RR, OR, HR)	Independent predictors (protectors) for fractures (p<0.05): Women (Ratio: RR, OR, HR)	Comments
Hippisley-Cox et al. 2009, England	1 183 663 women and 1 174 232 men aged 30-85 y, free of fractures at baseline.	10	**Both genders:** age, BMI, smoking, use of alcohol, rheumatoid arthiristis, cardiovascular diseases, type 2 diabetes, asthma, current tricyclic antidepressants, current corticosteroids, history of falls, lives disese. **Women:** previous + use of HRT, parental histoy of osteoporosis, menopausal symptoms, gastrointestial melabsorptions, other endocrinology disorders.	**Osteoporotic fractures[1]:** high age, BMI, smoking, use of alcohol, rheumatoid arthiristis, cardiovascular diseases, type 2 diabetes, asthma, current tricyclic antidepressants, current corticosteroids, history of falls, liver disese.	**Osteoporotic fractures[1]:** age, BMI, smoking, use of alcohol, rheumatoid arthiristis, cardiovascular diseases, type 2 diabetes, asthma, current corticosteroids, history of falls, liver disese, no use of HRT, parental history of osteporosis, menopausal symptoms, gastrointestial melabsorptions and other endocrinology disorders.	Fractures were recorded from general practice records. Multiple imputation to replace missing values in the data.
White et al. 2006, USA	13978 participants (2101 men and 8877 women), age 44-101 y. Mean age: 74.9 years in men, 73.7 years in women.	Median time 4.7 to 11.8	Gender and fracture site-specific adjustement. Age and previous fracture were included in all models in both genders and + BMI in women.	**Hip & wrist & spine fractures:** age per 10 years (HR 1.2 to 3.2), previous fracture (HR 1.8 to 3.2); **Hip & spine fractures:** ever or current smoker (HR 1.3 to 2.1), positive attitude (HR 0.7 to 0.8)	**Hip & wrist & spine fractures:** age per 10 years (HR 1.3 to 2.4), previous fracture (HR 1.4 to 2.6), high BMI (HR 0.7 to 0.8); **Hip & spine fractures:** current smoker (HR 1.5 to 1.8), positive attitude (HR 0.7 to 0.9)	Fractures were identified from health surveys, hospital disharge records and death certificates.
Nguyen et al. 2007, Australia	1647 (924 women, 723 men) without osteoporosis, mean age: women 70 (SD ± 6.4), men 72.2 (SD ± 6.3) y.	up to 15	Age, postural sway, quadriceps strenght, femoral neck BMD, fall, prior fracture.	**Any fracture:** Age (HR 1.4, 1.1-1.6); postural instability (HR 1.2, 1.1-1.3); history of fall (HR 1.9, 1.2-3.0); femoral neck BMD↓ (HR 1.2, 1.0-1.5).	**Any fracture:** advanced age (HR 1.2); postural instability (HR 1.1); history of fall (HR 2.1); prior fracture (HR 1.7); femoral neck BMD ↓ (HR 1.6).	Fractures were identified through radiologists' reports.
Huopio et al. 2000, Finland	3068 perimenopausal women (53.1-53.9 y) and 1931 random sample of women (53.2-54.2 y)	3.6	Age, weight, height, menopausal status, BMD, history of previous fracture, maternal hip fracture, use of HRT, smoking, intake of calsium, multiple chronic health disorders.		**Osteoporotic fractures[2]:** Low BMD (RR 1.6); history of previous fracture (RR 1.9); nonuse of HRT (RR 2.2). **Other fractures:** Low BMD (RR 1.3-1.4); history of previous fracture (RR 1.6); ≥3 chronic illnesses (RR 1.6); smoking (RR 1.8).	Self-reported fractures were validated by radiological reports.
Whooley et al. 1999, USA	7414 women at least 65 y, mean age 74.5 y with depression, 73.3 y without depression	6 (SD ± 2)	**Nonvertebral fractures:** Medical history, habits, current medication use, health and functional status, neuromuscular function. **Vertebral fractures:** history of vertebral fractures, history of falling, diabetes, steroid use, estrogen use, supplemental calsium use, cognitive function, hip BMD.		**Nonvertebral fractures:** depression (HR 1.3). **Vertebral fractures:** depression (OR 2.1).	Self-reported fractures were validated by radiological reports. Falls explained part of sustaining a nonvertebral fracture.
Albrand et al. 2003, France	672 healthy, postmenopausal women, mean age: 67 y (SD ± 9.4) with fracture, 58.1 y (SD ± 9.3) without fracture	5.3 (SD ± 1.1)	All variables statistically significant (p<0.05) in the univariate analyses, or were considered of interest a priori (not mentioned in detailed). At least age, years since menopause, past falls, all prevalent fractures, all prevalent fractures after 45 years, HRT, maternal history of fracture, fat body mass, physical activity score, left grip strenght, walking speed, tandem balance, chair stand, height loss, BMD.		**Fragility fractures[3]:** BMD total hip ≤ 0.736 g/cm2 (OR 3.2); history of fragility fracture (OR 3.3); physical activity score ≤ 14 (OR 2.1); low grip strenth (OR 2.1); age ≥ 65 years (OR 1.9); maternel history of fragility fractures (OR 1.8); past falls (RR 1.8).	Fractures confirmed by radiologist. Include type of fractures that are not nessesary related to fragility.
Kelsey et al. 1992, USA	9704 caucasian women at least 65 y (42% were 65-69 y, 31% 70-74 y, 16% 75-79 y, 10% ≥80 y).	mean 2.2	**Forearm fractures:** Age, BMD, previous fractures since age 50, blocks walked per week, corrected visual acuity score, previous falls, use of estrogen, weight, age at menopause. **Proximal humerus fractures:** age, BMD, height loss, health status, diabetes treated with insulin, blocks walked per week, balance, corrected visual acuity, waist to hip ratio, children breast-fed.		**Forearm fracture:** high BMD (RR 0.6), blocks walked per week (RR 1.2), higher age at menopause (RR 0.9); **proximal humerus fractures:** high BMD (RR 0.5), height loss (RR 1.1), diabetes treated with insulin (RR 3.8), waist to hip ratio (RR 1.4).	Fractures validated by radiological reports.

* At baseline unless stated otherwise. 1) Osteoporotic fract.: vertebral, distal radius, hip; 2) Osteoporotic fract.: vertebral, hip, proximal humerus, wrist ; 3) Fragility fract.: vertebral, wrist, hip, humerus, ankle, rib, patella, metatarsal, pelvis, sacrum. y= years, BMD = Bone minaral density, HRT= Hormone replacement therapy, BMI= body mass index, SD= standard deviation, fract.= fracture.

The most common independent risk factors of falls have been listed in a consensus paper by the American and British Geriatric Societies, and the American Academy of Orthopaedic Surgeons in year 2001 (The American Geriatrics Society et al. 2001) (Table 2) updated with the clinical practice guidelines and a review in 2010 (Figure 4) (The American Geriatrics Society 2010; Tinetti & Kumar 2010).

In the updated consensus paper, the strongest individual risk factors for falling include previous falls (fall history) (RR range 1.9-6.6), decreased muscle strength (RR range 2.2-2.6), impairment in balance (RR range 1.2-2.4) and gait (RR range 1.2-2.2), visual impairment (RR range 1.5-2.3), and the use of four or more medications or the use of psychoactive medications (RR range 1.1-2.4), (Figure 4) (Karinkanta et al. 2010; The American Geriatrics Society 2010; Tinetti & Kumar 2010).

For injurious falls, the risk factors are reported to be impaired ability to walk, and a variety of diseases and medications (especially opioids, benzodiazepines, neuroleptics, antidepressive medications, calcium blockers, digitalis and some anti-inflammatory drugs) (Koski et al. 1996).

Table 2. The most common risk factors for fall identified in 16 studies*.

Risk Factor	Significant of total †	Mean RR / OR**	Range of RR or OR
Muscle weakness	10 / 11	4.4	1.5 to 10.3
History of falls	12 / 13	3.0	1.7 to 7.0
Gait deficit	10 / 12	2.9	1.3 to 5.6
Balance deficit	8 / 11	2.9	1.6 to 5.4
Use of assistive device	8 / 8	2.6	1.2 to 4.6
Visual deficit	6 / 12	2.5	1.6 to 3.5
Arthritis	3 / 7	2.4	1.9 to 2.9
Impaired ADL	8 / 9	2.3	1.5 to 3.1
Depression	3 / 6	2.2	1.7 to 2.5
Cognitive impairment	4 / 11	1.8	1.0 to 2.3
Age > 80 years	5 / 8	1.7	1.1 to 2.5

* Adapted from the American Geriatrics Society (2001).
† Number of studies with significant odds ration (OR) or relative risk ratio (RR) in univariate analysis of the total number of studies included each factor.
** RR for prospective and OR for retrospective studies.

3.2.2 Falling and environmental hazards

The majority of falls (Leclerc et al. 2008) and fragility fractures (Bergström et al. 2008) occur indoors, especially among the oldest olds (Bergström et al. 2008). Among community-dwelling and persons aged 70 years or older, about 50% of the falls occur in home environments (Luukinen et al. 1994). Among those with a high risk of falling, the proportion of falls in home environments increases from 60% (Nachreiner et al. 2007) up to 82% (Leclerc et al. 2008). In case of hip fractures, 70% of fractures occur indoors in patients 50 to 59 years of age and the amount of indoors-related hip fractures rises up to 90% in persons 80 years of age (Lönnroos et al. 2006).

In community-dwelling persons, falls occur primarily during the daytime (Luukinen et al. 1994; Nachreiner et al. 2007), especially in the afternoons (Luukinen et al. 1994). In institutionalised persons, the proportion of falls is reported to be equal both during day- and night-time (Luukinen et al. 1994). In addition to falls, a majority (77%) of hip fractures are sustained during daytime (Formiga et al. 2004). This is true also in Finland, where the majority of hip fractures are reported to be sustained during active day-time and only 22% during night-time (Lönnroos et al. 2006).

In both institutionalised and community-dwelling persons, a majority of falls (Nachreiner et al. 2007), injurious falls (Luukinen et al. 1995) and fractures (Johansson 1998) occur during daily routines, especially in relation to walking (54% - 64%) but also while standing, rising to stand up, carrying objects, and reaching or leaning. In institutionalised persons, there are more unknown circumstances related to falls compared to home-dwelling older adults (20% vs. 2%, $p<0.001$) (Luukinen et al. 1995). It has been reported that falls from lower than 1 metre level are associated with a more proximal fracture location both in upper and lower extremities, whereas slipping tend to cause more distal extremity fractures (Bergström et al. 2008). In hip fracture patients, over 90% of fractures are sustained by falling from standing or sitting level (Honkanen 1990; Lönnroos et al. 2006). Falling less than one metre causes 53% of all fractures in persons 50 years and older but in those over 75 years of age, fall-related injuries cause over 80% of the fractures and in persons 90 years and over, the proportion is over 90% (Bergström et al. 2008).

The contribution of environmental hazards in sustaining falls that predispose fractures is most evident (Kannus et al. 2005a; Close 2009). However, prospective studies specifically aimed to detect home hazards in relation to falls have failed to demonstrate a clear association between the environment and falls (Close 2009). The influence of home hazards on falling has been shown to be contradictory (Lord et al. 2006). However, home environmental hazards have been found in 91% of homes among seniors receiving home-care services and the presence of hazards is significantly associated with all falls and fall-related medical consultations (Leclerc et al. 2010).

During a 12-month follow-up, falls have not been found to be strongly associated with the presence of home hazards among 325 voluntary and ambulatory persons aged 60 years or older with a history of previous falls (Northridge et al. 1995). However, in their study vigorous older persons living with home hazards were more likely to fall compared with those with fewer home hazards. The association between the amount of home hazards and falls was not found in frail older persons. In a population-based cohort study of persons 85-years of age, participants without a history of preceding falls were more prone to fall compared with those with a history of falls i.e. a higher overall risk of falling (van Bemmel et al. 2005). After adjustments for confounders, the risk of falling was 4-fold in the presence of six or seven home hazards in those without a history of falls compared with those with previous falls (van Bemmel et al. 2005). However, environmental hazards, when considered in isolation, are unlikely to predict falls (Close 2009).

As one part of the environmental hazards in sustaining fractures, seasonal variation, especially due to slippery weather conditions, has been shown (Bulajic-Kopjar 2000; Bischoff-Ferrari et al. 2007). During the winter or the autumn months, more distal radius fractures (Jacobsen et al. 1999; Bulajic-Kopjar 2000; O'Neill et al. 2001; Thompson et al. 2004; Bischoff-Ferrari et al. 2007; Flinkkilä et al. 2010) and hip fractures (Bulajic-Kopjar 2000; Mirchandani et al. 2005) have been reported.

It is noticeable that weather affects hip fracture risk differently compared with risk of sustaining distal forearm, proximal humerus or ankle fractures (Bischoff-Ferrari et al. 2007). According to the Finnish register data, small but clear seasonal variation in sustaining hip fractures has been recorded in persons aged 50 or older; 53.5% occurred during the winter/spring seasons compared with 46.5% during the summer/fall season (Sund 2007). However, this variation was almost completely due to non-institutionalised persons, and no seasonal variation in hip fractures was reported among institutionalised persons (Sund 2007). No seasonal variations in the incidence rates of hip fractures have been found in Oslo, Norway (Lofthus et al. 2001) and Tottori prefecture, Japan (Hagino et al. 1999) with rather similar climate conditions to south-western Finland.

3.2.3 Bone-related risk factors

Bone breaks when the applied load (force affecting bone) is greater than bone strength (Hayes et al. 1996; Silva 2007; Bouxsein 2008). Thus, low bone mineral density (BMD), less optimal bone geometry and less optimal bone architecture leading to bone fragility (osteoporosis) have an important role in sustaining fractures (Hayes et al. 1996; The WHO 2003). It has been shown that at least a low level of femoral neck bone mineral density (BMD) and that of calcaneal bone measured by ultrasound speed are associated with an increased risk of a proximal humerus fracture in women (Lee et al. 2002) and that of hip fracture in both genders (Greenspan et al. 1994; Greenspan et al. 1998). In community-dwelling fallers, the energy of a fall is reported to be associated with sustaining a hip fracture (Greenspan et al. 1994) but in more frail older individuals, the strength of the bone seems to become more important (Greenspan et al. 1998).

The risk factors for low bone strength (Nordin 2008; Papaioannou et al. 2009; Sweet et al. 2009; Waugh et al. 2009; Wu et al. 2009) and the risk between low bone strength and fractures (Seeley et al. 1991; Cummings et al. 1993; Kröger et al. 1995) are rather well reported. Risk factors for bone mass loss are presented in Table 3 and their association with fractures in Figure 4 (Espallargues et al. 2001).

Table 3. Risk factors for fractures related to bone mass loss in a meta-analysis*

High risk (RR ≥ 2)	Moderate risk (1< RR <2)
- Age over 75 years	- Female
- Low body weight	- Active smoking
- BMI < 20-25	- Low sunlight exposure
- weight < 40 kg	- Family history of osteporotic fracture
- Weight loss (>10%)	- Surgical menopause
- Physical inactivity	- Early menopause (<40 years)
- Corticosteroids	- Short fertile period (<30 years)
- Anticonvulsants	- Late menarche (>15 years)
- Primary hyperparathyroidism	- No lactation
- Diabetes mellitus type I	- Low calcium intake (<500-850 mg/day)
- Anorexia nervosa	- Hyperparathyroidism
- Gastrectomy	- Hyperthyroidism
- Pernicious anaemia	- Diabetes mellitus type II
- Prior osteoporotic fracture	- Rheumatoid arthritis

* Adapted from a systematic review and meta-analysis of Espallargues and colleagues including 94 cohort and 72 case-control studies (Espallargues et al. 2001).

3.3 Functional decline and fractures

In older persons, the development of functional decline and disability is a dynamic process (Verbrugge & Jette 1994) with considerable diversity (Gill & Kurland 2003). In the disablement process (Verbrugge & Jette 1994), disease or injury is defined as an activator (pathology) leading to dysfunction and structural abnormalities in a special body system (impairment). Such impairment can lead to functional limitations that are restrictions in performing fundamental physical and mental actions used in age- and gender-specific daily life (e.g walking). Disability is experienced as difficulty in doing activities in any domain of age- and gender-specific life (ADL, IADL, hobbies etc.). Due to functional limitations and reduced abilities to perform individual-based activities, functional disabilities lead to some kinds of compensatory activities: either to activity accommodation or reduction in individual-based activities by individuals themselves (intra-individual factors) or a need for external support by others as personal assistance in one or more activities of daily living (extra-individual factors) (Verbrugge & Jette 1994; Ferrucci et al. 1996; Gill et al. 2004).

The most used and internationally validated tests/questionnaires for assessing domestic daily living are Katz’s (Katz et al. 1963) and Barthel’s (Mahoney & Barthel 1965) indexes for assessing ADL tasks (ability of bathing, dressing, toileting, transfer, continence and feeding) and Lawton and Brody’s scale for IADL tasks (Lawton & Brody 1969). Also the abilities to move (mobility) within the home, the immediate neighbourhood and the larger community are usually assessed (German 1981). The IADL tasks include a variety of tasks; self-medicating, phone use, handling money, shopping, etc. In the 2000s, many variations in tests and questionnaires have been used in describing disability and function in different studies (Freedman et al. 2002; Rockwood 2007). However, there is no golden standard for measuring functional abilities after a fracture.

Most types of fractures are reported to be associated with long-standing pain, functional decline or dependence in activities of daily living (ADL) and admission into institutional care (Braithwaite et al. 2003; Melton 2003; Kannus et al. 2005b; Greendale & Barrett-Connor 2008). After a hip fracture, about every fifth to fourth of the patients who were independent before a fracture needed long-term institutional care, and about half of the patients were able to return to their own homes. In a study conducted in the southeast of Finland, 12.5% of those who survived after a sustained hip fracture and were living independently before a fracture needed long-term institutional care one year after a hip fracture (Nurmi et al. 2004). The increased risk of long-term institutionalisation is due to reduced mobility and ability to perform activities of daily living after a fracture, at least in hip fracture patients (Willig et al. 2001; Kirke et al. 2002). The impact of fractures on the process of functional decline and dependency is illustrated in Figure 5.

Recovery after a hip fracture (Young et al. 1997; Ingemarsson et al. 2003; Alegre-Lopéz et al. 2005; Hawkes et al. 2006; Pande et al. 2006) and a proximal humerus fracture (Gaebler et al. 2003) have been reported to be dependent on the person's health and functional status before the fracture. Therefore, a poor outcome after a fracture has been explained by the patient's pre-fracture status. The diversity in the study designs have left the independent impact of fractures on post-fracture functional performance unclear: only a few population-based studies (Willig et al. 2001; Magaziner et al. 2003; Alegre-Lopéz et al. 2005; Hasserius et al. 2005; Olsson et al. 2005) or studies with a comparison group without fractures and information about comorbidities (Willig et al. 2001; Magaziner et al. 2003) have been published.

Among all fractures, a sustained hip fracture has a special role in the development of functional decline and dependency in ADL tasks. The hip joint and the muscles attached to the region are critical for the ability to stand and walk. For this reason, a fracture at proximal femur has a great impact on managing activities of daily living. (Committee of the Institute of Medicine Division of Health Care Services 1990). The majority of the studies have focused on the consequences of hip fractures (Magaziner et al. 2000; Willig et al. 2001; Kirke et al. 2002; Magaziner et al. 2003; Alegre-Lopéz et al. 2005; Endo et al. 2005; Hawkes et al. 2006; Pande et al. 2006; Tsuboi et al. 2007; Givens et al. 2008; Holt et al. 2008).

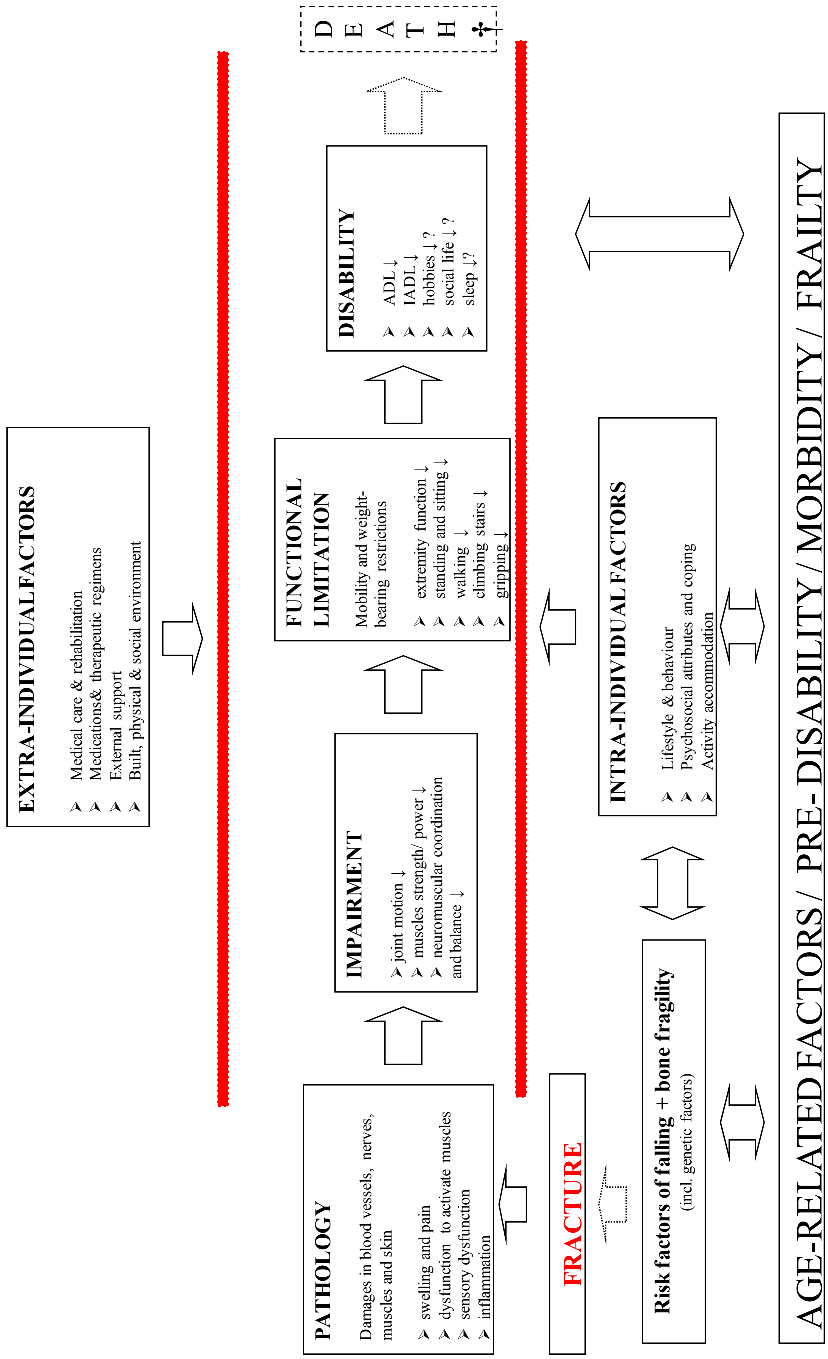


Figure 5. Bone fractures and the process of disability and death in older people. Modificated picture adapted from Verbrugge & Jette 1994.

3.3.1 Short-term follow-up

The short-term outcomes of lower body fractures on locomotion and physical performance are mainly reported in hip fracture patients. A variety of study designs have been used, ranging from a population-based case-control (Leibson et al. 2002; Magaziner et al. 2003), a case-control (Kirke et al. 2002; Pande et al. 2006) to a follow-up of fracture patients (Magaziner et al. 2000; Hannan et al. 2001; Ingemarsson et al. 2003; Rosell & Parker 2003; Alegre-Lopéz et al. 2005; Endo et al. 2005; Hawkes et al. 2006; Givens et al. 2008). In the follow-up studies (“cohorts”), the follow-up periods have varied from one month (Givens et al. 2008) up to two years (Magaziner et al. 2000; Kirke et al. 2002; Magaziner et al. 2003; Pande et al. 2006).

According to a well-designed population-based case-control study, hip fracture patients (n=594) are reported to be twice as disabled in walking, transferring from bed to chair and grooming (brushing hair and teeth, or washing face) compared with their matched controls from three different cohorts both in 12- and 24-month follow-ups after the fracture (Magaziner et al. 2003) (Table 4). Interestingly, hip fractures decreased also independent ability in managing ADL tasks related to upper body performances, such as grooming (Magaziner et al. 2003).

In other case-control studies, hip fracture patients are reported to be more disabled in mobility-related tasks after a hip fracture compared with gender- and age-matched controls without hip fractures (Kirke et al. 2002; Pande et al. 2006) (Table 4). In a 12-month follow-up, only 36% of hip fracture male patients could walk independently compared with 84% of the controls without a hip fracture (Pande et al. 2006). During a 2-year follow-up, more hip fracture patients have been reported not to get out of the house less than before the fracture compared with controls (80% hip vs. 46% controls) and more hip fracture patients have been reported to walk less than before (73% hip vs. 54% controls) (Kirke et al. 2002). Also the mean level of independence in ADL tasks has decreased significantly more in hip fracture patients in contrast to their controls with no history of hip fractures (Kirke et al. 2002) (Table 4).

Patients living in long-term care facilities are at much higher risk of not returning to prefracture functional levels following hip fracture compared with community-dwelling residents (Nurmi et al. 2004; Beaupre et al. 2007), even if not adjusted for age, baseline function, comorbidities or cognitive status (Beaupre et al. 2007). Six months after a hip fracture, more than half of long-term care residents are no longer ambulating without the help of another person, and they also require assistance in transfer (Beaupre et al. 2007). In contrast, the majority (over 77%) of community-dwelling patients remain independent in ambulation and transfer (Beaupre et al. 2007).

A second hip fracture has a significant further impact on the decline of patients’ mobility and social independence in a three month follow-up (Pearse et al. 2003). It has also been reported that intertrochanteric hip fracture patients are functionally more impaired compared with femoral neck patients after a fracture but the functional outcome has been reported to be similar among surviving patients after one year

(Haentjens et al. 2007). On the other hand, is has been shown that patients with extracapsular hip fractures are more likely to need long-term care compared with intracapsular hip fracture patients (Sund et al. 2009).

Little information is available about the impact of fractures other than hip fracture on functional abilities. In follow-up studies, tibial shaft (Skoog et al. 2001) and ankle fracture (Nilsson et al. 2007) patients are reported to experience functional limitations in using stairs as late as one year after the trauma. Less than half of the ankle fracture patients returned to their pre-activity level (Nilsson et al. 2007). In hospital-treated vertebral fracture patients, the decrease in ADL tasks and quality of life at 4 and 12 months after a fracture is similar compared with hip fracture patients (Theander et al. 2004). In contrast, a good or excellent result evaluated by the patients was achieved in 77% of distal forearm fracture patients with a follow-up of 6 months (Kaukonen et al. 1988).

It is noticeable that after minimally displaced humerus fractures in 507 cases with a one-year follow-up, poor outcome was related to other factors, such as co-morbidities and high age, rather than to the fracture itself (Gaebler et al. 2003). However, it has been shown that hip fractures, vertebral fractures and wrist fractures are all associated with the loss of quality of life one year after a fracture (Borgström et al. 2006).

3.3.2 Long-term follow-up

In a follow-up of seven years, patients sustaining a hip, arm or spine fracture have demonstrated to have a declined physical performance in balance, turning 360° circle, walking, chair standing and grip strength compared with subjects without fractures but similar to age and mean number of medical conditions at baseline (Greendale et al. 2000). However, the number of sustained fractures was very small (7 wrist fractures and 16 hip, arm or spine fractures) in the Greendale (2000) study. A retrospective case-control study with a 10-year follow-up showed that balance and gait were poorer in women who sustained a hip, vertebra or proximal humerus fracture compared with those without a fracture (Gerdhem et al. 2006). In older women, each additional fracture was associated with slower gait, and poor physical performance has been noticed especially in patients who have sustained several fractures (Gerdhem et al. 2006).

The evidence of functional decline is stronger after a hip fracture compared with other fractures. In hip fracture patients, mobility and physical performance has been shown to be impaired for up to 10 years (Willig et al. 2001; Gerdhem et al. 2006; Tsuboi et al. 2007). A 7-year follow-up showed that hip fracture patients have substantially more disability in ADL and physical performance compared with their age- and gender-matched controls without fractures (Willig et al. 2001) (Table 4). A study with a 10-year follow-up showed that the proportion of those able to walk independently outdoors decreased most during the first year after a hip fracture (Tsuboi et al. 2007). In their study, the proportion of those able to walk outdoors before a hip fracture was

68%, decreased to 56% one year after the fracture, and remained stable at 63% thereafter.

A case-control study showed physical performance to be impaired most commonly in women with hip and multiple fractures (Gerdhem et al. 2006). In a population-based cohort of 218 hip fracture patients in Spain, one year after a hip fracture women had more difficulties in functioning compared with men (Alegre-Lopéz et al. 2005). In a Finnish one-year cohort study in male and female hip fracture patients, no association was found between the female or male gender and poorer functional outcome at 2 or 4 months after the fracture. However, the women needed more help in transferring from or into bed, turning in bed and getting up from bed (Nurmi et al. 2004).

Upper extremities fractures limit old persons' joint function, physical performances and reduce their independence in activities of daily living (ADL) tasks for up to 13 years (Olsson et al. 2005; Földhazy et al. 2007). Wrist, forearm and proximal humerus fractures limit the functional ability and reduce the independence in daily living for up to 13 years (Greendale et al. 2000; Olsson et al. 2005; Földhazy et al. 2007). Almost one half of female patients with vertebral fractures report recurrent back pain and impaired health status for as long as 12 years after the fracture (Hasserius et al. 2005).

In the USA, the cumulative incidence of nursing home admission at 3 months after baseline was 60% (95% CI = 54-67) for hip fracture patients living outside a nursing home before a hip fracture versus 3% (95% CI 1-5) for similar controls (Leibson et al. 2002). The cumulative incidence at 1 year was 64% in hip fracture patients versus 7% for controls. The risk of nursing home admission remained elevated at least 5 years after the fracture (Leibson et al. 2002). In a Finnish study with a mean of 7-year follow-up, 27% of those who survived hip fracture were living in a nursing home or chronic care hospital compared with 2% of their age- and gender-matched controls randomly selected from the Finnish Population Register (Willig et al. 2001).

An increased risk for changing from home or sheltered housing into long-term institutional care is also associated with vertebral fractures (Greendale & Barrett-Connor 2008), whereas in forearm fracture patients there is no reported change in the living situation after a fracture (Endres et al. 2006). However, a subsequent injurious fall after a serious fall-related fracture increases the risk for further injurious falls, readmitting to hospital and transferring to nursing home (Lord et al. 1992; Tinetti & Williams 1997).

Authors, year and country	Participants	Controls	Follow-up period	Measures of outcome	Adjusted variables	Results	Comments
Magaziner et al. 2003, USA	65+ y, n=594, mean 80.5 y, 75% women, community-dwelling	65+ y, three cohorts (n= 594 in each), 75% women, community-dwelling	12 mo 24 mo	Disabled or dependent in - walking indoors (3 m), - transferring from bed to chair, - grooming (hair, teeth)	age, sex, comorbidities, ability of walking	After **12 mo: dependent in walking** 54% hip fr.p. vs. 21-22% controls; in **transferring** 38% hip fr.p. vs. 10-13% controls; in **grooming** 17% hip fr.p. vs. 7-11% controls. After **24 mo dependent in walking** 53% hip fr.p. vs. 25-29% controls; **in transferring** 39% hip fr.p. vs. 14-18% controls; in **grooming** 18% hip fr.p. vs. 10-14% controls	8% of patients had a history of a previous hip fracture. Controls from a prospective study of risk factors for chronic disease, loss of fuctioning and mortality including three cohorts (n= from 2539 to 3492) from three US states. Controls matched from the original cohorts by sex, age and ability to walk indoors.
Leibson et al. 2002, USA	Mean age 81 y, n=312, 81% women, 18% in institution	Mean age 81 y, n=312, 81% women, 28% in institution	12 mo	Ranking disability score (1=no significant disability, 5=severe disability)	age, sex	**Score at 12 mo:** 3.2 +/- 1.2 in hip fr.p. vs. 2.3 +/- 1.3 in controls (p<0.001)	Isolated trochanteric and subtrachenteric fractures were excluded. Controls from Mayo Clinic of whom 18 sustained a hip fracture during the follow-up.
Pande et al. 2006, United Kindom	50+ y, n=100, mean age 80 y,100% men, 15% in institution	50+ y, n=100, mean age 75 y, 100% men, 2% in institution	12 mo 24 mo	Inability to walk independently. Functional ability: Health Assessment Questionaire (HAQ) (range 0-3; higher score indicating more difficulties).	age, sex	After **12 mo inable to walk:** 15% hip fr.p. vs. 1% controls , **24 mo inable to walk:** 20% hip fr.p. vs. 0% controls, Mean **HAQ score** at 12 and 24 mo: 1.2 in hip fr.p. vs. 0.39 in controls	Controls from a local general practioner register with no history of a hip fracture.
Kirke et al. 2002, Ireland	50+ y, n=106, mean age 80 y, 100% women, 24% in institution (no moderate or severe dementia)	50+ y, n=89, mean age 77.8 y, 100% women, 20% in institution (no moderate or severe dementia)	24 mo	Inability to walk 100 yards unaided. ADL score by Katz and Akpom (score 0= total independence, 6= total dependence).	age, sex	**Inable to walk** 58% hip fr.p. vs. 11.5% controls, p<0.001, **Change in ADL score +**1.4 (from 0.56 to 1.95) in hip fr.p. vs. +0.23 (from 0.36 to 0.58) in controls (p<0.001)	Controls with no history of hip fractures attended accident & emergency or in-patient department of the hospital or lived in community residence for older people in the catchment area of a hospital. Hip fr.p. and controls did not differ from controls in place of residence, social class or marital status.
Willig et al. 2001, Finland	Original n=200. At follow-up: n=62, mean age 79 y, 81% women	Original n=200. At follow-up: n=92, mean age 77 y, 81% women	Mean 7 y (from 4.5 to 10.5 y)	Ability in walking and in ADL functions. Need for care/assistance at home.	age, sex	**Ability to walk alone outdoors**: 42 (36%) of the hip fr.p. Vs. 73 (79%) in controls. **Ability in ADL tasks:** worse in every* task in hip fr.p. vs. in controls (p < at least 0.005). **No need for care/assistance at home**: 28 (45%) in hip fr.p. Vs. 53 (58%) in controls.	Included only trochanteric hip fracture patients. Controls from Finnish Population Register (the sampling method from the register is not informed).

y= years, mo= month, hip fr.p. = hip fracture patient(s), ADL= activities of daily living

* Worse in all tasks except in eating.

3.4 Excess mortality and fractures

Several types of fractures are associated with excess mortality (Center et al. 1999; Bliuc et al. 2009). The standardised mortality rate of sustaining any fracture is 1.76 (95% CI, 1.59 – 1.95) for women and 1.96 (95% CI, 1.69 – 2.28) for men compared with general Australian population aged 60 years or older (Bliuc et al. 2009).

The term excess mortality is used to describe deaths which are connected with a special event (e.g. a hip fracture) and which could be prevented without the accelerating impact of the event in the process of dying (Tosteson et al. 2007). The difficulty in attributing excess impact of fractures to excess death, especially as to the hip fracture *per se*, is related to the fact that increased risk of fractures is associated with advanced age (Endres et al. 2006; Bergström et al. 2008; Ahmed et al. 2009). Especially hip fractures occur in those individuals who are already at an increased risk of dying from other causes (Browner et al. 1996; Tosteson et al. 2007). In a Dubbo population-based study among individuals 60 years or older with a follow-up of 18 years, an increased mortality risk was found during the first 5 years following all major (femur, pelvic, proximal humerus) fractures, except for hip fractures where the impact of a fracture on mortality remained elevated even longer (Bliuc et al. 2009). A subsequent fracture resulted in an elevated mortality risk for 5 years (Bliuc et al. 2009).

In addition to advanced age, quadriceps weakness and subsequent fracture but not comorbidities are shown to be associated with excess mortality after any fragility facture for both older men and women (Bliuc et al. 2009). After a fracture, low bone mineral density, previous smoking and increased body sway are also predictors for accelerated death in older women, and less physical activity in older men (Bliuc et al. 2009).

3.4.1 Hip fractures

Hip fractures have a significant impact on excess mortality (Melton 1995; Lüthje et al. 1995a; Roberts & Goldacre 2003; Nurmi-Lüthje et al. 2009; Haentjens et al. 2010). In a Finnish register-based data, mortality has proven to be similar among patients with an intra- or extracapsular hip fracture (Sund et al. 2009), but noticeably high mortality is reported in inter- or pertrochanteric hip fracture patients (Endres et al. 2006; Haentjens et al. 2007).

About 6 to 14% of the hip fracture patients die after the first admission to the hospital (Rissanen & Noro 1999; Roberts & Goldacre 2003; Sund et al. 2008) and 22 to 40% of the patients die within the first year (Rissanen & Noro 1999; Leibson et al. 2002; Roberts & Goldacre 2003; Nurmi et al. 2004; Haleem et al. 2008; Sund et al. 2009). Global geographic (Haleem et al. 2008) and even within-country (Sund et al. 2008) variations exist in the mortality rates.

In the most recently published meta-analysis including 24 prospective cohort studies in hip fracture patients aged 50 years or older, with 578 436 women and 154 276 men, patients with a hip fracture have 5 to 8-fold risk of mortality during the first 3 months after hip fracture compared with those without a hip fracture (Haentjens et al. 2010) (Table 5). The excess mortality risk after a hip fracture decreases over time, especially during the first 2 years after fracture (Haentjens et al. 2010), but the risk of dying remains elevated for up to 10 years when compared with age- and gender-matched population without hip fractures (Bliuc et al. 2009; Haentjens et al. 2010).

Table 5. Relative hazard of all-cause mortality for women and men with hip fracture compared with control patients over a 10-year follow-up *.

Follow-up	**Women**		**Men**	
	RH (95% CI)	**p-value**	**RH (95% CI)**	**p-value**
0-3 mo	5.75 (4.95 - 6.69)	<0.001	7.95 (6.13 - 10.30)	<0.001
3-6 mo	3.32 (2.18-5.07)	<0.001	3.56 (2.64-4.80)	<0.001
6-9 mo	1.92 (1.59-2.32)	<0.001	2.33 (1.91-2.85)	<0.001
9-12 mo	1.59 (1.26- 2.00)	<0.001	2.30 (1.81- 2.93)	<0.001
0-1 y	2.87 (2.52 - 3.27)	<0.001	3.70 (3.31 - 4.14)	<0.001
1-2 y	1.86 (1.60 - 2.16)	<0.001	1.90 (1.58 - 2.30)	<0.001
2-3 y	1.58 (1.09 - 2.29)	0.016	1.69 (1.36 - 2.10)	<0.001
3-4 y	1.71 (1.35 - 2.16)	<0.001	1.76 (1.44 - 2.14)	<0.001
4-5 y	1.91 (1.53 - 2.38)	<0.001	1.71 (1.37 - 2.13)	<0.001
5-6 y	1.81 (1.30 - 2.53)	<0.001	1.51 (1.33 - 2.71)	<0.001
6-7 y	1.50 (1.23 - 1.83)	<0.001	1.29 (0.98 - 1.72)	0.073
7-8 y	1.69 (1.16 - 2.45)	0.006	1.66 (0.96 - 2.87)	0.069
8-9 y	1.96 (1.30 -2.95)	<0.001	1.91 (1.32 -2.78)	<0.001
9-10 y	1.99 (1.42 -2.78)	0.001	1.79 (1.14 -2.81)	0.012

* Table adapted from the meta-analysis of Haentjens et al 2010.

The mortality rate after a hip fracture increases with age (Haentjens et al. 2010) and is the highest in the oldest age groups (Roberts & Goldacre 2003; Tosteson et al. 2007; Bliuc et al. 2009; Haentjens et al. 2010). There is strong evidence that mortality after a hip fracture is higher among older men than women (Roberts & Goldacre 2003; Bruyere et al. 2008; Bliuc et al. 2009; Haentjens et al. 2010). However, there are also studies in which women are found to be at higher risk of mortality (Nurmi et al. 2004; Nurmi-Lüthje et al. 2009), especially when adjusted for pre-fracture health status (Tosteson et al. 2007). The gender-specific excess mortality rates have also been reported to vary between health care regions in Finland (Lüthje et al. 1995a).

Other independent conditions associated with excess hip fracture mortality are reported to be osteoarthritis and related conditions, dementia, no surgical procedure, and 2 or more co-morbid conditions at baseline (Bentler et al. 2009) as well as severe systemic diseases according to American Society of Anesthesiologists (ASA) classification (Owens et al. 1978), and increasingly severe cognitive dysfunction (Söderqvist et al. 2009). The existence of chronic lung disease is associated with increased risk of death after a hip fracture (Panula et al. 2009).

Recent studies have shown a decline in the subsequent mortality rates after a hip fracture both in men and women aged 65 years or older from 1986 to 2004 in the US (Brauer et al. 2009) and from the early 1980s to 1998 in England (Roberts & Goldacre 2003). In Finland, the proportion of deaths within one year after a hip fracture was about 20% in year 2007 (Sund et al. 2008).

3.4.2 Fractures of the proximal humerus

In many studies, the association of proximal humerus fractures with excess mortality has been analysed by combining humerus fractures to a group of other fractures, usually to a group of "major fractures" including also distal femur, pelvic, proximal tibia and multiple rib fractures (Center et al. 1999; Bliuc et al. 2009). In these studies, gender-specific and standardised five-year (Center et al. 1999) and 18-year (Bliuc et al. 2009) mortality ratios have been significantly higher in persons who have sustained any of the major fractures compared with mortality in the general population. Nevertheless, proximal humerus fractures themselves have been shown to increase mortality both in women (Browner et al. 1996; Johnell et al. 2004c; Shortt & Robinson 2005) and in men (Johnell et al. 2004c; Shortt & Robinson 2005) older than 60 years of age (first year HR ratios have varied from 1.4 to 1.9 in persons over 65 years of age) (Shortt & Robinson 2005). The association is highest during the first year after a fracture (Johnell et al. 2004c; Shortt & Robinson 2005).

3.4.3 Vertebral fractures

There is evidence that a vertebral fracture in the thoracic or lumbar spine increases mortality in men and women along with age (Cooper et al. 1993; Center et al. 1999; van Staa et al. 2001; Hasserius et al. 2003; Johnell et al. 2004c; Pongchaiyakul et al. 2005). After a vertebral fracture, the age- and gender-specific standardised mortality rate per 100 PY is 1.82 (95% CI, 1.52-2.17) for women and 2.12 (95% CI, 1.66-2.72) for men compared with the overall mortality rate of Dubbo population aged 60 years or older in Australia (Bliuc et al. 2009).

Mortality rate is reported to be especially high in those with a vertebral deformity who had had a subsequent symptomatic fracture (HR 9.0, 95% CI: 3.1-26.0) (Pongchaiyakul et al. 2005). A part of this excess mortality is explained by health and lifestyle factors (Ismail et al. 1998), and it is shown that the risk of death decreases after 5 years after a sustained vertebral fracture (Johnell et al. 2004c).

3.4.4 Forearm and wrist fractures

Previous studies have not shown forearm and wrist fractures to be associated with higher mortality in an older population (Cooper et al. 1993; Browner et al. 1996; Johnell et al. 2004c). There is even evidence that persons sustaining a wrist fracture may have significantly improved survival rates compared with general population in a five-year follow-up (Shortt & Robinson 2005). However, somewhat controversial results have been reported in studies which included distal forearm and wrist fractures in a group of "minor fractures" including also lower leg fractures (Center et al. 1999; Bliuc et al. 2009). In these studies gender-specific and standardised five-year mortality in men (Center et al. 1999) and 18-year mortality in women (Bliuc et al. 2009) who have sustained any of the minor fractures have been significantly higher compared with mortality in the general population.

3.4.5 Other fractures

In nursing home residents at least 65 years of age, an excess mortality has been found during the first months in both genders after pelvic fracture (in women: HR 1.83, 95% CI: 1.42-2.37, and in men: HR 2.95, 95% CI: 1.57-5.54 for the first month). The increased mortality appeared to last longer in men than in women (Rapp et al. 2010).

Rib fractures are related to both mild and severe traumas (Sirmali et al. 2003). In patients with high age and high Injury Severity Score, they are shown to be associated with both high mortality and the presence of pneumonia (Bulger et al. 2000; Brasel et al. 2006). Pneumonia is more common in older patients compared with young ones (Bulger et al. 2000). In addition, other complications have been noted in rib fracture patients, also in older patients who have sustained their fractures either in traffic or fall-related accidents (Sirmali et al. 2003). The greater the number of fractured ribs, the higher the mortality rate (Bulger et al. 2000; Sirmali et al. 2003) even though this association has not been noticed in all studies (Brasel et al. 2006). The overall mortality in rib fracture patients admitted to trauma centres has been reported to be 4% (Brasel et al. 2006) and in patients 65 years and over as high as 22% (Bulger et al. 2000) compared with patients without rib fractures.

There is no clear evidence of excess mortality risk associated with other fracture types.

3.5 Summary and need for further research

The number of fractures is high among older people causing many challenges both for the individual and society. Incidence data on fractures obtained from population-based studies have been published (Melton et al. 1998; Sanders et al. 1999; Ismail et al. 2002; Chang et al. 2004; Jonsson et al. 2004) but updated information about the rates, trends, risk factors and consequences of fractures is needed. In addition, only a few studies have been published concerning the incidence of all kinds of fractures (Jones et al. 1994; Baron et al. 1996; Johansen et al. 1997; Sanders et al. 1999; Melton et al. 1999b; Jonsson et al. 2004). This information is needed for evaluating the trends in all kinds of fractures to facilitate allocating public health resources for the prevention and treatment of fractures.

In previous studies, the inclusion or exclusion criteria of fractures have varied. For example, only 'osteoporotic fractures' have been included (Jones et al. 1994; Kanis et al. 2000; Ismail et al. 2002; Chang et al. 2004) or fractures due to high-impact accidents have been excluded (Jones et al. 1994; Chang et al. 2004). Thus, the influence of osteoporosis on fracture rates may have been overestimated (Sanders et al. 1998). In most studies, only the first fracture has been taken into account (Baron et al. 1996; Sanders et al. 1999; Kanis et al. 2000; Ismail et al. 2002) although all patients with a fracture need at least some medical attention. In many studies the incidence of hip fractures has been derived from hospital discharge registers (Baron et al. 1996; Gullberg et al. 1997; Kannus et al. 1999; Schwartz et al. 1999) leading to possible inaccuracies (Langley et al. 2002). There are studies in which only people with health care insurance have been included (Baron et al. 1996). Using only self-reported information on fractures (Honkanen et al. 1999; Ismail et al. 2002) the accuracy of fracture data is poor, at least in the case of minor, vertebral and rib fractures. Based on previous studies, the loading impact of fractures on emergency treatment departments and health services may have been underestimated.

Information is available about the risk factors of fractures. There is even a series of meta-analyses published on some specific risk factors of fractures (Kanis et al. 2004a; Kanis et al. 2004b; De Laet et al. 2005; Kanis et al. 2005b; Kanis et al. 2005c), but there are rather few prospective population-based studies (Jacqmin-Gadda et al. 1998; Huopio et al. 2000; Stel et al. 2004; Nguyen et al. 2007) on predictors of all types of fractures both in men and women. Gender-based differences have been noticed in predictors of falls (Campbell et al. 1989) and fractures (White et al. 2006; Hippisley-Cox & Coupland 2009). However, more information about gender-specific risk factors of fractures is needed.

Some information about the consequences of fractures, predictors of survival after fracture or predictors of decline in functional ability due to fracture have been reported, but a majority of the studies have focused on hip fracture (Magaziner et al. 2000; Willig et al. 2001; Ingemarsson et al. 2003; Magaziner et al. 2003; Rosell & Parker 2003; Alegre-Lopéz et al. 2005; Endo et al. 2005; Olsson et al. 2005; Hawkes et al. 2006; Pande et al. 2006; Tsuboi et al. 2007; Holt et al. 2008). There are rather few prospective population-based studies reporting consequences (Stel et al. 2004) of all types of fractures both in men and women. More research in this field is needed.

4. AIMS OF THE STUDY

The aims of the present study were to describe incidence, predictors and consequences of fractures among Finnish people aged 65 years or older during long-term follow-up.

In detail, the aims were:

1. To describe the age-specific incidence of fractures by type of fracture among older men and women (study I).
2. To analyse secular changes in the age-adjusted incidence of fractures among the older people (study I).
3. To identify gender-specific predictors of fractures among the older people (study II).
4. To analyse independent associations between fractures and functional ability in an unselected older population both in short- and long- term follow-ups (study III).
5. To analyse gender-specific factors predicting mortality after fractures among older people (study IV).

5. MATERIALS AND METHODS

5.1 Study settings and subjects

This study is part of a larger, longitudinal, population-based study of subjects aged 65 years or older living in the semi-industrialised municipality of Lieto, south-western Finland (Isoaho et al. 1994a; Isoaho et al. 1994b; Ahto et al. 1998; Linjakumpu et al. 2002; Löppönen et al. 2003). The baseline data were collected between 1990 (October 1) and 1991 (December 31) (Lieto Study I) (Isoaho et al. 1994a). The original population consisted of all residents in Lieto born in 1926 or earlier (N=1283), of whom 1196 (93%), 488 men and 708 women, participated.

The occurrence of fractures among the participants of the Lieto Study I were derived from medical records from October 1990 to the end of December 2002. The fracture data was obtained for 1177 (92%) persons, 482 men and 695 women. These 1177 persons formed the study population for the studies I, II and IV (Figure 6).

The second wave of the Lieto study (Lieto Study II) was carried out between March 1998 and September 1999 (n=1260) (Löppönen et al. 2003). Re-examinations were performed for 616 participants (241 men, 375 women), who had participated in the Lieto Study I. These 616 persons having taken part both in the Lieto Study I and in the Lieto Study II formed the subjects for this dissertation's study III (Figure 6).

5.2 Informed consent and ethical approvals

The study was conducted according to the guidelines of the Declaration of Helsinki. Informed consent was obtained from all participants or their caregivers. The Joint Ethics Committee of the University of Turku and the Hospital District of Southwest Finland approved the study plan. The Finnish Ministry of Social Affairs and Health, the Finnish National Research and Development Centre for Welfare and Health, and the Lieto District Health Authority approved the collection of fracture and mortality data during the follow-ups.

5.3 Data collection

Wide-ranging data about socio-demographic, education, previous occupation, economical, functional abilities, health behaviour, cognitive and psychological abilities, health, illnesses and other clinical factors in the Lieto Study were collected by structured interviews, tests and measurements (Isoaho et al. 1994a; Ahto et al. 1998; Löppönen et al. 2003). In addition, information was gathered from the Finnish Hospital Discharge Register and Cause of Death Statistics.

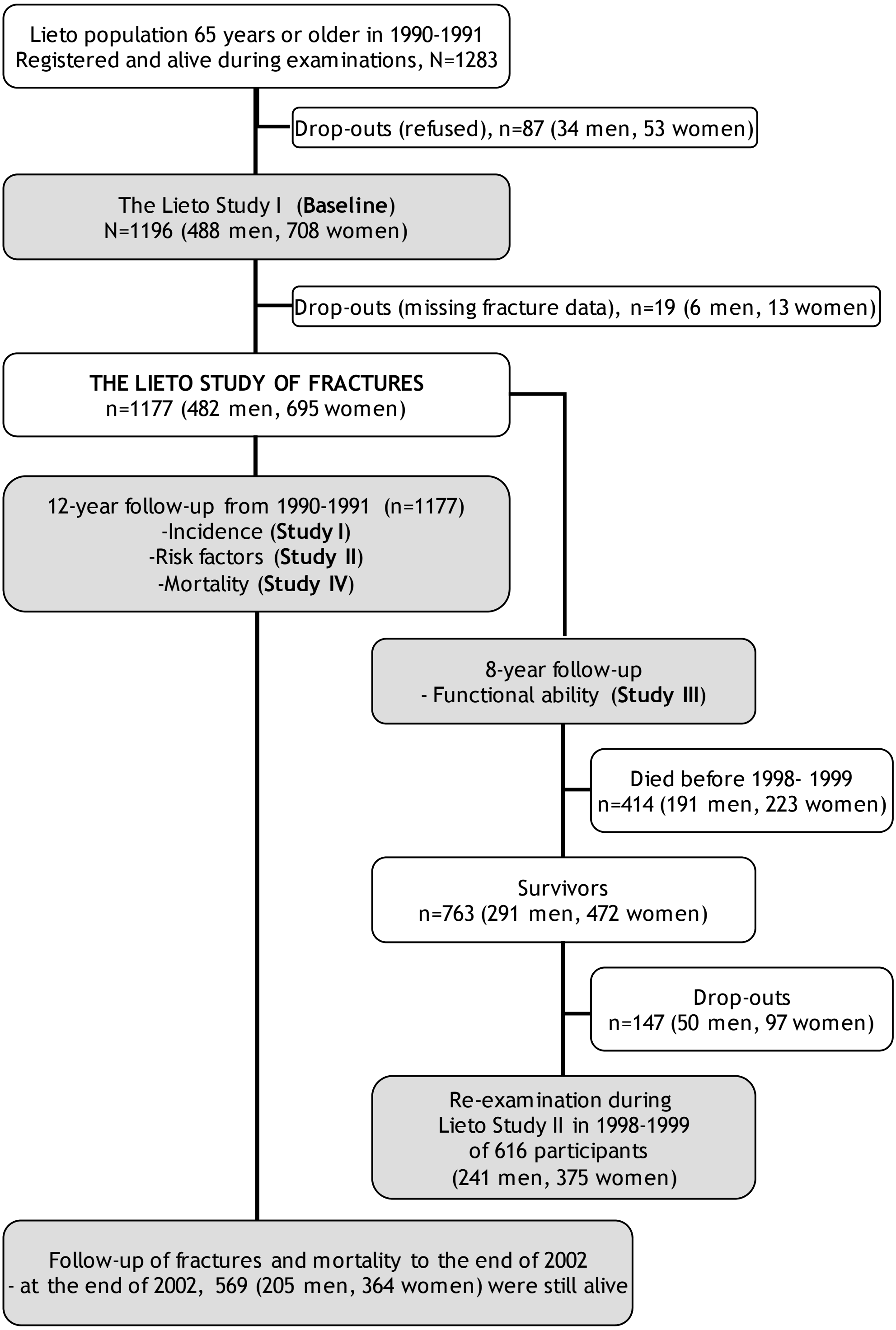


Figure 6. Study flow of the Lieto study of fractures.

The participants made two visits to the Lieto Health Centre during both data collection waves (Lieto Study I and Lieto Study II). The interviews, tests and measurements were carried out by two trained nurses and the clinical examinations were performed by two experienced general practitioners, GPs (Raimo Isoaho in 1990-1991 and in 1998-1999, Minna Löppönen in 1998-99). If a person was not able to visit the Health Centre, a home visit or a visit to the nursing home was made. Proxy interviews were carried out for 75 (6%) out of 1177 subjects in 1990-1991 and for 79 (13%) out of 616 subjects in 1998-1999.

The author of this doctoral thesis was not involved in planning and collecting the baseline data for the original Lieto cohort studies implemented in 1990-1991 (Lieto I) and 1998-1999 (Lieto II). However, the author of this doctoral thesis planned the study protocol and data collection of the Lieto Study of fractures and acquired all necessary permissions for data collection from the authorities of The Finnish Ministry of Social Affairs and Health, the Finnish National Research and Development Centre for Welfare and Health, and the Lieto District Health Authority. She collected, recoded and re-checked the data of fractures from 1990 to the end of 2002 individually for 1177 study subjects and added the data into the original databases of Lieto Study I and II.

5.3.1 Baseline interviews, tests and measurements

Socio-economic factors included information about gender, age, marital status, accommodation, education, previous occupation and economical status.

The interview included 14 questions about functional abilities (Heikkinen et al. 1983; Waters et al. 1989). Mobility was assessed by questions about ability to walk outdoors, walk between rooms, negotiate stairs, and walk at least 400 metres. Managing activities of daily living (ADL) was assessed with questions of abilities to go to toilet, wash and bath, dress and undress, get in and out of bed, and eat. Managing instrumental activities of daily living (IADL) was assessed with questions about abilities to prepare meals, do light housework, do heavy housework, carry a 5-kg load at least 100 metres, and cut one's toe nails. The use of mobility aids was recorded.

Health behaviour was assessed by questions about smoking and engagement in physical activity. Smoking was categorised as non-smoker, ex-smoker and current smoker. Leisure time physical exercise was assessed by one dichotomised question "In addition to your ordinary household work, do you do physical exercise as a hobby?"

Cognitive abilities were measured with the Mini-Mental State Examination test (MMSE) (Folstein et al. 1975) and depressive symptoms with the Zung Self-rating Depression Scale (ZSDS) (Zung 1965). Subjects were coded as having a large number of depressive symptoms if they scored 45 or more points on the ZSDS (Rainio 1991; Salminen et al. 2005).

Questions about health and medical status included information about diagnosed diseases, symptoms, and use of drugs. All prescription and non-prescription drugs used in the previous seven days were recorded. Medical diagnoses and the use of prescription drugs were confirmed from the health centre medical records. The number of drugs was used as an indicator of co-morbidity (Perkins et al. 2004).

Weight, height, visual acuity, hearing ability, blood pressure and handgrip strength were measured. Body mass index (BMI) was calculated as kilograms per height squared (kg/m2) and categorised according to the WHO recommendations as <25, 25-29.9 and ≥ 30. Binocular visual acuity was tested with the Snellen E-Chart. Subjects using glasses were asked to wear them in the test. The ability to read normal print (font 12) was tested in a sitting position from a distance of 40 cm. The ability to hear normal speech with or without a hearing aid at a distance of one to five metres was tested. Diastolic and systolic blood pressures were measured in a sitting position and categorised using quartiles. Handgrip strength was measured with an Elmed Vigorimeter ® (hand dynamometer) consisting of three different-sized rubber balls, and the measurement was used as an index of muscle strength. The research nurse selected a suitable rubber ball for each person. One technically successful attempt was accepted for both hands. If a subject could not use one or the other hand, only one hand was tested.

5.3.2 Fractures

Information about fractures (date, type and cause of fracture, type and place of accident, type of dwelling at the time of fracture, treatment and rehabilitation) confirmed with radiology reports from October 1990 until the end of December 2002 was collected from the medical records of the Lieto and Turku Health Centre units, from the Finnish Hospital Discharge Register and Cause of Death Statistics. Data on fractures from all sources were obtained for 1177 of the 1196 subjects (98 %). The double calculation error of fractures due to hospital transfers was eliminated by following the treatment path of each fracture individually during the whole 12-year follow-up period. Twenty-three of the subjects (6 men and 17 women) sustained more than one fracture within the same accident. In these cases, the main fracture contributing to the need for treatment and rehabilitation was taken into account.

Chest roentgenograms were taken from two different angles during the Lieto Study I baseline examination (1990-1991), and the pictures were checked by one experienced GP (RI). A compressed fracture in thoracic and upper lumbar (mainly L1) vertebra was diagnosed if the vertebra was obviously compressed to a wedge shape. In addition to roentgenograms, possible information about kyphotic spine and history of back pain were obtained. Only definite compression fractures (all severe and most of moderate deformities in Genant's classification) were recorded (Genant et al. 1993). One or more compression fractures in the thoracic and upper lumbar vertebra were used as an indicator of bone fragility in this study.

Fractures were categorised according to the International Classification of Diseases (ICD), by 9 codes during 1990-1995 and by ICD 10 codes from 1996 onwards. All codes were converted into ICD 10 codes (The WHO 1995), and fractures were grouped as follows: all fractures, hip fractures (S72.0, S72.1, S72.2), forearm and wrist fractures (S52), tibial and ankle fractures (S82), thoracic and upper lumbar vertebral compression fractures (S 22.0, S 32.0) and other fractures (all fractures other than S72.0, S72.1, S72.2, S52, and S82) (Studies I-III). In addition, proximal humerus fractures (S42.2) and rib fractures (S22.3, S22.4) were used in analysing the association of fractures with excess mortality (study IV). In analysing the impact of fractures on functional abilities, the fractures were grouped by the impact of a fracture site on managing mobility or ADL or IADL tasks and were therefore divided into lower body fractures (S32, S72, S82, S92) and upper body fractures (S22, S42, S52, S62) (Study III). Lumbar vertebral compression fractures were included into lower body fractures because of their influence on weight-bearing and mobility-related tasks.

Accidents were coded according to ICD-9 injury codes (E-codes), and also the place of accident was recorded. Fractures were marked as fall-induced injuries in cases of moderate accidents (falling from standing height or less). Fractures due to falling from stairs or higher than standing height, but not higher than two metres, were classified as serious high-impact injuries. Fractures sustained in traffic accidents or falling from higher than two metres were coded as extremely serious high-impact injuries.

The review of medical records also covered information about previous fractures sustained by subjects before the follow-up period, from their early childhood up to the age of 65 years. All information about these previous fractures was collected. Data on fractures sustained by the subjects after the age of 45 years but before the baseline examination (1990-91) were not included in the calculations of incidence rates, but they were used as a covariate in studies II-IV. The age limit of 45 years was chosen to coincide with the beginning of the menopause in women and to exclude wartime injuries (1939-1945) especially in men.

5.3.3 Functional ability in the 8-year follow-up

Functional abilities were recorded during the Lieto Study II in 1998-1999. The interview included the same 14 questions about functional abilities (Heikkinen et al. 1983; Waters et al. 1989) as used in the baseline interview.

5.3.4 Mortality

Causes of deaths during the follow-up were collected from the Finnish Cause of Death statistics and coded according to the ICD 10 codes (The WHO 1995). The main cause of death was included in the analyses.

5.4 Statistical analyses

Continuous baseline variables were categorised using clinical cut-off points reported in literature when possible or using quartiles (blood pressure and grip strength). In studies I, II and IV, analyses were performed separately for men and women. In analysing the association of fractures with functional abilities, gender was used as one of the covariates.

Pathological fractures caused by cancer etc. (n<5) were excluded from all analyses. In analysing risk factors for fractures (study II), consequences of fractures on functional ability (study III) and impact of fractures on mortality (study IV), fractures caused by the most serious accidents (falling from higher than two metres, impact of a falling object, or traffic accident) were excluded (n=14 in studies II and IV; n=12 in study III).

Differences between categorical variables were analysed by the Chi Square Test or Fisher's Exact Test. Statistical analyses were performed with the SAS System for Windows, version 8.2 or 9.1. (SAS Institute Inc, Cary, NC). In the analyses, p-values of less than 0.05 were considered statistically significant.

5.4.1 Incidence rates of fractures

Incidence rates were calculated for all sustained fractures and for the first fracture of each subject during the 12-year follow-up. Analyses were performed by gender, type of fracture, and age (five-year age groups). Ninety-five per cent confidence intervals (95% CI) for incidences were calculated, based on the assumption that the number of fractures followed the Poisson distribution (Breslow & Day 1987). Person-years (PY) for all fractures were calculated from the beginning of participants' individual follow-up to the end of 2002, or death. Person-years for first fractures during follow-up were calculated from the beginning of follow-up to the occurrence of the first fracture sustained by the subject, to the end of year 2002 or to death. Incidences of fractures were calculated by dividing the number of all fractures or the number of first fractures that occurred during follow-up by person-years (number of fractures/PY).

In addition to the standard Poisson method, the confidence intervals of the incidence were calculated by the generalised estimation equations (GEE) by taking into account the correlation between fractures sustained by the same persons (Agresti 2002). However, the GEE analyses showed similar confidence limits compared with those obtained by the standard method, and these results are not reported here.

Age-adjusted incidences were calculated for all fractures in each year of follow-up. In these analyses, person-years were calculated for each calendar year of follow-up, or to death. Age was determined as age at the time of the fracture or at the end of the corresponding year. The differences in fracture incidences between follow-up years (categorical independent variable) were analysed using Poisson's regression. Age (continuous) was used as a covariate in Poisson regression calculations.

Incidence rates were also analysed by the season of the year. Seasons were categorised as winter (December 1 to the end of February), spring (March to May), summer (June to August) and autumn (September to November).

5.4.2 Predictors (risk factors) of fractures

A 12-year follow-up period (October 1, 1990 – December 31, 2002) was used in analysing the predictors of fractures. Those who had sustained at least one fracture during the follow-up made up a group of fractured persons and those who had sustained no fractures served as a reference group. The first fracture of each individual was included into the analyses.

Diagnosed diseases and health behaviour variables with evidence from literature or otherwise potential to serve as predictors of fractures were included in the analyses. The ability to manage ADL and IADL functions was categorised into three classes: 1) independent, 2) independent with difficulties, and 3) dependent. Handgrip strength was calculated as the mean of both hands' best values. Systolic and diastolic blood pressures and handgrip strength recordings were categorised as follows: the lowest quartile, the second and the third quartiles combined, and the highest quartile, separately by gender.

Univariate and age-adjusted Poisson regression analyses (Breslow & Day 1987) were applied first. The variables showing significant associations with fractures in age-adjusted analyses were further included in multivariate analyses. Age was used as a continuous variable in age-adjusted and multivariate analyses. All analyses were made separately for men and women. Follow-up periods in each analysis were calculated as person-years (PY). Person-years were calculated from the beginning of the follow-up to the occurrence of a fracture or, for persons with no fractures, to the end of the follow-up period (2002) or to death. The results were presented using relative risks (RR) with their 95% confidence intervals (95% CI).

5.4.3 Fractures and functional ability

Mobility, ADL, and IADL functions were categorised in three levels: 1) independent, with no difficulties in any of the included tasks, 2) able to carry out the tasks independently but having difficulties in at least one task and 3) dependent on at least one task. In analysing the impact of fractures on functional abilities, the question of cutting one's toe nails was left out from IADL tasks.

The follow-up period comprised the time from the first baseline measurement in 1990-91 to the re-examination in 1998-99. Functional decline in mobility, or ADL, or IADL performance was detected if the ability to perform tasks at the baseline was changed into a lower level at the re-examination. The 8-year follow-up was split into two periods (Figure 7). The long-term consequences of fractures were analysed for fractures sustained between the years 1990 and 1997. The short-term consequences of fractures were analysed for fractures sustained over the most recent two years before the re-examination in 1998-1999. One fracture of each individual per a follow-up period was included. If the same person sustained more than one fracture during the period, hip or proximal humerus fractures were favoured. In case of several fractures that were likely to have an equal effect on functional decline, the most recent fracture before re-examination in 1998-1999 was included in the analyses.

Cumulative logistic regression model was used in the analyses (Agresti 2002). The dependent variables (mobility, ADL and IADL) consisted of three, ordinal-type categories, and thus cumulative logistic models (proportional odds models) instead of binary logistic regression were used. Variables showing significant associations with a decline in mobility, or ADL or IADL tasks after adjusting age and functional ability at baseline were further included in the multivariate analyses. If there were several variables significantly related to a functional decline and highly correlating with each other, the variables with the strongest relationship with the decline were included in the final multivariate models to avoid multicollinearity. The results were presented using cumulative odds ratios (COR) with their 95% confidence intervals (95% CI).

5.4.4 Fractures and mortality

The follow-up months were calculated from the first baseline measurement to the end of the follow-up period (December 31, 2002) or death. One-year mortality in hip fracture patients was calculated from the date of the fracture. Potential confounding factors for survival at the baseline were analysed using age-adjusted Cox Proportional Hazards model (Collett 2003). The assumptions of proportional hazards were checked by using the plots of log minus log survival functions against log time. The variables showing significant associations with mortality in the age-adjusted analyses were included in the multivariate analyses. The variables with the strongest relationship with excess mortality within a given subcategory in age-adjusted analyses were included in the final multivariate models. Age was used as a continuous variable. The first fracture of each individual was included, and the fractures were used as time-dependent variables (Collett 2003). The results were presented using Hazard Ratios (HR) with their 95% confidence intervals (95% CI). All analyses were made separately for men and women.

A gender-specific external validation of mortality between the study subjects and persons over 65 in the total Finnish population in 1991 was analysed using mortality data derived from the Finnish Cause of Death Statistics. Age-standardised mortality was calculated with the direct method by grouping persons into three age categories (65-74, 75-84, 85+) by gender.

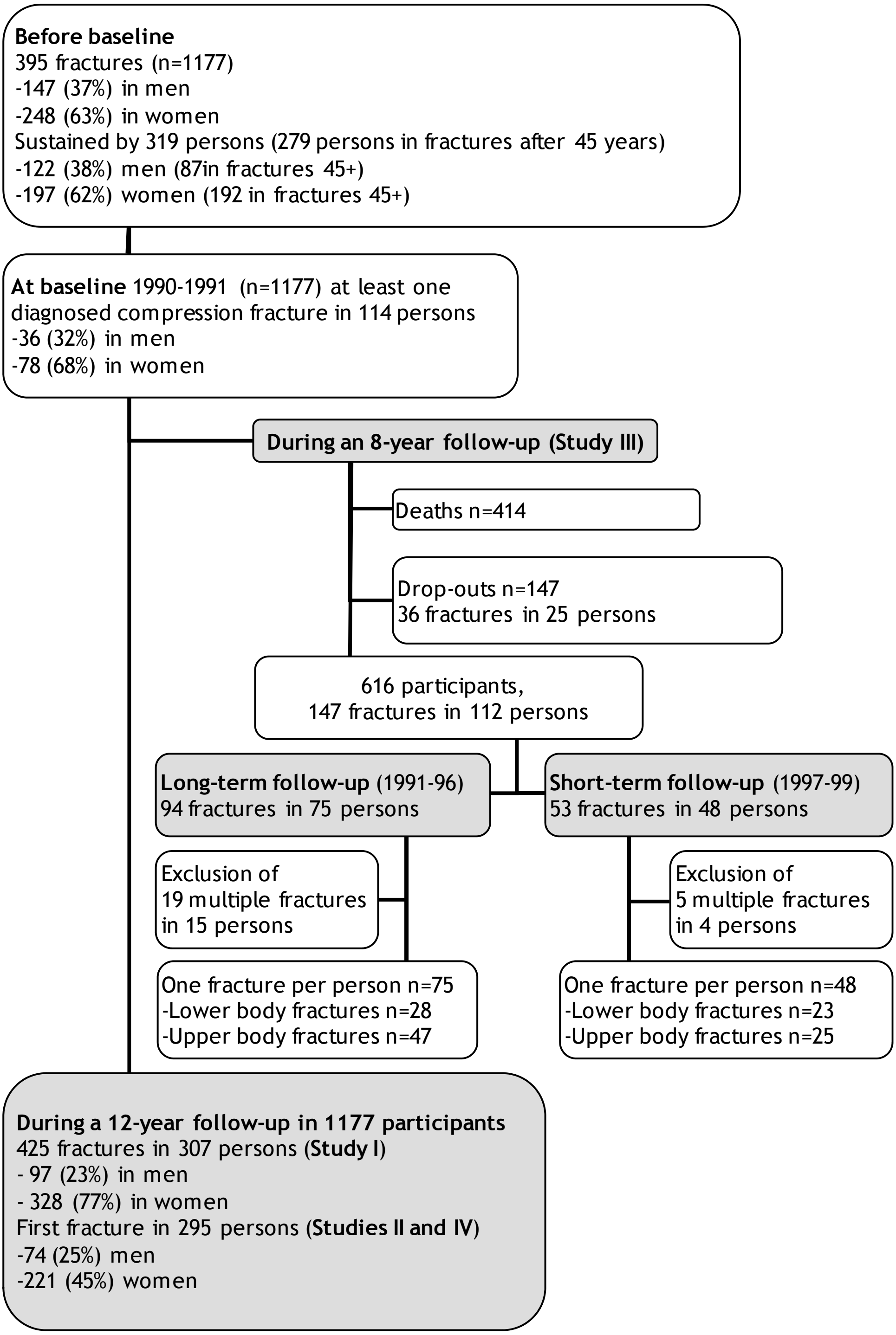


Figure 7. Sustained fractures in the Lieto Study of fractures.

6. RESULTS

6.1 Background data

A follow-up of 12 years (1991-2002) in 1177 participants was used for analysing the incidences and predictors of fractures and the association of fractures with excess mortality. An 8-year follow-up was used for analysing the impact of fractures on functional abilities in 616 survivors who had participated in both examinations. The full background characteristics of the subjects in studies I-II and IV (n=1177) and in study III (n=616) at baseline are presented in appendices (Table appendices 1-4).

Among the participants in the 12-year follow-up, the mean age of the 1177 participants was 72.4 years (standard deviation, SD 6.6) in men and 73.8 (SD 7.0) in women (range of both genders 65-97) at baseline. The median number of diagnosed diseases in men was 5.0 (lower – upper quartile: 3-7) and in women 5.0 (3-8), and the median number of drugs used 2.0 (0-4) and 3.0 (1-5), respectively.

In the 616 participants included in the analyses for functional decline during the 8-year follow-up, the mean age was 70.2 years (standard deviation, SD 5.2) in men and 71.4 (SD 5.7) in women (range in both genders 64-92) at baseline.

6.2 Sustained fractures

6.2.1 During the 8- and 12-year follow-ups

The 12-year follow-up

Altogether 307 (26%) persons (83 [17%] men and 224 [32%] women) sustained 425 fractures during the 12-year follow-up (Table 6, Figure 7). Women sustained 77% of all fractures. One fracture was sustained by 222 (19%) subjects (men 15%, women 22%), and two or more fractures by 85 (7.2%) subjects (men 2.3%, women 10%). The total number of all fractures was highest among persons aged 75 to 84 years and it was especially high among those from 80 to 84 years (Figure 8).

Out of 425 fractures, 79% were sustained by fall-induced injuries, 7.5% by serious high-impact injuries, and 3.5% by extremely serious high-impact injuries. The external cause of injury causing 10% of the fractures was unknown. The place of sustaining fracture was indoors in 44% and outdoors in 20% of the cases (Table 7). The place was not mentioned in 36% of the cases.

Table 6. Number and distribution of fracture types by follow-up period and gender.

Fracture type	12-year		8-year**	
	Men n (%)	**Women** n (%)	**Long-term§ follow-up** n (%)	**Short-term* follow-up** n (%)
Hip	27 (28)	73 (22)	10 (13)	10 (21)
Femoral neck (S72.0)	*17 (63)*	*38 (52)*	*6 (60)*	*8 (80)*
Pertrochanter (S72.1)	*9 (33)*	*32 (44)*	*4 (40)*	*2 (20)*
Subtrochanter (S72.2)	*1 (4)*	*3 (4)*	-	-
Forearm and wrist	9 (9)	95 (29)	23 (31)	12 (25)
Tibial and ankle	13 (13)	28 (8)	7 (9)	6 (13)
Proximal humerus	4 (4)	25 (8)	7 (9)	1 (2)
Rib(s)	20 (21)	22 (7)	11 (15)	5 (10)
Vertebral compression	6 (6)	22 (7)		
Miscellaneous	18 (19)	63 (19)	17 (23)	14 (29)
	n= 97	**n=328**	**n=75**	**n=48**

** Includes both genders.
The eight-year follow-up period is divided into two periods: long-term (1991 - 1996) § and short-term (1997 - 1999)*.

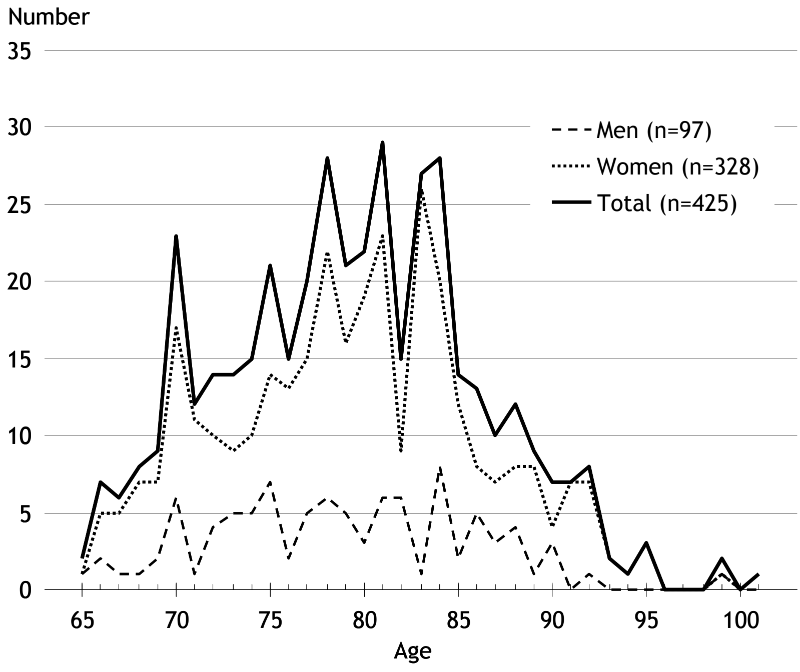


Figure 8. Number of fractures by age and gender between 1990 and 2002.

Table 7. Number and distribution of fractures (n=425) by type and place of occurrence.

Type of fracture	Place of occurrence Indoors n (%)	 Outside n (%)	 Not recorded n (%)	 Total n (%)
Hip	67 (67)	11 (11)	22 (22)	100 (24)
Forearm and wrist	31 (30)	31 (30)	42 (40)	104 (24)
Proximal humerus	10 (35)	7 (24)	12 (41)	29 (7)
Ankle and tibia	13 (32)	10 (24)	18 (44)	41 (10)
Rib(s)	24 (57)	8 (19)	10 (24)	42 (10)
Vertebral compression	8 (29)	2 (7)	18 (64)	28 (7)
Miscellaneous	34 (42)	17 (20)	30 (37)	81 (19)
Total	**187 (44)**	**86 (20)**	**152 (36)**	**425 (100)**

Altogether, 68 (16%) fractures occurred in long-term institutional care (men 9%, women 18%) and the rest of the fractures occurred in the aged living in their homes or sheltered housing (Table 8). There were no significant differences in the occurrence of fractures by season in either men (p=0.105) or women (p=0.482). Nor did seasonal numbers differ between institutionalised persons and home-dwellers in men (p=0.448) or women (p=0.085).

Table 8. Numbers and distributions of fractures by type of dwelling and season.

Season/ Dwelling	Winter n (%)	Spring n (%)	Summer n (%)	Autumn n (%)	Total n (%)
Institution	14 (21)	15 (22)	24 (35)	15 (22)	68 (100)
At own home or sheltered housing	103 (29)	85 (24)	74 (21)	95 (27)	357 (100)
Total	**117 (27.5)**	**100 (23.5)**	**98 (23)**	**110 (26)**	**425 (100)**

In analysing the predictors (risk factors) of fractures and the impact of fractures on excess mortality (Studies II and IV), the fractures caused by extremely serious high-impact injuries were excluded from the data. In this data, 295 persons (74 men [15% of all men] and 221 women [32% of all women]) had sustained at least one fracture. Of the first fracture of each individual, 21 (28%) in men and 44 (20%) in women were hip fractures, while 7 (10%) and 73 (33%) were wrist fractures, 11 (15%) and 22 (10%) tibial and ankle fractures, 4 (5%) and 20 (9%) proximal humerus fractures, 16 (22%) and 11 (5%) rib(s) fractures, 5 (7%), and 14 (6%) vertebral compression fractures and 10 (13%) and 37 (17%) “miscellaneous” fractures, respectively.

The 8-year follow-up
Among the population for the 8-year follow-up (Study III), 112 persons (28 men [12% of all men], 84 women [22% of all women]) sustained altogether 147 fractures (Figure 7, Table 7). Of the subjects, 11 persons sustained fractures during both 1991-1996 (long-term) and 1997-1999 (short-term) follow-ups. Altogether 123 fractures were included in the final analyses. The long-term follow-up contained 75 fractures (10 hip, 23 wrist, 7 proximal humerus, 7 tibial or ankle, 11 ribs and 17 other fractures) which were categorised to 28 (37%) lower body fractures and 47 (63%) upper body fractures. The corresponding number for the short-term follow-up period was 48 fractures (10 hip, 12 wrist, 1 proximal humerus, 6 tibial or ankle, 5 ribs and 14 other fractures), which were categorised to 23 (48%) lower body fractures and 25 (52%) upper body fractures.

6.2.2 Before the baseline

Altogether 319 (27%) persons had sustained a total of 395 fractures during their previous lifespan before the baseline in 1991-99 (Figure 7). Of the previous fractures, 11 (7%) in men and 20 (8%) in women were hip fractures, 16 (11%) and 109 (44%) wrist fractures, 35 (24%) and 41 (17%) tibial and ankle fractures, 6 (4%) and 10 (4%) proximal humerus fractures, 37 (25%) and 15 (6%) rib(s) fractures, 6 (4%), and 15 (6%) vertebral compression fractures, and 36 (25%) and 38 (15%) “miscellaneous” fractures, respectively. The median period between the previous fracture and the baseline examination was 7 years (from 0 to 74). A total of 279 persons (87 men and 192 women) sustained at least one fracture after the age of 45 years but before the baseline examination (1990-91).

6.2.3 During the whole lifespan

At the end of 2002, 45% of all subjects had sustained at least one fracture during their whole lifespan. Among participants who had not sustained a fracture before the follow-up started, 24% (men 17%, women 30%) sustained at least one fracture during the follow-up. The corresponding proportion was 30% (men 19%, women 38%) among those who had sustained at least one fracture before the beginning of follow-up.

6.3 Incidence of fractures (Study I)

A total of 10 040 PY were observed for calculating the incidences of all fractures (3892 in men, 6148 in women). The overall incidence rate of all fractures was 24.9 per 1000 PY with 95% confidence intervals (95% CI) 20.4-30.4 in men, and 53.4 per 1000 PY (95% CI 47.9-59.5) in women (Table 9, Figure 9). Age-specific incidence increased with age in both men and women, and fractures were more common in women than in men in all age groups.

Table 9. Number of fractures, person-years (PY), age-specific incidence and 95% confidence intervals (95% CI) by type of fracture in men and women aged 65 years or older in the Lieto study of fractures, 1991-2002.

	MEN			WOMEN		
	Number of fractures	PY	Incidence (95% CI)/1000 PY	Number of fractures	PY	Incidence (95%CI)/1000 PY
All fractures	**97**	**3892**	**24.9 (20.4 - 30.4)**	**328**	**6148**	**53.4 (47.9 - 59.5)**
65-69	7	600	11.7 (5.6 - 24.5)	25	687	36.4 (24.6 - 53.8)
70-74	21	1143	18.4 (12.0 - 28.2)	57	1494	38.2 (29.4 - 49.5)
75-79	25	1076	23.2 (15.7 - 34.4)	80	1755	45.6 (36.6 - 56.8)
80-84	24	679	35.4 (23.7 - 52.7)	97	1246	77.9 (63.8 - 95.0)
85+	20	394	50.7 (32.7 - 78.6)	69	966	71.4 (56.4 - 90.4)
Hip fractures*	**27**	**3892**	**6.9 (4.8 - 10.1)**	**73**	**6148**	**11.9 (9.4 - 14.9)**
65-69	0	600	0	0	687	0
70-74	3	1143	2.6 (0.8 - 8.1)	8	1494	5.4 (2.7 - 10.7)
75-79	9	1076	8.4 (4.4 - 16.1)	14	1755	8.0 (4.7 - 13.5)
80-84	8	679	11.8 (5.9 - 23.6)	27	1246	21.7 (14.9 - 31.6)
85+	7	394	17.8 (8.5 - 37.2)	24	966	24.8 (16.7 - 37.1)
Proximal humerus fractures	**4**	**3892**	**1.0 (0.4 - 2.7)**	**25**	**6148**	**4.1 (2.7 - 6.0)**
65-69	0	600	0	2	687	2.9 (0.7 - 11.6)
70-74	0	1143	0	5	1494	3.3 (1.4 - 8.0)
75-79	3	1076	2.8 (0.9 - 8.6)	8	1755	4.6 (2.3 - 9.1)
80-84	1	679	1.5 (0.2 - 10.5)	5	1246	4.0 (1.7 - 9.6)
85+	0	394	0	5	966	5.2 (2.2 - 12.4)
Forearm and wrist fractures	**9**	**3892**	**2.3 (1.2 - 4.4)**	**95**	**6148**	**15.5 (12.6 - 18.9)**
65-69	0	600	0	12	687	17.5 (9.9 - 30.7)
70-74	2	1143	1.8 (0.4 - 7.0)	22	1494	14.7 (9.7 - 22.4)
75-79	4	1076	3.7 (1.4 - 9.9)	29	1755	16.5 (11.5 - 23.8)
80-84	3	679	4.4 (1.4 - 13.7)	22	1246	17.7 (11.6 - 26.8)
85+	0	394	0	10	966	10.4 (5.6 - 19.2)
Vertebral compression fractures	**6**	**3892**	**1.5 (0.7 - 3.4)**	**22**	**6148**	**3.6 (2.4 - 5.4)**
65-69	1	600	1.7 (0.2 - 11.8)	1	687	1.5 (0.2 - 10.3)
70-74	2	1143	1.8 (0.4 - 7.0)	4	1494	2.7 (1.0 - 7.1)
75-79	1	1076	0.9 (0.1 - 6.6)	8	1755	4.6 (2.3 - 9.1)
80-84	1	679	1.5 (0.2 - 10.5)	3	1246	2.4 (0.8 - 7.5)
85+	1	394	2.5 (0.4 - 18.0)	6	966	6.2 (2.8 - 13.8)
Tibial and ankle fractures	**13**	**3892**	**3.3 (1.9 - 5.8)**	**28**	**6148**	**4.6 (3.1 - 6.6)**
65-69	2	600	3.3 (0.8 - 13.3)	2	687	2.9 (0.7 - 11.6)
70-74	4	1143	3.5 (1.3 - 9.3)	8	1494	5.4 (2.7 - 10.7)
75-79	1	1076	0.9 (0.1 - 6.6)	5	1755	2.8 (1.2 - 6.8)
80-84	3	679	4.4 (1.4 - 13.7)	7	1246	5.6 (2.7 - 11.8)
85+	3	394	7.6 (2.5 - 23.6)	6	966	6.2 (2.8 - 13.8)
Rib(s) fractures	**20**	**3892**	**5.1 (3.3 - 8.0)**	**22**	**6148**	**3.6 (2.4 - 5.4)**
65-69	3	600	5.0 (1.6 - 15.5)	2	687	2.9 (0.7 - 11.6)
70-74	5	1143	4.4 (1.8 - 10.5)	3	1494	2.0 (0.6 - 6.2)
75-79	3	1076	2.8 (0.9 - 8.6)	1	1755	0.6 (0.1 - 4.0)
80-84	3	679	4.4 (1.4 - 13.7)	12	1246	9.6 (5.5 - 17.0)
85+	6	394	15.2 (6.8 - 33.9)	4	966	4.1 (1.6 - 11.0)
Other fractures*	**18**	**3892**	**4.6 (2.9 - 7.3)**	**63**	**6148**	**10.2 (8.0 - 13.1)**
65-69	1	600	1.7 (0.2 - 11.8)	6	687	8.7 (3.9 - 19.4)
70-74	5	1143	4.4 (1.8 - 10.5)	7	1494	4.7 (2.2 - 9.8)
75-79	4	1076	3.7 (1.4 - 9.9)	15	1755	8.5 (5.2 - 14.2)
80-84	5	679	7.4 (3.1 - 17.7)	21	1246	16.9 (11.0 - 25.8)
85+	3	394	7.6 (2.5 - 23.6)	14	966	14.5 (8.6 - 24.5)

* Incidence: 3 hip fractures transferred from other fractures to hip fractures (paper I)

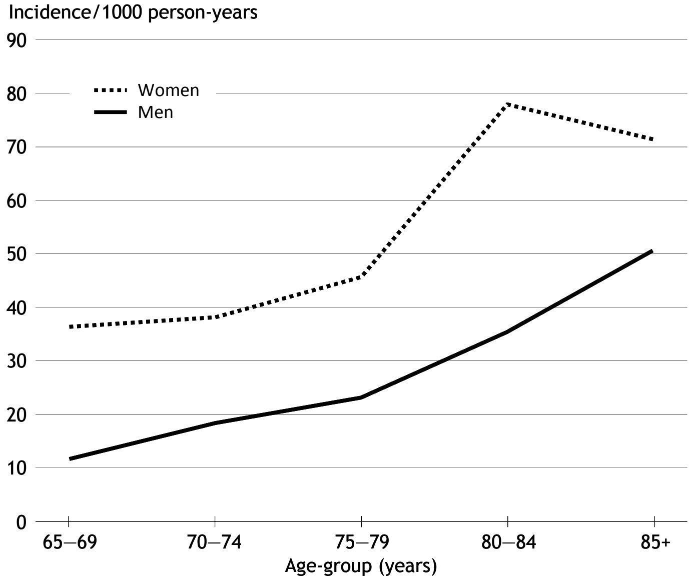


Figure 9. Age-specific incidence rates of all fractures by gender.

6.3.1 Incidence of the first fracture

The incidence of the first fracture of any kind sustained by subjects during the follow-up period was also calculated. The crude incidence of first fracture during follow-up was 23.2 per 1000 PY (95%CI: 18.7 to 28.7) in men and 44.0 per 1000 PY (95%CI: 38.6 to 50.1) in women.

6.3.2 Incidence of upper limb fractures

Proximal humerus fractures were uncommon in men compared with women (ratio 1:5) (Table 9, Figure 10). The crude incidence was 1.0 per 1000 PY (0.4 to 2.7) in men and 4.1 per 1000 PY (2.7 to 6.0) in women. In women, age-specific incidence tended to be highest in the age group of 85 years and over but in average the incidence rate was stable in all age groups.

Forearm and wrist fractures were far more common in women compared with men (ratio 10:1) (Table 9, Figure 10). The crude incidence of wrist factures was 2.3 per 1000 PY (1.2 to 4.4) in men and 15.5 per 1000 PY (12.7 to 18.8) in women. Forearm and wrist fractures were more common among women than among men in all age groups. In women, incidence was not related to age. In men, no forearm or wrist fractures were observed in the youngest and oldest age groups.

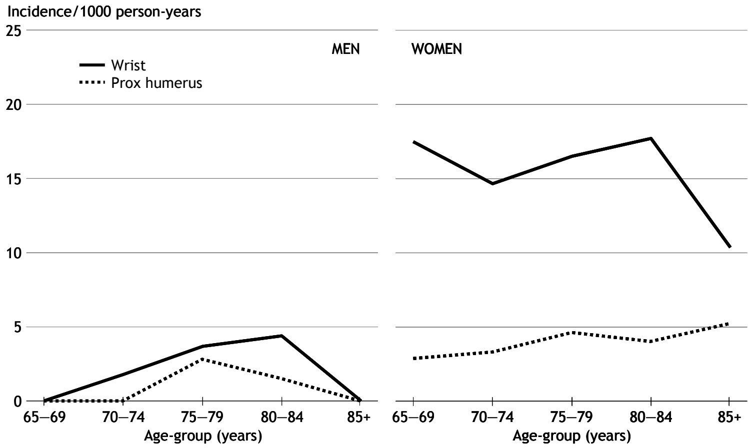


Figure 10. Age-specific incidence rates of upper limb fractures per 1000 PY by gender.

6.3.3 Incidence of lower limb fractures

The crude incidence of hip fractures was 6.9 per 1000 PY (4.8 to 10.1) in men and 11.9 per 1000 PY (9.4 to 14.9) in women (Table 9). Age-specific incidence tended to be higher among women than among men, especially in the age group of 80 years or over (Figure 11). Age-specific incidence increased with increasing age in both genders.

In general, tibial and ankle fractures were equally common in both genders and the age-specific incidence tended to be stable in all age groups (Table 9, Figure 11). The crude incidence of tibial and ankle factures was 3.3 per 1000 PY (1.9 to 5.8) in men and 4.6 per 1000 PY (3.1 to 6.6) in women.

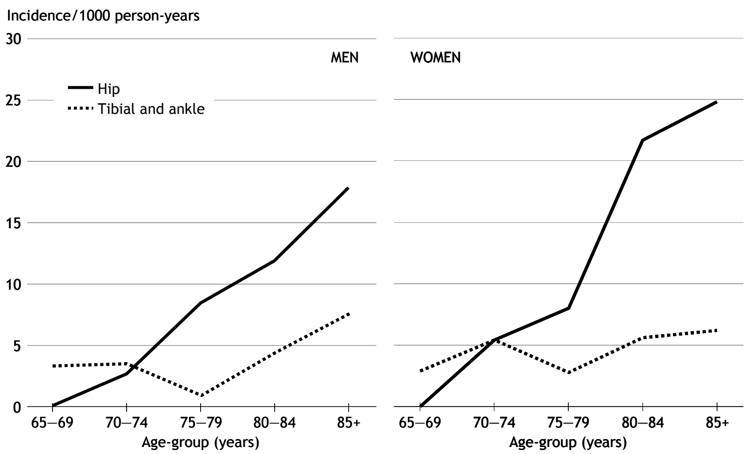


Figure 11. Age-specific incidence rates of lower limb fractures per 1000 PY in men and in women.

6.3.4 Incidence of other fractures

The crude incidence of the diagnosed compression fractures in thoracic and upper lumbar vertebral fractures was 1.5 per 1000 PY (0.7 to 3.4) in men and 3.6 per 1000 PY (2.4 to 5.4) in women (Table 9). In men, the incidence rates of compression fractures were small in all age groups. In women, there was a rising tendency in incidence rates by increasing age.

Rib(s) fractures were more common in men compared with women, especially after the age of 85 years (Table 9). In men, the crude incidence of rib(s) factures was 5.1 per 1000 PY (3.3 to 8.0) and in women 3.6 per 1000 PY (2.4 to 5.4). In women, the incidence rate was especially high in the age group of 80 to 84 years of age.

The incidence rates of miscellaneous fractures rose with increasing age in both genders (Table 9).

6.3.5 Changes in number and incidence of fractures over time

The number of sustained fractures each year varied very little during the follow-up period (Figure 12, Table 10). The age-adjusted incidence of all fractures, calculated separately for each calendar year of follow-up, varied from 14.5 to 43.3 per 1000 PY among men and from 41.8 to 73.8 per 1000 PY among women (Table 10). There were no significant differences in age-adjusted incidences between calendar years in either men (p=0.145) or women (p=0.385).

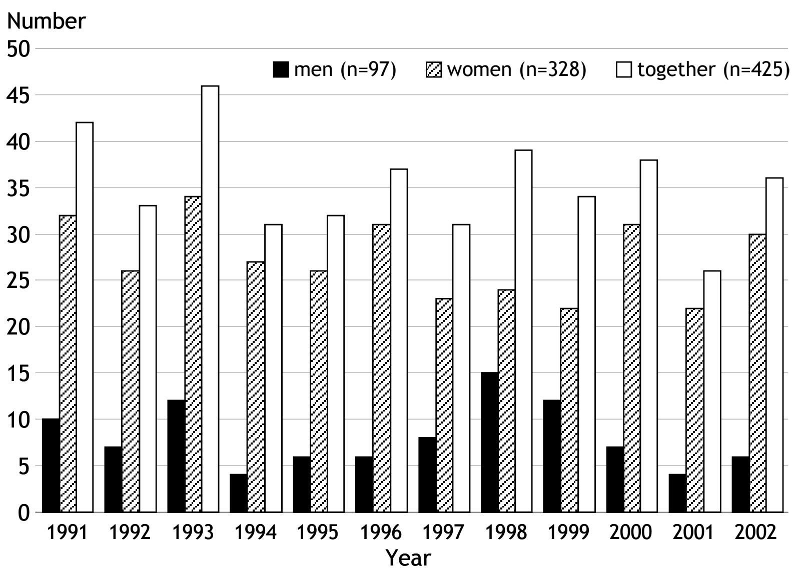


Figure 12. Number of fractures among men and women between 1991 and 2002.

Table 10. Number of subjects 65 years or older and all fractures, person-years (PY), age-adjusted incidence of all fractures and 95% confidence intervals (95% CI) by gender and year in the Lieto study of fractures, 1991-2002.

	MEN				WOMEN			
Year	N†	Fractures (n)	PY	Incidence‡ (95% CI)	N†	Fractures (n)	PY	Incidence‡ (95% CI)
1991	482	10	338	33.9 (18.2 - 63.1)	695	32	474	73.8 (52.1 - 104.5)
1992	460	7	448	17.0 (8.1 - 35.6)	676	26	667	41.8 (28.4 - 61.4)
1993	437	12	421	30.0 (17.1 - 52.9)	656	34	636	56.3 (40.2 - 78.8)
1994	405	4	388	10.5 (3.9 - 28.0)	612	27	597	46.7 (32.0 - 68.1)
1995	376	6	362	16.2 (7.3 - 36.1)	583	26	574	45.6 (31.0 - 66.9)
1996	351	6	344	16.3 (7.3 - 36.4)	565	31	546	55.8 (39.2 - 79.4)
1997	338	8	326	22.2 (11.0 - 44.6)	527	23	514	43.0 (28.5 - 64.7)
1998	315	15	304	43.3 (25.8 - 72.6)	497	24	483	46.7 (31.2 - 69.8)
1999	288	12	276	37.2 (20.9 - 66.3)	468	22	456	44.5 (29.2 - 67.8)
2000	266	7	252	23.1 (10.9 - 49.1)	444	31	425	65.9 (46.1 - 94.2)
2001	234	4	223	14.5 (5.4 - 39.1)	412	22	401	48.6 (31.8 - 74.3)
2002	216	6	210	22.2 (9.8 - 50.2)	390	30	375	69.4 (48.1 - 100.2)
Total		**97**				**328**		

† Number (N) of male / female subjects alive at the beginning of the year in question.
‡ Adjusted for age at the time of the fracture or age at the end of follow-up year.

6.4 Predictors of fractures (Study II)

In age-adjusted Poisson regression analysis among women, handgrip strength <76 kPa, BMI scores <30, a previous fracture sustained after the age of 45 years but before the baseline, and a compression fracture in one or more thoracic or upper lumbar vertebra were significantly related to the risk of fractures. Among men, significant predictors were a large number of depressive symptoms (ZSDS score 45 or over) and a compression fracture in one or more thoracic or upper lumbar vertebra at baseline.

The variables showing significant association with fractures in age-adjusted analyses were selected to be adjusted in gender-specific multivariate Poisson regression analyses (Table 11). In the analyses, reduced handgrip strength and body mass index (BMI) <30 among women, and a large number of depressive symptoms among men were identified as predictors of fractures during the 12-year follow-up. A compression fracture in one or more thoracic or upper lumbar vertebra on chest radiography at baseline was associated with fractures in both genders.

Table 11. Predicting factors and relative risks (RR) with their 95% confidence intervals (95% CI) for fractures in multivariate Poisson regression analyses among men* and women# who sustained at least one fracture during the 12-year follow-up.

Predicting factor**	Men *		Women #	
	RR (95% CI)	p-value	RR (95% CI)	p-value
Handgrip strength (kPa)				
76+			1	
48- 75			**1.6 (1.1 – 2.3)**	**0.021**
≤47			**2.2 (1.4 - 3.5)**	**0.004**
Body mass index (BMI)				
≥30			1	
25-29.9			**1.9 (1.3 – 2.7)**	**0.0003**
<25			**2.0 (1.4 – 2.9)**	**0.0004**
ZSDS score				
20-44	1			
45-80	**2.1 (1.2 – 3.6)**	**0.012**		
Previous fracture after age of 45 years ##				
no			1	
yes			1.1 (0.8 – 1.5)	0.428
Compression fracture/s in thoracic or upper lumbar vertebrae				
no	1		1	
yes	**3.5 (1.9 – 6.7)**	**<0.0001**	**2.0 (1.3 – 3.0)**	**0.0006**

* Age (a continuous variable), ZSDS and compression of thoracic or upper lumbar vertebrae were included in multivariate Poisson regression model in men.
# Age (a continuous variable), handgrip strength, BMI, occurrence of a previous fracture after 45 years of age and compression of thoracic or upper lumbar vertebrae were included in multivariate Poisson regression model in women.
** Include variables showing significant association ($p < 0.05$) with fractures in gender-specific age-adjusted analyses.
At least one registered fracture after the age of 45 years but before baseline (1990-19

6.5 Functional ability in the 8-year follow-up

6.5.1 Change in functional ability

During the eight-year follow-up, the proportion of those who reported difficulties or dependence in tasks increased from 29.7% to 63.4 % in mobility, from 13% to 38.9% in ADL tasks, and from 35.4% to 75.6% in IADL tasks (Appendix Tables 5-7).

Gender, cognitive ability, leisure-time physical exercise, handgrip strength, body mass index (BMI), number of drugs, depressive symptoms and fractures sustained during either follow-up periods (2 years or 6 years) significantly predicted a decline in mobility or in managing ADL or IADL tasks after adjusting for age and functional abilities at baseline, and were therefore chosen to be controlled and analysed in the multivariate analyses.

6.5.2 Fractures and functional decline (Study III)

In the multivariate analyses, lower body fractures predicted decline in mobility ($p<0.001$) and in ADL functions ($p=0.012$) in the short-term follow-up, whereas upper body fractures did not (Table 12). In the long-term follow-up, lower body fractures predicted decline in mobility ($p=0.029$) and in ADL functions ($p<0.001$). In addition, upper body fractures predicted decline in ADL functions ($p=0.009$). Sustained fractures were not related to a decrease in managing IADL tasks in short-term or longer-term follow-ups.

6.5.3 Other predictors of functional decline (Study III)

There were several other variables that were statistically significantly associated with the functional decline during the 8-year follow-up (Table 12). High age, inactivity in leisure-time physical exercise and difficulties or dependency in mobility or ADL or IADL tasks at baseline were related to all three dimensions of functional decline (mobility, ADL and IADL).

6.5.4 Drop-out analysis

There were 147 subjects (19%) (50 men and 97 women) who were alive in 1998-1999 but who did not participate in the Lieto Study II (Figure 7). Of the drop-out persons, 100 (68%) cancelled their participation or did not participate in a re-examination without telling a specific reason, 23 (16%) were not invited, 19 (13%) were too tired to participate, 3 had moved and were not reached, and 2 did not participate because their relatives did not allow them to participate.

There were only minor differences between participants (n=616) and non-participants (drop-outs=147) in re-examinations. Drop-outs had more difficulties or were more dependent in moving outdoors ($p=0.034$), walking at least 400 metres ($p=0.039$) and carrying a 5-kg load at least 100 metres ($p=0.014$). In addition, a greater share of drop-outs had elevated diastolic blood pressure (over 90 mmHg) ($p=0.016$) and belonged to the highest quartile in systolic blood pressure categorisation (over 168 mmHg in men and 170 mmHg in women) ($p=0.027$) compared with those participating in the study. The proportions of those with a diagnosed cardiovascular disease were equal in both groups.

Table 12. Relationships between variables and the risk of functional decline during the 8-year follow-up. Cumulative odds ratios (COR) with their 95% confidence intervals (95%CI) in the multivariate cumulative logistic regression analyses* (n=616).

Characteristics †	Mobility (n=594) COR (95% CI)	ADL tasks (n=590) COR (95% CI)	IADL tasks (n=598) COR (95% CI)
At least one fracture during the short-term follow-up (1997-99)			
– no	1	1	1
– lower body	**4.7 (1.9 – 11.7)**	**3.1 (1.3 – 7.6)**	3.4 (0.9 – 12.4)
– upper body	1.6 (0.7 – 3.6)	1.4 (0.6 – 3.4)	1.8 (0.7 – 4.9)
At least one fracture during the long-term follow-up (1991-96)			
– no	1	1	1
– lower body	**2.6 (1.1 – 6.2)**	**4.7 (2.0 – 11.4)**	0.7 (0.2 – 1.8)
– upper body	1.7 (0.9 – 3.2)	**2.5 (1.3 – 4.8)**	1.8 (0.8 – 3.9)
Gender			
– male	1	1	1
– female	1.3 (0.9 – 1.8)	0.8 (0.5 – 1.2)	**1.5 (1.0 – 2.2)**
Cognitive ability (MMSE)			
– 24-30	1	1	1
– <24	1.8 (0.9 – 3.6)	**3.7 (1.8 – 7.8)**	1.3 (0.5 – 3.3)
Leisure-time physical exercise			
– yes	1	1	1
– no	**2.3 (1.6 – 3.4)**	**1.9 (1.3 – 2.9)**	**1.8 (1.2 – 2.7)**
Sumvariable of mobility or ADL tasks or IADL tasks at baseline			
– independent in all tasks	1	1	1
– difficulties in at least one task	**3.0 (1.9 – 4.8)**	**2.3 (1.2 – 4.2)**	**2.6 (1.4 – 4.6)**
– dependent in at least one task	**5.7 (2.6 – 12.2)**	**7.8 (1.3 – 45.9)**	**26.5 (6.1 – 114.6)**
Handgrip strength (kPa) (M= men; W= women)			
– M 86 + W 76 +	1	1	1
– M 55 -85 W 48 -75	1.1 (0.7 – 1.5)	1.3 (0.8 – 2.0)	1.1 (0.7 – 1.6)
– M ≤ 54 W ≤ 47	1.5 (0.8 – 2.7)	**2.4 (1.3 – 4.5)**	1.9 (0.9 – 3.9)
Body mass index (BMI)			
– <25	1	1	1
– 25 -29.9	1.4 (0.9 – 2.2)	0.8 (0.5 – 1.4)	1.5 (0.9 – 2.4)
– 30 +	**1.7 (1.1 – 2.8)**	1.1 (0.6 – 1.9)	**2.3 (1.3 – 4.1)**
Number of prescribed drugs			
– 0	1	1	1
– 1-5	**1.6 (1.1 – 2.4)**	**2.7 (1.6 – 4.4)**	1.1 (0.7 – 1.7)
– ≥6	1.6 (0.8 – 2.9)	**2.1 (1.0 – 4.3)**	1.8 (0.7 – 4.7)

* Adjusted with age, gender, cognitive abilities (Mini Mental State Examination), leisure time physical exercise, level of mobility or managing in activities of daily living or instrumental activities of daily living, handgrip strength, body mass index, number of prescription drugs in use, depressive symptoms (Zung Self-rating Depression Scale) at baseline, and sustained fractures by site during the follow-up periods.

† Only variables showing a significant (p-values <0.05) association with decline of mobility or in managing ADL or IADL functions in multivariate analyses are shown. COR > 1 indicates decline in functioning.

6.6 Mortality (Study IV)

At the end of 2002, 608 people (52%) out of 1177 (277 men and 331 women) had died. Age-adjusted mortality was higher in men than in women (HR 1.6, 95% CI: 1.4-1.9).

The main causes of death in both genders were cardio- and cerebro-vascular diseases. More men died due to coronary heart disease and myocardial infarction (p=0.003) and pulmonary diseases (p=0.011) compared with women (Study IV). In women, dying due to mental disorder was more common compared with men (p=0.019).

In hip fracture patients, coronary heart disease and myocardial infarction were significantly more common causes of death in men than in women (52% vs. 10%, p=0.0019). There were no other gender-specific differences in the main causes of deaths by fracture type.

6.6.1 General predictors of excess mortality

Several variables were related to excess mortality in the gender-specific and age-adjusted analyses. In the multivariate analyses, being single (HR 1.4, 95% CI: 1.1 - 1.9), or having difficulties at least in one mobility, ADL, or IADL tasks (HR 1.7, 95% CI: 1.2 - 2.5) predicted death in women, while cognitive impairment (MMSE <17) (HR 5.7, 95% CI: 1.6 - 20.0) and ex-smoking (HR 1.4, 95% CI: 1.0 - 2.0) predicted death in men. In addition, current smoking (men: HR 2.0, 95% CI: 1.3 - 3.2), (women: HR 2.2, 95% CI:1.1 - 4.7); the use of prescribed drugs (men: HR 1.7-2.1, 95% CI: 1.2 - 3.4) ; (women: HR 2.0, 95% CI: 1.2 – 3.2) and lack of leisure-time physical exercise (men: HR 1.5, 95% CI: 1.1 - 2.1); (women: HR 1.6, 95% CI: 1.1 - 2.2) were independently associated with increased mortality both in men and women.

6.6.2 Fractures as predictors of excess mortality

In 1991, age-standardised mortality per 1000 persons in Lieto among persons 65 years or older was 41.3 (95% CI 22.5-60.0) in men and 29.2 (95% CI 16.0-42.4) in women. Among men, mortality was 62% (n=46) in those sustaining at least one fracture during the follow-up compared with 57% (n=231) in those without any fractures (p=ns). In women, the corresponding figures were 49% (n=231) and 45% (n=100) (p=ns). In the follow-up period of six months to three years after a sustained hip fracture, the proportion of dead patients was higher in men than in women (57-81 vs. 18- 43%, respectively), (p<0.007).

In the age-adjusted analyses, sustaining any kind of fracture was associated with excess mortality in both men (HR 2.2, 95% CI: 1.6-3.1) and women (HR 1.6, 95% CI: 1.3-2.1) during the 12-year follow-up. In addition, vertebral compression fractures at baseline predicted death both in men and in women, but previous fractures sustained before the baseline did not predict excess mortality in either gender (Table 13). In fracture-specific analyses, hip fractures in both genders and proximal humerus fractures in men predicted mortality.

In the multivariate analyses, sustaining any kind of fracture was associated with the excess mortality in both genders during the 12-year follow-up: men (HR 2.1, 95% CI: 1.5-3.1) and women (HR 1.5, 95% CI: 1.1-2.0) (Table 13). In fracture-specific analyses, sustaining a hip fracture was an independent risk factor for mortality both in men (HR 8.1, 95% CI: 4.4-14.9) and in women (HR 3.0, 95% CI: 1.9-4.9), whereas proximal humerus fractures were associated with excess mortality only in men (HR 5.4, 95% CI: 1.6-17.7). Other fracture types sustained during the follow-up or vertebral compression fractures at baseline did not predict excess mortality.

Table 13. Prediction of death by an occurrence of fracture during the 12-year follow-up in the Lieto study of fractures. Gender-specific Hazards Ratios (HR) with their 95% confidence intervals (95% CI) in the age-adjusted and multivariate Cox Proportional Hazards regression analyses.

	Men		**Women**	
Fracture	Age-adjusted HR (95% CI)	Multivariate* HR (95% CI)	Age-adjusted HR (95% CI)	Multivariate* HR (95% CI)
At least one previous fracture after age of 45 years but before baseline				
– no	1		1	
– yes	1.0 (0.8 - 1.4)		1.9 (0.7 – 1.2)	
At least one fracture during follow-up†				
– no fracture	1	1	1	1
– hip	**6.6 (4.0 – 10.8)**	**8.1 (4.4 – 14.9)**	**2.7 (1.8 – 3.9)**	**3.0 (1.9 – 4.9)**
– forearm or wrist	1.9 (0.6 – 5.8)	1.5 (0.4 – 6.4)	1.3 (0.8 – 2.0)	1.3 (0.8 – 2.1)
– tibial or ankle	1.6 (0.8 – 3.5)	1.8 (0.8 – 4.0)	1.3 (0.6 – 2.5)	1.2 (0.6 – 2.3)
– proximal humerus	**6.6 (2.1 – 20.7)**	**5.4 (1.6 – 17.7)**	1.5 (0.8 – 2.9)	1.0 (0.4 – 2.3)
– rib(s)	0.6 (0.2 – 1.6)	0.5 (0.1 – 1.5)	1.4 (0.6 – 3.2)	1.8 (0.8 – 4.2)
– vertebral compression	3.6 (1.3 – 9.6)	2.1 (0.6 – 6.8)	1.0 (0.3 – 3.1)	0.6 (0.1 – 2.3)
– other	1.6 (0.7 – 3.5)	1.9 (0.7 – 4.8)	1.6 (1.0 – 2.5)	1.6 (0.9 – 2.8)
– any	**2.2 (1.6 – 3.1)**	**2.1 (1.5 – 3.1)**	**1.6 (1.3 – 2.1)**	**1.5 (1.1 – 2.0)**
Vertebral compression fracture/-s at baseline				
– no	1	1	1	1
– yes	**1.6 (1.1 – 2.4)**	1.4 (0.8 - 2.2)	**1.6 (1.2 – 2.2)**	1.3 (0.9 - 2.0)

* Age (continuous variable), marital status, education, mobility, ADL tasks, IADL tasks, MMSE score, smoking, leisure-time physical exercise, hand grip strength, body mass index, drug use, depressive symptoms, fractures during the follow-up, and compression fractures at baseline were included in multivariate analyses.

† Fractures sustained during the 12-year follow-up were analysed as time-dependent variables.

ADL=activities of daily living, IADL= instrumental activities of daily living, kPa= kiloPascals, MMSE= Mini-Mental State Examination, ZSDS = Zung Self-rating Depression Scale.

7. DISCUSSION

7.1 Strengths and limitations of the study

The Lieto Study is a population-based cohort study with a 93% participation rate at baseline and a 98% participation rate in fracture collection ensuring an unselected population. Differences in health care systems and registers may decrease comparability of study results in different countries. In this work, studies with population-based or cohort studies are favoured, when our results are compared with other published studies. The long follow-up time and detailed and verified information in older adults, morbidity, functional status and mortality in older men and women increase the validity of the Lieto Study.

The internal validity is determined by how well the design, data collection and analyses are carried out or threatened by selection, measurement or confounding biases (Fletcher & Fletcher 2005). External validity (generalisability) refers to the extent to which the results achieved hold true in other settings (Fletcher & Fletcher 2005). In a population-based cohort study where a cohort is representative of a well-defined population (by geographic boundaries or by other criteria), selection bias is minimised and the external validity is high (Szklo 1998). Because the sampling, recruitment, data collection and follow-up of the participants were exhaustive in the Lieto Study, at least three advantages have been achieved: 1) estimation of distributions and prevalence rates of relevant variables in the reference population, 2) risk factor distributions measured at baseline in the Lieto Study and periodic examinations of the cohort allow comparison with distributions in future cross sectional samples to assess risk factor trends over time, and 3) a representative sample that "is the ideal setting in which to carry out unbiased evaluations of relations, not only of confounders to exposures and outcomes, but also among any other variables of interest, even those which were not specified in the original study hypotheses" (Szklo 1998).

Majority of measurements used in data collection in the Lieto Study have been assessed internationally as valid and reliable. This decreases the possibilities of measurement biases. The wide and detailed baseline and follow-up data provided also a possibility to adjust for confounding variables related both to mortality and functional decline, especially to morbidity and functional limitations. The data on participants' health status used in the adjusted analyses were collected in the beginning of the study, 1990-1991. In follow-up studies, changes in health status may take place after the baseline examination (Gill et al. 2004). These changes may have affected the individual's survival and the development of functional limitations also in the Lieto Study. In the Lieto Study, the baseline variables were collected during years 1990-91 and the consequences of fractures were assessed for fractures sustained in 1991-2002. It is obvious that there have been changes in health and functional ability between the baseline measurements and the occurrence of fractures. Hence the cumulative odds ratios for the impact of fractures on functional decline are only approximations. However, the baseline data was used in a way which is common in prospective epidemiological studies.

Population-based follow-up studies are expensive, and thus multiple hypotheses are included in their plans (Szklo 1998). This was also true in the Lieto Study. The Lieto Study was designed in order to describe and analyse occurrences and risk factors of several common health disorders among the aged (Isoaho et al. 1994a; Isoaho et al. 1994b; Ahto et al. 1998; Linjakumpu et al. 2002). It was not originally designed for describing and analysing the occurrence and risk factors of fractures. Despite of comprehensive data collection, some previously reported risk factors of fractures (bone mineral density, calcium and vitamin D intake, family history of fractures, height loss, alcohol consumption, leanness, body balance, and strength of lower extremities) were not included in the baseline measurements. Several risk factors of fractures differ by type of fracture (Honkanen et al. 1998; Hippisley-Cox & Coupland 2009; Kelsey & Samelson 2009; Jokinen et al. 2010) but the risk factors of fractures were analysed for all fractures only in Lieto. Unfortunately the small number of fractures did not allow fracture-specific analyses in Study III. Thus the association between fractures and functional limitation was analysed in two major groups: upper and lower body fractures. Fractures were categorised due to their association to mobility. In addition, none of our results were adjusted by amount or quality of rehabilitation after a fracture. Thus, confounding may always be present in observational studies. However, the best available statistical methods and a careful assessment of statistical power as well as careful consideration of the variables from the clinical perspective have been used in developing the multivariate models and in analysing the results.

Fracture data

We used the data on fractures collected from three sources: baseline examination (1990-1991), second wave of the Lieto Study (1998-99), and follow-up data collected from the registers. Previously sustained fractures were asked from the participants and reported during the Lieto Study II in 1998-1999. Altogether, 616 of the 1177 subjects participating in the first wave of the Lieto Study in 1990-1991 (baseline) also participated in the second wave during 1998-1999. The fracture data was collected individually from the health records for the present study and it was compared with the self-reported information collected during Lieto Study II in 616 participants; no diagnosed fractures that had occurred in these 616 participants were missed. However, only one third of vertebral fractures are diagnosed clinically (Haczynski & Jakimiuk 2001; Old & Calvert 2004). In addition, the Genant's classification (Genant et al. 1993) was not used in diagnosing compression fractures in Lieto at baseline and mainly only moderate to severe wedge-shaped deformities were included. Furthermore, in most cases a compressed fracture in upper lumbar vertebra was diagnosed from the L1 level only. It is most likely that the sensitivity of diagnosing all vertebral compression fractures has been poor. However, it has been shown that the agreement of diagnosing a vertebral compression fracture is higher in severe compression fractures (Härmä et al.

1986; Gehlbach et al. 2000). In Lieto, a deformity of a vertebra was diagnosed only if it was obviously compressed to a wedge shape (Genant's classification at least moderate). Thus, the specificity of diagnosing osteoporotic vertebral fractures is high in Lieto. It is probable that vertebral compression factures are underreported in Lieto, but otherwise, the data cover nearly 100% of all fractures sustained in 1991-2002.

Even though it has been shown that the accuracy of coding fractures in health registers is high (93-98%) (Mönkkönen et al. 1989; Lüthje et al. 1995b; Sund et al. 2007), it is possible that the registers used may have contained inaccuracies in coding fractures. However, in Lieto all fractures were collected individually with their ICD codes and written information about the fracture. The codes were double-checked in relation to written information and patient records. When transferring ICD-9 codes into ICD-10 codes, the written information about the type and site of fracture was carefully taken into account. The fracture data of the present study were collected and coded by a single collector with particular care; thus the data accuracy should be of high quality.

Lieto is a semi-rural municipality. There is evidence that the incidence of hip fractures is higher in urban residents than in their rural counterparts (Brennan et al. 2010). The reason for the difference is unknown. However, the difference in hip fracture incidence ratios between rural and urban populations has not been reported in all studies (Lüthje et al. 1995c). It is noticeable that information is scarce about differences in incidence rates of other types of fractures by living area. It is possible that the lower fracture incidence in rural areas might be true also for other fracture types.

In the Lieto Study, the numbers of individual fracture types were rather small leading to wide confidence intervals of risk ratios and limiting the power of statistical analyses. Especially low numbers of fractures were detected among those over 80 years of age, which decreases the accuracy of age-specific incidences among the oldest-old population.

Mortality data

Statistics Finland produces statistics on causes of death and on the change of mortality in the Finnish population. The causes of death are compiled from data obtained from death certificates and supplemented with data from the population information system of the Population Register Centre. The databases cover all the persons who died in Finland or abroad during the calendar year and who were domiciled in Finland at the time of death (Statistics Finland 2009). The quality and coverage of the Statistics on Deaths database is high (Statistics Finland 2010).

In the Lieto Study, causes of death among persons with fractures were compared with causes of death among persons without sustained fractures. In many cohort studies, mortality is evaluated by calculating the difference between the observed number of dead persons and the number of dead persons in a general population with similar age and gender during the follow-up period (expected death) (Bliuc et al. 2009). Usually standard life-table methods applied to population-based data with age- and gender-specific mortality is used (Haentjens et al. 2010). However, in their meta-analysis Haentjens and colleagues (2010) summarised that in many studies, the data are not stratified or adjusted by important risk factors for death (Haentjens et al. 2010). This raises the value of the Lieto Study; the data are both valid and adjusted by important risk factors of excess mortality. Other fractures sustained are also included in the multivariate analyses in the Lieto Study.

The age-standardised mortality in 1991 was 1.6 times higher in the total Finnish population aged 65 years or older than in the corresponding Lieto population. In Lieto, the mortality was 41.3 in men and 29.2 in women compared with 65.5 per 1000 persons in men and 48.9 in women in 1991 in the total Finnish population. This finding is supported by the results of previous Finnish epidemiological studies which have shown the rate of coronary heart disease mortality to be lower in south-western Finland compared with the north-eastern areas (Pekkanen et al. 1992). This difference is explained by differences in socioeconomic, nutritional and genetic factors (Mähönen et al. 2000).

7.2 Results

7.2.1 All fractures

The results showed that fractures are common among an older Finnish population and as many as every fourth person aged 65 years or older sustains at least one fracture later in life.

Incidence of fractures

The overall incidence rate of sustaining any kind of fracture was 53.4 per 1000 PY in women and 24.9 per 1000 PY in men. Thus the fracture risk in older women was 2-fold compared with older men. The incidence of fractures in older women has been reported to be higher compared with older men also in other studies (Baron et al. 1996; Gullberg et al. 1997; Sanders et al. 1999). The male fracture rate in Lieto was 39% lower than that in Iceland (Jonsson et al. 2004), but 30% higher in men and 64% higher in women than among persons aged 60 years or older living in Australia (Jones et al. 1994). In the Australian Dubbo Study (Jones et al. 1994; Chang et al. 2004), only the first fractures were taken into account. When the incidence is calculated for the first fractures only, the rate remains lower than when all fractures are taken into account.

Seasonal variation was not found in the incidence rate of all fractures in Lieto. No statistically significant differences were observed in seasonal incidence rates in distal radius, hip or proximal humerus fractures in Japan, either (Hagino et al. 1999). Opposite results have also been reported suggesting that fractures occur more frequently during the autumn or winter months (Bulajic-Kopjar 2000; O'Neill et al.

2001; Thompson et al. 2004; Mirchandani et al. 2005; Bischoff-Ferrari et al. 2007; Sund 2007; Flinkkilä et al. 2010). These differences may be explained by the differences of the age structure of the subjects and by the differences in types or the severity of fractures included in analyses. For example, in the study of Kaukonen et al. (1985) the seasonal variation (higher number in winter) was found only among out-patient distal forearm patients, not in hospitalised cases. In addition, Sund et al. (2007) reported that the number of hip fractures was higher in winter/ spring season compared with that of hip fractures in summer/ autumn season in non-institutionalised persons. It has also been shown that hip fractures have a smaller winter/ summer difference than those of distal forearm, proximal humerus or ankle fractures (Bischoff-Ferrari et al. 2007). The winter-summer variation in fracture rates has also been reported to be higher in men than women, and winter peaks appear to be more pronounced in those younger than 80 years of age (Bischoff-Ferrari et al. 2007). However, it is possible that the use of seasonal division in our study had an effect on our results; in Finland snowfalls are common even in March. Unfortunately, the small number of fractures did not allow analysing seasonal variation by the types of fractures.

Trend of fracture incidences

The trend in the age-adjusted incidence of all fractures was stable from 1991 to 2002 in Lieto. Unfortunately, the amount of fractures was too small to analyse fracture-specific trends. The trend of hip fractures has been studied widely, most likely because hip fractures are easily derived from registers. There is evidence that the incidence of hip fractures has increased among older persons in Central Finland (Lönnroos et al. 2006). However, an overall declining trend of hip fractures has been reported covering Finland as a whole (Kannus et al. 2006; Sund 2011 unpublished data). Globally, the age-adjusted incidence of hip fracture seems to be stabilised (Lofthus et al. 2001) or declined among the aged during the last decade (Kannus et al. 2006; Fisher et al. 2009; Leslie et al. 2009; Melton et al. 2009). This decline has been noticed especially in older women (Kannus et al. 2006; Fisher et al. 2009; Leslie et al. 2009; Melton et al. 2009). Among older men, there is also evidence that the incidence trend is increasing in Germany and that the annual incidence of hip fractures has risen in very old persons (≥90 years) in Sweden (Bergström et al. 2009).

It is possible that older people in high-income countries are healthier and have improved functional abilities and reduced risk of injurious falls compared with earlier cohorts (Kannus et al. 2006). The risen average body weight and body mass index may contribute higher bone density, aromatisation of oestrogen and padding over the trochanter reducing the fracture rates (Leslie et al. 2009). It is also possible that preventive actions, such as non-smoking and physical activity and fall prevention interventions, and improvement in calcium and vitamin D intake as well as the use of hip protectors have affected the hip fracture rates at the population level (Kannus et al. 2006; Gates et al. 2008; Leslie et al. 2009). However, if the amount of very old people keeps increasing and the trend of hip fractures keeps shifting more and more towards the oldest old people all over the western world, future healthcare will face major challenges (Bergström et al. 2009).

Predictors of fractures

A predictor is a characteristic associated with the increased rate of a subsequently occurring disease/injury; causality may or may not be implied (Dorland's illustrated medical dictionary 2000). It is noticeable that the predictors are always related to the population from which they are derived. The possibility to use wide-based confounders in analysing independent risk factors for fractures in other studies is limited compared with the Lieto Study. The use of confounding variables may explain the difference in some of the results of the present study compared with other studies.

The risk factors for fractures found in this study were similar to the risk factors of both falls and bone fragility identified also in several previous studies (Hippisley-Cox & Coupland 2009; Karinkanta et al. 2010). However, in screening people with specific risk of fractures, the differences in the predictors (risk factors) of fractures between genders need to be noticed. In the Lieto study, variables associated with an increased risk of fractures differed between men and women. Even though men and women share many of the risk factors for fractures (White et al. 2006; Hippisley-Cox & Coupland 2009), gender differences have been noticed in the variables associated with both falls (Campbell et al. 1989) and fractures (White et al. 2006; Hippisley-Cox & Coupland 2009).

In Lieto, prior fractures were not associated with future fractures. In former studies, not only prior forearm fractures (Cuddihy et al. 1999; Honkanen et al. 2000) but also prior vertebral fractures (Melton et al. 1999a; Johnell et al. 2004b) and prior hip fractures (Johnell et al. 2004b) have been shown to be associated with future fractures, in both genders (Kanis et al. 2004b). However, in a Swedish study (Johnell et al. 2004b) prior spine and hip fractures were not associated with future forearm fractures in older women. There is also strong evidence that parental history of fracture, especially a family history of hip fracture, is related to the risk of future fractures (Kanis et al. 2004a). In Lieto, the information on parental history of fractures was not available.

The explanation for the association between prior and future fractures has been searched from bone strength. Low BMD has been shown to be one of the risk factors for osteoporosis and fragility fractures (Cheng et al. 1997; Albrand et al. 2003; Johnell et al. 2005; Cummings et al. 2006). However, not all persons with a low BMD value sustain a fracture after a fall (Sambrook & Cooper 2006; Järvinen et al. 2008). There is also evidence that falling accidents and fall-related factors predict fractures independently regardless of BMD values (Kaptoge et al. 2005; Schwartz et al. 2005). Thus, the importance of the falling accident itself has been emphasised (Kanis et al. 2005a; Kannus et al. 2005b; Järvinen et al. 2008). In Lieto, BMD was not measured but vertebral compression at baseline was used as an indicator of bone fragility. It is noticeable that compression fractures predicted future fractures both in men and in women in Lieto. It is likely that the impact of prior fractures (and low BMD) on sustaining future fractures vary by the type of fracture and it is evident that bone quality has also an important impact if a fracture is sustained after a fall, especially in advanced age (Bouxsein 2008; Kelsey & Samelson 2009). In future studies more emphasis need to be focused especially on the falling mechanism and bone quality.

Smoking impairs formation of new bone, absorption of calcium and adversely affects hormones and enzymes involved in bone regulation leading to decreased bone mass (Nieves 2008). Thus, smoking has been identified as a significant risk factor for both osteoporosis (Nieves 2008) and many fracture types (Vestergaard & Mosekilde 2003; Kanis et al. 2005c; Nieves 2008; Hippisley-Cox & Coupland 2009). However, smoking was not associated with the risk of fracture in Lieto. One explanation for the difference in this result compared with previous studies is that smoking has more impact on hip and spine fractures (fragility fractures) compared with other fracture types (Vestergaard & Mosekilde 2003). On the other hand, it has been shown that smoking is also associated with ankle fractures in women (Valtola et al. 2002). In Lieto, a majority of the fractures were other than typical fragility fractures, and the proportion of hip, spine and proximal humerus fractures was only 37% of all fractures. Another explanation is related to smoking cessation and the small proportion of smokers in Lieto. It has been shown that cessation of smoking decreases the risk of fractures (Vestergaard & Mosekilde 2003; Nieves 2008). The proportion of smokers who have stopped smoking is high among the elderly in Finland (Laitalainen et al. 2008).

A BMI value <30 at baseline predicted a new fracture in women in Lieto. Low BMI is a well-documented risk factor for future fractures, but the significance of BMI as a risk factor depends on BMD and varies according to the classification of BMI (De Laet et al. 2005). In older people, low BMI predicts an overall poor health status and mortality (Klenk et al. 2009) as well as an increased risk for falls and fractures (Karinkanta et al. 2010). According to a meta-analysis of 12 prospective population-based studies (De Laet et al. 2005), low BMI predisposes to fracture and this finding is independent of age and gender, but dependent on BMD. However, in the meta-analysis of De Laet et al. (2005), no other risk factors than age, BMI and BMD were adjusted in evaluating the risk factors for fractures. Thus, the importance of low BMI as an independent risk factor for fractures can only be speculated.

The protecting factor behind high BMI is likely the high amount of muscle mass instead of overweight itself (Beck et al. 2009). Poor muscle strength has also been proven to be an independent risk factor for falls (The American Geriatrics Society 2010; Tinetti & Kumar 2010). There is evidence that overweight serves as a risk factor for ankle fracture in middle-aged women (Valtola et al. 2002), and obesity is associated with higher all-cause mortality in both genders (Klenk et al. 2009). In the elderly women, a decrease in BMI value may, however, serve as an alarm signal for increased risk of fractures and thus, the weight of older persons should be regularly followed. Poor muscle strength, low handgrip strength as an indicator in this study, predicted fractures in women. It is likely that especially aging women need to take care of their muscle strength both in order to prevent fractures and severe consequences after an injury.

The Lieto study showed that depressive symptoms measured with ZSDS independently predicted fractures in men but not in women. This result is opposite to that obtained in a Norwegian study (Søgaard et al. 2005), where long-term mental distress was associated with a risk of all non-vertebral fractures and osteoporotic fractures in middle-aged women, but not in men. Although the association between depressive symptoms and fractures has been shown especially in women (Whooley et al. 1999; Mussolino 2005; Søgaard et al. 2005), the overall association between depressive symptoms and BMD decrease or fractures has not been shown in all prospective cohort studies (Whitson et al. 2008). In a recent meta-analysis (Wu et al. 2009), depression was associated with a significant decrease in mean BMD of spine and hip both in men and women. Furthermore, a substantially greater BMD decrease was observed in depressed women and in those with diagnosed clinical depression.

However, there is previous evidence that depressive symptoms are related to falls in both genders (Whooley et al. 1999; Biderman et al. 2002; Tinetti & Kumar 2010). A low quality of life measured with the SF-36 physical component summary score has been reported to predict fractures in menopausal women (Papaioannou et al. 2005). A large number of depressive symptoms in addition to cognitive impairment has been shown to be a risk factor for functional decline (Mehta et al. 2002). Depressed persons may be passive in physical exercise and they may have poor appetite, which may lead to a decrease in BMD, muscle strength and body balance. Depression is associated with poor physical health both in older men and women (Päivärinta et al. 1999). Thus, the high risk of sustaining fractures may be explained by these factors. However, the negative impact of depressive symptoms on BMD has been shown to be independent of body weight or other behavioural factors such as calcium compliance or exercise in postmenopausal women (Milliken et al. 2006). It is possible that mental distress influences bone metabolism both directly and indirectly via health behaviour and functional decline (Mezuk et al. 2008).

Functional decline

Older women report more disabilities and functional limitations in ADL tasks than older men (Merrill et al. 1997). In the Lieto study, no clear gender differences were observed in managing mobility- or ADL-related tasks in the 616 surviving participants but more women were more often than men dependent in at least one IADL-related task both in 1990-1991 and 1998-1999 examinations. Several reasons for gender differences in functioning have been proposed. One hypothesis is that women have more nonfatal but disabling conditions and diseases. A Dutch population-based sub-cohort study with one-year follow-up showed that neither men nor women regained their pre-injury levels of ADL functioning after an injury (Kempen et al. 2003). In the present study, older men were able to reach their pre-injury level. Men who survived an injury needed up to 12 months to recover, whereas women's recovery ceased at 5 months after injury. In a short-term follow-up (up to 5 months), recovery does not seem to be influenced by gender but rather, by the severity of the injury and high age.

The Lieto data shows that fractures have an impact on the development of impairments both in short- and longer perspectives. The results support and bring new evidence for the previously reported studies (Willig et al. 2001; Nurmi et al. 2004; Gerdhem et al. 2006; Tsuboi et al. 2007). The participants in this study represented an unselected population with a great variability in health status and functioning. The functional tests might not be sensitive for minor changes in functioning among the healthiest participants, but they are sensitive for major limitations and dependences. A decline in self-reported mobility and in self-reported ADL performance after a fracture, which were used as functional outcomes, may thus be an underestimate of functional decline among older fracture patients. It is also likely that the variables assessing functional tasks were not sensitive in analysing the impact of fractures on hobby-related tasks.

Functional decline is usually defined as a reduced ability to perform basic mobility tasks, e.g. walking, and daily tasks, such as eating, washing and cleaning (Inouye et al. 2000). In this study, leisure-time physical inactivity in exercise predicted increased risk of functional decline and mortality independently of other predictors, which supports earlier reports (Stuck et al. 1999). Most ADL functions are based on walking and require balance and muscle strength. After a fracture, physical exercise, especially progressive resistance training, is important in reducing physical disability and ADL limitations (Binder et al. 2004).

Also psychosocial factors are associated with the development of disabilities, especially in older persons (Kempen et al. 2005). Positive self-efficacy, perceived control, positive life attitude and belief of having control over own health (internal locus of control) seems to have positive effects on recovery after injurious falls and even in chronic conditions (Kempen et al. 2003; Proctor et al. 2008). There is evidence that a falling accident increases the fear of falling (Lord et al. 2001). It is therefore likely that many old persons limit also their social activities after a fracture. Patients with fear of falling or unrealistic expectations on their recovery (overexertion) or patients underestimating their capabilities are at risk of anxiety, frustration, and reduced motivation for physical activation. In addition, they are at risk of negative self-efficacy and excess disability (Proctor et al. 2008). Fractures and consequences of fractures may also narrow social roles and increase depressive symptoms (Greendale & Barrett-Connor 2008).

Personal resources and ability to benefit from social support seem to promote patients' recovery from fall-related injuries (Kempen et al. 2001). Persons with stronger support cope better with their situation after a hip fracture (Johansson et al. 1998). The assessment of patients' cognitions and beliefs about their recovery is essential for the rehabilitation process of fracture patients. In addition to setting realistic goals for the rehabilitation process, it is important to increase patients' feelings of self-efficacy and control over the process of rehabilitation (Proctor et al. 2008).

Mortality
Sustaining any kind of fracture was associated with excess mortality both in men and women in the Lieto Study. However, it is likely that the impact of fracture on mortality risk varies by the type of fracture.

7.2.2 Hip fractures

Incidence rates
The crude incidence of hip fractures in both genders was quite similar to the results obtained in persons aged 60 years or older in Australia (Chang et al. 2004). In previous studies (Jones et al. 1994; Kannus et al. 1999; Sanders et al. 1999; Lofthus et al. 2001; Boufous et al. 2004), the age-specific incidences have been quite similar to the results of this study among persons younger than 80 years, but among the population 85 years of age or older, the incidence of hip fractures was lower in this study. In Sweden (Kanis et al. 2000), the incidence in older men was quite similar to the results of this study, but the rate among women 75 years or older was higher in every age group compared with Lieto. In Mexican Americans, and in Africa and Asia, the incidence rates of hip fractures are reported to be lower in both genders compared with the results of this study (Espino et al. 2000; Lau et al. 2001; Zebaze & Seeman 2003). The reasons for gender-specific rate difference between countries can only be speculated but differences in life-style, health behaviour and genetic factors cannot be ruled out (Moayyeri et al. 2006).

The female/male incidence ratio of hip fracture was 1.7. Age-adjusted female/male incidence ratios of hip fracture have varied in different populations across the world from 0.9 to 2.9 (Moayyeri et al. 2006). In the majority of studies, including information from the last two decades, the female/male ratio of hip fracture incidence is approximately 2.5. In the Finnish PERFECT data in the years 2005, 2006 and 2007, the ratios have been 2.4, 2.3 and 2.1, respectively (Sund et al. 2008). Thus, the ratio in the present study was somewhat lower compared with those reported previously (Moayyeri et al. 2006; Sund et al. 2008). The incidence of hip fractures is higher in some Asian men (Middle-East and China) compared with men in European and North-American countries.

Predictors
Specific predictors for hip fractures were not analysed in this study. A majority of hip fractures are sustained indoors (Lofthus et al. 2001), and this was also true in the Lieto Study, in which about 70% of the hip fractures were sustained indoors. Factors affecting hip fracture incidence differ between urban populations within a restricted geographical region (Falch et al. 1995). Predictors of hip fractures vary even between

countries geographically close to each other and among populations representing people of similar race and social structures (Falch et al. 1995; Moayyeri et al. 2006). This may be due to different registration systems, but more focus should also be directed on genetic and life-style factors in analysing predictors for hip fractures (Moayyeri et al. 2006).

The latitude and seasonal variation have been discussed as potential reasons for the high fracture incidence in the Scandinavian countries (Bulajic-Kopjar 2000; Lofthus et al. 2001). Seasonal variations of fractures were not analysed by type of fracture in the Lieto Study. However, in Lieto, every fourth fracture was a hip fracture, and no seasonal variation in any kind of fractures was found either in men or in women. Similarly, no seasonal variations in the incidence rates of hip fractures were found in Oslo, Norway (Lofthus et al. 2001), in Birmingham, the United Kingdom (Parker & Martin 1994) or in Rochester, Minnesota, USA (Jacobsen et al. 1995). However, considerable seasonal variation in the hip fracture incidence has been observed in a number of other studies (Bulajic-Kopjar 2000; Bischoff-Ferrari et al. 2007; Grønskag et al. 2010). It is possible that the nonexistence of the seasonal variation is due to the small number of fractures and grouping of months into seasons in Lieto. However, ice and snow are related to hip fractures among women 45 to 74 years of age but not among those aged 75 years and older (Jacobsen et al. 1995). It has also been shown that hip fractures have a smaller winter/summer difference than other fractures (Bischoff-Ferrari et al. 2007). Thus, it is understandable that the oldest old people fall and sustain hip fractures for other reasons than icy conditions (Bischoff-Ferrari et al. 2007).

However, reduced sunlight during the winter periods in Northern parts of the world reduces the synthesis of vitamin D (Bulajic-Kopjar 2000) and there is evidence that half of the patients with hip fracture suffer from hypovitaminosis D (Nurmi et al. 2005). The winter season and cold weather may also decrease physical activity and increase bone loss (Bergstralh et al. 1990). All these factors increase the risk of fractures, especially the risk of hip fracture and thus winter may increase the risk of sustaining a hip fracture, especially in those active and moving outside their homes in all seasons of the year. However, at least in patients with a history of recurrent falling (≥3 previous falls), intrinsic risk factors are likely to be more important than extrinsic risk factors for sustaining a hip fracture (Formiga et al. 2008).

Functional decline

The relationship between hip fracture and functional decline was not analysed in the Lieto Study. However, it has been shown that hip fractures are highly associated with loss of quality of life (Borgström et al. 2006). Thus, it is assumed that hip fractures had the greatest impact on the results regarding the effect of lower-body fractures.

In another Finnish study, only 36% of the hip fracture patients were able to move independently outdoors compared with 79% of their age- and gender-matched controls after a mean of 7 years follow-up (Willig et al. 2001). More hip fracture patients needed walking aids, had difficulties in managing ADLs and required home help than the controls (Willig et al. 2001). In a 12- month follow-up, only 36% of male hip fracture patients could walk independently compared with 84% of the controls without a hip fracture (Pande et al. 2006). During a 2-year follow- up, 58% of women who sustained a hip fracture were unable to walk 100 yards unaided compared with 11.5% of the controls (at baseline: 13.6% and 6.3%, respectively) (Kirke et al. 2002).

In the previous studies, the results are adjusted only by age and gender. There is some evidence about the independent relationship of hip fractures on functional decline in 12 and 24 month follow-ups (Magaziner et al. 2003). The long-term findings of this study give new evidence compared with previous reports; lower-body fractures are independent risk factors for decreased mobility and ADL functioning.

Dementia, delirium and depression are common in older persons admitted to hospitals due to a hip fracture (Magaziner et al. 2000; Givens et al. 2008). These symptoms, alone and in combinations, debilitate recovery after a fracture (Givens et al. 2008). In the Lieto Study, no information about cognitive and mood disorders at the time of hip fracture was available, but adjustments could be made with the baseline information about depressive symptoms and cognitive ability. The MMSE score <24 and a high amount of depressive symptoms at baseline were related to a decline in ADL abilities during the 8-year follow-up even without fractures. It is likely that all of these factors together inflate the poor outcome after a fracture.

In hip fracture patients, muscle strength may remain persistently poor. An asymmetrical leg extension power impairs stair-climbing, a mobility task requiring unilateral force production (Portegijs et al. 2008b). It is likely that lower body fractures lead to reduced muscle strength that impairs ability to perform ADL functions requiring balance and gait. The first six months after the trauma are the most rapid recovery time for femur fracture patients (Magaziner et al. 2000; Sanders et al. 2008). After a fracture, physical exercise, especially progressive resistance training, is important in the reduction of physical disability and ADL limitations (Binder et al. 2004). Intensive progressive resistance training may decrease self-reported difficulties in outdoor mobility even several years after a hip fracture (Portegijs et al. 2008a). A rather long follow-up with effective rehabilitation after sustained fracture, at least after a hip fracture, may be needed to avoid mobility problems and ADL dependence.

In addition to low muscle power, high level of interleukin-6 in serum, reflecting inflammation reaction, is associated with poor recovery of lower extremity function after hip fracture (Miller et al. 2006b). One explanation may be vitamin D deficiency at the time of hip fracture that can interact on higher serum interleukin-6 level (Miller et al. 2007). Low vitamin D level (Visser et al. 2003) and high interleukin-6 level (Miller et al. 2008) either alone or together can impair muscle strength and further impair lower extremity function. Anyhow, in addition to intensive physical rehabilitation (at least 60 minutes per day), a sufficient dose of vitamin D supplementation (Bischoff-

Ferrari et al. 2010; Nurmi-Lüthje et al. 2011 [Epub ahead of print]) can be recommended for hip fracture patients.

Mortality

A hip fracture was a powerful independent predictor of long-term excess mortality in both older men and women during the 12-year follow-up. It has been suggested that in people aged 50 years or more, 17-32% of all death cases associated with hip fracture may be causally related to the fracture itself (Kanis et al. 2003). Together with a Danish study (Vestergaard et al. 2007), the finding here supports that hip fracture, not the pre-existing co-morbidity alone, is an independent predictor of excess mortality. The relation between the type or severity of hip fracture and mortality was not analysed in the Lieto study. No differences in mortality rates between intra- and extracapsular hip fractures have been noticed in Finland (Sund et al. 2009). However, patients with extracapsular hip fractures have been reported to require longer total inpatient treatment and they are more likely transferred into long-term care (Sund et al. 2009). The type of hip fracture may have some impact on the functional recovery to performing activities of daily living after the fracture.

In Lieto, excess mortality after a hip fracture was particularly high in men in which the risk of death was eight-fold compared with men without a hip fracture. Overall, the risk of dying after a hip fracture has been reported to be about two times greater for men than for women (Center et al. 1999; Forsén et al. 1999; Kanis et al. 2003; Johnell et al. 2004c; Shortt & Robinson 2005). However, some studies have given opposite results: the female mortality after a hip fracture has been higher than the male mortality (Nurmi et al. 2004; Nurmi-Lüthje et al. 2009). The reason for this difference is unclear. It is noticeable that in Lieto, coronary heart disease and myocardial infarction were found to be significantly more common causes of death in male hip fracture patients than in female patients. Coronary heart disease is related with excess death in hip fracture patients also in another Finnish cohort study (Panula et al. 2009). However, the use of prescribed calcium plus vitamin D after a hip fracture has been reported to reduce three-year mortality especially in male hip fracture patients compared with female patients (Nurmi-Lüthje et al. 2009). In a recent nationwide Finnish study, the post-fracture mortality was 26 per cent lower among males who used calcium plus vitamin D supplements than among those who did not. Among women the corresponding figure was 21%. There was a tendency to even better survival in both genders if calcium plus vitamin D or vitamin D supplements and anti-osteoporotic drugs were used simultaneously (Nurmi-Lüthje et al. 2011 [Epub ahead of print]).

A hip fracture is associated with substantial increases in proinflammatory cytokines such as interleukin-6 (Miller et al. 2008; Colon-Emeric et al. 2010). These elevated proinflammatory markers are associated with perioperative complications and worse long-term functional outcomes and are therefore hypothesised to explain the excess infections and cardiovascular events observed during the first two years after hip fracture. Men are more prone to postoperative complications such as pneumonia, arrhythmia, delirium and pulmonary embolism compared with women after a hip fracture (Endo et al. 2005). These postoperative complications themselves may increase the risk of death, and they may delay the rehabilitation process after a hip fracture and may indirectly increase the risk of death. Thus one speculative explanation for differences in mortality rates between men and women after a hip fracture may be associated with proinflammatory cytokines. Unfortunately, postoperative complications or proinflammatory markers were not recorded in the Lieto study.

Another explanation for men's higher mortality rate after a hip fracture may also be found in the care and rehabilitation process after a hip fracture and it is related to inflammation reactions after a hip fracture. No differences in practical rehabilitation interventions after hip fracture surgery have been reported between men and women (Lieberman & Lieberman 2004), but there is evidence that diagnosis and treatment of osteoporosis may be inadequate especially in men (Kiebzak et al. 2002; Riley et al. 2002; Nurmi-Lüthje et al. 2011 [Epub ahead of print]).

7.2.3 Proximal humerus

Even though proximal humerus fractures are relatively common, especially among fit, home-dwelling older women (Court-Brown et al. 2001), little is known about the epidemiology of all kinds of proximal humerus fractures. This is because most of them (80%) are non-displaced or minimally displaced, and therefore, can be managed non-operatively. Thus, they are treated on an outpatient basis and only the most severe cases can be identified from the Hospital Discharge Register. The articles written by the specialists of shoulder traumas and surgery have focused on complex humerus fractures or their complications. For this reason, the epidemiology of all proximal humerus fractures has remained superficial at the population level.

Incidence

Proximal humerus fractures are one of the most frequent fracture types in elderly people (Baron et al. 1996; Ismail et al. 2002). In the Lieto Study, the age-specific incidence of proximal humerus fractures among women and men aged 65 years or over varied from 1.5 to 2.8 per 1000 PY in men and from 2.9 to 5.2 per 1000 PY in women. The incidence rate rose with age in women and was highest among those 85 years and older. The incidence rates in both genders in Lieto are higher compared with data collected in England (Court-Brown et al. 2001), in Tasmania (Cooley & Jones 2001) or Europe (Ismail et al. 2002). In another Finnish study among women 80 years and older who were admitted to hospital because of a proximal humerus fracture, the age-adjusted incidence was 3.0 per 1000 PY (298 per 100 000 PY) (Kannus et al. 2009b) and the rates were lower among men compared with women (Kannus 2010 unpublished data). The number of proximal humerus fractures was 4 in men and 25 in women in this study that will debilitate the generalisation of the results.

Functional decline
The Lieto results support and give new evidence that upper body fractures predict difficulties in managing activities of daily living as long as eight years after a fracture. Proximal humerus fractures have most probably had the strongest influence on these results. Also a follow-up study of proximal humerus fracture patients in Sweden (Olsson et al. 2005) has shown negative consequences of proximal humerus fractures up to 13 years. The study of Olsson and colleagues (2005) did not have a control group or adjustments of other variables related to functional decline.

Mortality
In the present study, proximal humerus fractures independently predicted long-term excess mortality in older men. Previously, proximal humerus fractures are shown to increase short-term mortality both in men and women (Johnell et al. 2004c; Shortt & Robinson 2005). There are only a few studies with long-term follow-up and data on other covariates associated with mortality (Browner et al. 1996). Sustaining a humerus fracture or a hip fracture may be indicative of remarkably poor underlying health, especially in men.

7.2.4 Other fractures

Forearm and wrist fractures
The incidence rates of forearm and wrist fractures have been reported to be higher among aged women than men (Kaukonen 1985; Jones et al. 1994; Melton et al. 1998; Kanis et al. 2000; O'Neill et al. 2001; Ismail et al. 2002; Thompson et al. 2004; Flinkkilä et al. 2010). The results in the Lieto Study support these findings. In addition, the age-specific incidence of wrist fractures among women and men aged 65 years or over in this study tended to be similar to those found in Sweden (Kanis et al. 2000) among all age groups, with the exception of women aged 65-79, for whom the rate in Finland was higher. In Australia (Jones et al. 1994), the UK (O'Neill et al. 2001; Thompson et al. 2004) and the USA (Melton et al. 1998), the rates were lower among both men and women over 65 years of age.

One fifth of the patients with non-surgically treated distal radius fractures have been reported to experience severe impairments in functional abilities sometimes even a decade after the trauma (Földhazy et al. 2007), but the results are inconsistent (Greendale et al. 2000). The study of Földhazy et al. (2007) was a case follow-up study without a control group without fractures or adjustments of other variables related to functional decline. In the study of Greendale et al. (2000), a follow-up of 7 years was used and the study was a case-control study with relevant adjustments, but in their study individuals with wrist fractures did not experience a statistically significant decline in any performance measure compared with the no fracture group. Therefore, the results of the present study give new findings: upper body fractures predicted difficulties in activities of daily life after 8 years. It was surprising that the decline in ADL functions was not found in short-term follow-ups. It is possible that the number of upper-body fractures was too small, and statistical tests could not show the relationship. In addition, hand grip strength was not measured during the follow-up. However, wrist fractures seem to reduce quality of life, at least in a 1-year follow-up (Borgström et al. 2006).

Wrist and forearm fractures did not predict higher mortality in this study. This result is similar to the results from previous studies (Cooper et al. 1993; Johnell et al. 2004c). Wrist fracture patients are on average 10 years younger (average age 67.6 years) than hip fracture patients (average age 77.5 years) when sustaining a fracture (Endres et al. 2006). They also have less co-morbidities and better functional abilities compared with hip fracture patients (Endres et al. 2006).

Vertebral compression fractures

It is reported that only 30% of all vertebral fractures are diagnosed clinically (Haczynski & Jakimiuk 2001; Old & Calvert 2004). Thus, it is likely that vertebral fractures have been missed also in Lieto during the follow-up. The incidence of clinically diagnosed vertebral fractures was low in this study with only a slight increase with age. Previous studies have shown that vertebral fractures are associated with older age in both genders (Felsenberg et al. 2002).

In the present study, neither vertebral fractures at the baseline nor new vertebral fractures during the follow-up predicted increased mortality. The follow-ups of the previous studies have been shorter and the number of confounding variables has been more restricted (Cooper et al. 1993; Center et al. 1999; van Staa et al. 2001; Johnell et al. 2004c) which may explain the differences between the results. The number of clinically detected vertebral fractures in this study was too small to allow subgroup analyses. When vertebral fractures at the baseline were entered into the multivariate analyses, no association between vertebral fractures and mortality during the follow-up was found. Even though, this study was underpowered to show association between vertebral fractures sustained during the follow-up, it seems that vertebral fractures are associated with mortality through other causes of death rather than being a direct cause. There is also evidence that this excess can be partly explained by an association with other health and lifestyle factors associated with death (Ismail et al. 1998). Short-term mortality after a fracture was not analysed here, which may explain some results contradictory to previous results (Cooper et al. 1993; Center et al. 1999; van Staa et al. 2001; Johnell et al. 2004c).

Almost one half of female patients with vertebral fractures have been reported to have recurrent back pain and impaired health status for as long as 12 years after the fracture (Hasserius et al. 2005). The consequences of vertebral fractures may include also compromised respiratory functions (Greendale & Barrett-Connor 2008). Unfortunately, the amount of vertebral fractures was too small in this study to allow analysing the associations of these fractures with the abilities of daily living. It is noticeable that vertebral fractures have considerable impact on the quality of life (Borgström et al. 2006).

7.3 Implications for further studies

The high incidence and severe consequences of fractures are major reasons that emphasize the importance of fracture prevention. Even though the trend of hip and proximal humerus fractures has been reported to have stabilised during the last decade (Kannus et al. 2006; Kannus et al. 2009b), these conclusions are based mainly on hospital-based records and Cause of Death Statistics. These records can be used only in analysing the change in the incidences of the most severe fractures needing inpatient hospital treatment. We do not know if the incidence rates of other fractures have changed. There is a need for several cross-sectional population-based studies assessing the changes in the incidence of fractures.

Risk factors vary by type of fracture (Honkanen et al. 1998; Hippisley-Cox & Coupland 2009; Kelsey & Samelson 2009; Jokinen et al. 2010). Thus, sustaining a fracture depends most likely on the gender and the individual risk profile. For determining these fracture-specific dependencies, a huge data including wide-range background data of the subjects and a long follow-up about the fractures are needed. This requires collaboration between researchers both nationally and internationally, for comparing data and conducting meta-analyses.

The true impact of fractures on functional decline is mostly unknown, especially in physically more active persons. Because older people are a highly heterogeneous group, more sensitive assessment tools should be developed in assessing the impact of fractures on functional capacities especially in the most active persons. In addition, we should assess the impact of different fractures as well as follow the results of the care and rehabilitation on functional abilities more regularly (van Beeck et al. 2007) and more individually, including also hobby-related tasks (Rockwood 2007).

The first task is to identify individuals at risk of falling and sustaining a fracture. Even though screening tools for identifying persons at high risk of fractures have been developed (Black et al. 2001; Kanis et al. 2008b), these tools do not specify gender differences. More focus should also be given on resolving individual genetic and life-style factors in analysing predictors for hip fractures (Moayyeri et al. 2006).

Besides positive evidence about fall prevention, less is known about the effectiveness of programs directed at the prevention of fall-related injuries and fractures. More information is needed regarding the effects of multifactorial interventions designed to focus on both fall prevention and bone strength. It is most likely that people who have both fragile bones (osteoporosis) and increased risk of falling should receive the highest priority for preventive actions (Kanis et al. 2002; Lee et al. 2002; Woolf & Åkesson 2003). In these actions, national-, race- and gender-specific individual risk factors should be taken into account. More specific risk calculator programmes could be useful in daily clinical use.

8. CONCLUSIONS

1. Fractures are a common public health problem among the elderly in Finland: every fourth person aged 65 years or older sustains at least one fracture during the 12-year follow-up. The majority of the fractures occur in women. The age-adjusted incidence of all fractures remained stable between 1991 and 2002.
2. In general, the incidence of fractures increased with age, except for forearm and wrist fractures.
3. Predictors of fractures differ between genders: reduced handgrip strength and low or normal body mass index predict fractures in women, whereas depressive symptoms predict fractures in men. Vertebral compression fracture predicts subsequent fractures in both genders.
4. A hip fracture predicts mortality both in men and women, whereas fracture of the proximal humerus predicts mortality only in men. The impact of hip and proximal fractures on mortality is stronger in men than in women.
5. Physical inactivity in leisure time predicts excess mortality and functional decline.
6. Fractures decrease functional ability. A lower body fracture predicts decline in mobility and in ADL functions while an upper body fracture predicts decline in ADL functions during a long-term follow-up.

9. RECOMMENDATIONS

1. Since fractures are common in older people and a costly problem for the public health sector, attention should be paid on the prevention of fractures. Even though the majority of fractures occur in women, attention should be focused also on fractures of older men.

2. Prevention of fractures requires the maintenance and promotion of physical activity, muscular strength and nutritional status, and the prevention of depression. Special attention needs to be focused on prevention of bone fragility.

3. Fractures decrease mobility and ability to maintain ADL functions. Thus, fracture patients should be followed more intensively until full recovery. Rehabilitation after a fracture is important.

4. In minimising the influence of fractures on functional decline and death, research about treatment and rehabilitation effect is needed.

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APPENDICES

Appendix Table 1. Baseline characteristics of socio-demographic, education, occupation and economical factors among men and women during the 12-year (n=1177) and 8-year (n=616) follow-ups in the Lieto study of fractures.

Characteristics	**Men**		**Women**	
	12 years n=482 n (%)	**8 years** n=241 n (%)	**12 years** n=695 n (%)	**8 years** n=375 n (%)
Socio-demographic				
Age group at baseline				
- 64-74	318 (66)	192 (80)	406 (58)	270 (72)
- 75-84	145 (30)	46 (19)	226 (33)	94 (25)
- 85+	19 (4)	3 (1)	63 (9)	11 (3)
Marital status				
- married or co-habiting				
- single, widowed, divorced or judicial	361 (75)	197 (82)	288 (41)	182 (49)
separation	121 (25)	44 (18)	407 (59)	193 (51)
Type of dwelling				
- own home or sheltered housing				
- with another person	372 (77)	206 (85)	377 (54)	220 (59)
- alone	91 (19)	31 (13)	273 (39)	152 (41)
- long-term institutional care	19 (4)	4 (2)	45 (6)	3 (1)
Education, occupation and economical status				
Education				
- more than basic	35 (7)	24 (10)	45 (7)	26 (7)
- basic	400 (83)	198 (82)	579 (83)	321 (86)
- less than basic	47 (10)	19 (8)	71 (10)	28 (7)
Previous occupation				
- teaching, administration, home work and work in office	396 (82)	44 (18)	447 (64)	134 (36)
- constructive, manual work in industry or farming	86 (18)	197 (82)	248 (36)	241 (64)
Economical status				
- highest	15 (3)	11 (5)	4 (1)	3 (1)
- middle	379 (79)	190 (79)	406 (58)	219 (58)
- lowest	88 (18)	40 (17)	285 (41)	153 (41)

Appendix Table 2. Baseline characteristics of physical functional abilities among men and women during the 12-year (n=1177) and 8-year (n=616) follow-ups in the Lieto study of fractures.

Characteristics	**Men**		**Women**	
	12 years n=482 n (%)	**8 years** n=241 n (%)	**12 years** n=695 n (%)	**8 years** n=375 n (%)
Managing in mobility, ADL and IADL tasks* (missing values 3)				
- independently with no difficulties in any task	255 (53)	155 (64)	265 (38)	203 (54)
- with difficulties or dependence in at least one task	227 (47)	86 (36)	427 (62)	172 (46)
Mobility[†]				
- independent in all tasks	317 (66)	182 (76)	360 (52)	251 (67)
- difficulties at least in one task, but not dependent in any task	92 (19)	42 (17)	180 (26)	90 (24)
- dependent at least in one task	73 (15)	17 (7)	155 (22)	34 (9)
ADL[††]				
- independent in all tasks	372 (77)	215 (89)	507 (73)	321 (86)
- difficulties at least in one task, but not dependent in any task	59 (12)	23 (10)	94 (13,5)	41 (11)
- dependent at least in one task	51 (11)	3 (1)	94 (13,5)	13 (3)
IADL [†††]				
- independent in all tasks	283 (59)	175 (73)	296 (43)	223 (59)
- difficulties at least in one task, but not dependent in any task	69 (14)	36 (15)	107 (15)	57 (15)
- dependent at least in one task	130 (27)	30 (12)	292 (42)	95 (25)
Mobility aids (missing values 6)				
- no aids	410 (85)	224 (93)	546 (79)	337 (90)
- walking aids	61 (13)	17 (7)	106 (15)	33 (9)
- wheelchair or other	10 (2)	0 (0)	40 (6)	3 (1)

* Includes 14 questions about mobility (moving outdoors, walking between rooms, negotiating stairs, walking at least 400 metres), ADL (toileting, washing and bathing, dressing and undressing, getting in and out of bed, eating) and IADL (doing one's cooking, doing light housework, doing heavy housework, carrying a 5 kg load, cutting one's toe nails).
[†] Mobility functions include 4 questions about moving outdoors, walking between rooms, negotiating stairs, walking at least 400 metres. [††] ADL functions include 5 questions about toileting, washing and bathing, dressing and undressing, getting in and out of bed, eating. [†††] IADL functions includes 4 questions about doing one's cooking, doing light housework, doing heavy housework and carrying a 5 kg load.

Appendix Table 3. Baseline characteristics of health behaviour, cognitive ability and depressive symptoms among the men and women during the 12-year (n=1177) and 8-year (n=616) follow-ups in the Lieto study of fractures.

Characteristics	**Men**		**Women**	
	12 years n=482 n (%)	**8 years** n=241 n (%)	**12 years** n=695 n (%)	**8 years** n=375 n (%)
Smoking (missing values 3)				
- non-smoker	148 (31)	81 (34)	629 (91)	341 (91)
- ex-smoker	263 (55)	128 (53)	40 (6)	21 (6)
- current smoker	71 (15)	32 (13)	23 (3)	13 (3)
Self-reported leisure-time physical exercise (missing values 1)				
- yes	243 (51)	147 (61)	273 (39)	196 (52)
- no	238 (49)	94 (39)	422 (61)	179 (48)
Cognitive ability (MMSE score) (missing values 7)				
- 24-30	393 (82)	226 (94)	553 (80)	337 (90)
- 18-23	61 (13)	12 (5)	84 (12)	31 (8)
- ≤ 17	25 (5)	3 (1)	54 (8)	6 (2)
Depressive symptoms (missing values 111) (ZSDS score)				
- 20 -44	358 (82)	202 (86)	512 (81)	308 (84)
- 45 -80	78 (18)	33 (14)	118 (19)	60 (16)

Appendix Table 4. Baseline characteristics of clinical and medical data among men and women during the 12-year (n=1177) and 8-year (n=616) follow-ups in the Lieto study of fractures.

Characteristics	Men		Women	
	12 years n=482 n (%)	**8 years** n=241 n (%)	**12 years** n=695 n (%)	**8 years** n=375 n (%)
Systolic blood pressure (mmHg) (M= men; W= women)				
- M 168+ W 170+	125 (26)	57 (24)	185 (27)	99 (26)
- M 136-167 W 140-169	237 (49)	121 (50)	350 (50)	195 (52)
- M <136 W <140	120 (25)	63 (26)	160 (23)	81 (22)
Diastolic blood pressure (mmHg)				
- 90+	168 (35)	92 (38)	234 (34)	120 (32)
- 78-89	215 (45)	105 (44)	304 (44)	182 (49)
- ≤77	99 (21)	44 (18)	157 (23)	73 (19)
Handgrip strength (kPa) (missing values 52) (M= men; W= women)				
- M 86 + W 76 +	120 (26)	79 (33)	169 (26)	112 (30)
- M 55 -85 W 48 -75	232 (50)	124 (52)	330 (50)	200 (54)
- M ≤ 54 W ≤ 47	116 (25)	36 (15)	158 (24)	60 (16)
Body mass index (BMI) (missing values 2)				
- 30 +	96 (20)	49 (20)	228 (33)	121 (32)
- 25 -29.9	234 (49)	135 (56)	271 (39)	167 (45)
- <25	151 (31)	57 (24)	195 (28)	87 (23)
Binocular sight				
- 0.3 +	448 (95)	234 (98)	613 (92)	357 (96)
- < 0.3	24 (5)	6 (2)	50 (8)	16 (4)
Ability to read printed text				
- yes	453 (96)	238 (100)	636 (95)	366 (98)
- no	20 (4)	1 (0)	36 (5)	8 (2)
Ability to hear whisper or talk within 1-5 meters (bilateral) (missing values 5)				
- yes	455 (95)	233 (97)	662 (96)	370 (99)
- no	26 (5)	8 (3)	29 (4)	5 (1)

(**Appendix Table 4** continues)

Characteristics	**Men**		**Women**	
	12 years n=482 n (%)	**8 years** n=241 n (%)	**12 years** n=695 n (%)	**8 years** n=375 n (%)
Number of prescribed drugs	124 (26)	78 (32)	127 (18)	87 (23)
- 0	279 (58)	142 (59)	398 (57)	233 (62)
- 1-5	16 (79)	21 (9)	170 (24)	55 (9)
- ≥6				
Parkinson’s disease				
- no	478 (99)	241 (100)	690 (99)	75 (100)
- yes	4 (1)	0 (0)	5 (1)	0 (0)
Diabetes				
- no	426 (88)	226 (94)	618 (89)	351 (94)
- yes	56 (12)	15 (6)	77 (11)	24 (6)
Rheumatoid arthritis				
- no	471 (98)	237 (98)	680 (98)	370 (99)
- yes	11 (2)	4 (2)	15 (2)	5 (1)
Osteoarthosis				
- no	363 (75)	171 (71)	423 (61)	233 (62)
- yes	119 (25)	70 (29)	272 (39)	142 (38)
Cardiovascular disease (missing values 51)				
- no	335 (72)	185 (78)	516 (78)	298 (83)
- yes	133 (28)	51 (22)	142 (22)	63 (17)
Cancer				
- no	453 (94)	231 (96)	659 (95)	362 (97)
- yes	29 (6)	10 (4)	36 (5)	13 (3)
At least one previous fracture after the age of 45 years but before the baseline				
- no	395 (82)	196 (81)	503 (72)	265 (71)
- yes	87 (18)	45 (19)	192 (28)	110 (29)
Vertebral compression fracture/s on a chest radiogram at baseline (missing values 6)				
- no	445 (93)	228 (95)	612 (89)	350 (94)
- yes	36 (7)	13 (5)	78 (11)	24 (6)

Appendix Table 5. Change in independency in managing mobility-related tasks during the 8-year follow-up (1991-99) in the Lieto study of fractures (n=616).

	Baseline 1990-91			**Follow-up 1998-99**			
	Men (n=241) n (%)	**Women (n=375)** n (%)	**Total (n=616)** n (%)	**Men (n=241)** n (%)	**Women (n=375)** n (%)	**Total (n=616)** n (%)	**Mis** n
All mobility tasks together*							
- independent	182 (75.5)	251 (66.9)	433 (70.3)	102 (43.0)	122 (32.6)	224 (36.7)	
- difficulties	42 (17.4)	90 (24.0)	132 (21.4)	94 (39.7)	141 (37.7)	235 (38.5)	
- dependent	17 (7.1)	34 (9.1)	51 (8.3)	41 (17.3)	111 (29.7)	152 (24.9)	5
		p=0.074			p=0.112		
Moving outdoors							
- independent	195 (80.9)	280 (74.7)	475 (77.1)	128 (53.1)	152 (40.5)	280 (45.5)	
- difficulties	44 (18.3)	89 (23.7)	133 (21.6)	92 (38.2)	157 (41.9)	249 (40.4)	
- dependent	2 (0.8)	6 (1.6)	8 (1.3)	21 (8.7)	66 (17.6)	87 (14.1)	
		p=0.182			p=0.001		
Walking between rooms							
- independent	209 (86.7)	309 (82.4)	518 (84.1)	175 (72.6)	232 (62.6)	407 (66.2)	
- difficulties	32 (13.3)	64 (17.1)	96 (15.6)	57 (23.7)	117 (31.3)	174 (28.3)	
- dependent	0	2 (0.5)	2 (0.3)	9 (3.7)	25 (6.7)	34 (5.5)	1
		p=0.313			p=0.020		
Negotiating stairs							
- independent	188 (78.0)	256 (68.3)	444 (72.1)	118 (49.4)	140 (37.5)	224 (36.7)	
- difficulties	47 (19.5)	100 (26.7)	147 (23.8)	94 (39.3)	144 (38.6)	235 (38.5)	
- dependent	6 (2.5)	19 (5.1)	25 (4.1)	27 (11.3)	89 (23.9)	152 (24.9)	4
		p=0.024			p<0.001		
Walking at least 400 metres							
- independent	192 (79.7)	276 (73.6)	468 (76.0)	133 (55.7)	157 (41.9)	290 (47.2)	
- difficulties	32 (13.3)	72 (19.2)	104 (16.9)	71 (29.7)	129 (34.4)	200 (32.6)	
- dependent	17 (7.0)	27 (7.2)	44 (7.1)	35 (14.6)	89 (23.7)	124 (20.2)	2
		p=0.152			p=0.002		

* All mobility tasks together include ability to move outdoors, walk between rooms, negotiate stairs and walk at least 400 metres and the sum variable was classified into three categories: 1) independent and no difficulties in any of the included tasks, 2) able to carry out the tasks independently but having difficulties at least in one task and 3) dependent on assistance at least in one task.

P-values are calculated with two-sided Chi-Square or Fisher's Exact Tests and represents differences between genders at time of the examination.
Mis= missing.

Appendix Table 6. Change in independency in managing ADL tasks during the 8-year follow-up (1991-99) in the Lieto study of fractures (n=616).

	Baseline 1990-1991			Follow-up 1998-1999			
	Men (n=241) n (%)	**Women (n=375)** n (%)	**Total (n=616)** n (%)	**Men (n=241)** n (%)	**Women (n=375)** n (%)	**Total (n=616)** n (%)	**Mis** n
All ADL tasks together[†]							
- independent	215 (89.2)	321 (85.6)	536 (87.3)	152 (63.9)	219 (59.4)	371 (59.4)	
- difficulties	23 (9.5)	41 (10.9)	64 (10.4)	47 (19.8)	67 (18.2)	114 (18.8)	
- dependent	3 (1.2)	13 (3.5)	16 (2.6)	39 (16.4)	83 (22.5)	122 (20.1)	9
	p=0.099			p=0.186			
Toileting							
- independent	230 (95.4)	321 (85.6)	574 (93.2)	173 (71.8)	248 (66.5)	421 (68.5)	
- difficulties	10 (4.2)	29 (7.7)	39 (6.3)	56 (23.2)	93 (24.9)	149 (24.3)	
- dependent	1 (0.4)	2 (0.5)	3 (0.5)	12 (5.0)	32 (8.6)	44 (7.2)	1
	p=0.173			p=0.181			
Washing and bathing							
- independent	225 (93.4)	330 (88.0)	555 (90.1)	182 (75.5)	258 (69.0)	440 (71.6)	
- difficulties	14 (5.8)	32 (8.5)	46 (7.5)	22 (9.1)	36 (9.6)	58 (9.4)	
- dependent	2 (0.8)	13 (3.5)	15 (2.4)	37 (15.4)	80 (21.4)	117 (19.0)	1
	p=0.047			p=0.156			
Dressing and undressing							
- independent	226 (93.8)	343 (91.5)	569 (92.4)	189 (78.4)	276 (73.6)	465 (75.5)	
- difficulties	14 (5.8)	30 (8.0)	44 (7.2)	25 (10.4)	54 (14.4)	79 (12.8)	
- dependent	1 (0.4)	2 (0.5)	3 (0.5)	27 (11.2)	45 (12.0)	72 (11.7)	
	p=0.609			p=0.303			
Getting in and out of bed							
- independent	225 (93.4)	335 (89.3)	560 (90.9)	194 (81.5)	296 (79.8)	490 (80.5)	
- difficulties	16 (6.6)	38 (10.1)	54 (8.8)	34 (14.3)	50 (13.5)	84 (13.8)	
- dependent	0	2 (0.5)	2 (0.3)	10 (4.2)	25 (6.7)	35 (5.8)	7
	p=0.176			p=0.418			
Eating							
- independent	238 (98.8)	369 (98.4)	607 (98.5)	229 (95.4)	338 (90.6)	567 (92.5)	
- difficulties	3 (1.2)	5 (1.3)	8 (1.3)	8 (3.3)	14 (3.8)	22 (3.6)	
- dependent	0	1 (0.3)	1 (0.2)	3 (1.3)	21 (5.6)	24 (3.9)	3
	p=1.000			p=0.023			

[†] All ADL tasks include ability to move outdoors, walk between rooms, negotiate stairs and walk at least 400 metres and the sum variable was classified into three categories: 1) independent and no difficulties in any of the included tasks, 2) able to carry out the tasks independently but having difficulties at least in one task and 3) dependent on assistance at least in one task.

P-values are calculated with two-sided Chi-Square or Fisher's Exact Tests and represents differences between genders at time of the examination.

ADL=Activities of daily living, Mis=missing.

Appendix Table 7. Change in independency in managing IADL tasks during the 8-year follow-up (1991-99) in the Lieto study of fractures (n=616).

	Baseline 1990-1991			Follow-up 1998-1999			
	Men (n=241) n (%)	**Women (n=375)** n (%)	**Total (n=616)** n (%)	**Men (n=241)** n (%)	**Women (n=375)** n (%)	**Total (n=616)** n (%)	**Mis** n
All IADL tasks together‡							
- independent	175 (72.6)	223 (59.5)	398 (64.6)	81 (33.6)	69 (18.5)	150 (24.4)	
- difficulties	36 (14.9)	57 (15.2)	93 (15.1)	39 (16.2)	57 (15.2)	96 (15.6)	
- dependent	30 (12.5)	95 (25.3)	125 (20.3)	121 (50.2)	248 (66.3)	369 (60.0)	1
	p<0.001			p<0.001			
Preparing meals							
- independent	219 (90.9)	326 (86.9)	545 (88.5)	128 (53.1)	243 (64.8)	371 (60.2)	
- difficulties	11 (4.6)	38 (10.1)	49 (8.0)	41 (17.0)	47 (12.5)	88 (14.3)	
- dependent	11 (4.6)	11 (2.9)	22 (3.6)	72 (29.9)	85 (22.7)	157 (25.5)	
	p=0.029			p=0.015			
Doing light housework							
- independent	207 (85.9)	303 (80.8)	510 (82.8)	140 (58.1)	195 (52.1)	371 (59.4)	
- difficulties	25 (10.4)	55 (14.7)	80 (13.0)	30 (12.5)	72 (19.3)	102 (16.6)	
- dependent	9 (3.7)	17 (4.5)	26 (4.2)	71 (29.4)	107 (28.6)	178 (28.9)	1
	p=0.251			p=0.079			
Doing heavy housework							
- independent	182 (75.5)	241 (64.3)	423 (68.7)	101 (41.9)	91 (24.3)	91 (31.2)	
- difficulties	33 (13.7)	59 (15.7)	92 (14.9)	28 (11.6)	59 (15.7)	87 (14.1)	
- dependent	26 (10.8)	75 (20.0)	101 (16.4)	112 (46.5)	225 (60.0)	337 (54.7)	
	p=0.005			p=<0.001			
Carrying a 5-kg load							
- independent	192 (79.7)	357 (68.5)	449 (72.9)	127 (52.7)	107 (28.6)	234 (38.1)	
- difficulties	33 (13.7)	47 (12.5)	80 (13.0)	43 (17.8)	66 (17.7)	109 (17.7)	
- dependent	16 (6.6)	71 (18.9)	87 (14.1)	71 (29.5)	201 (53.7)	272 (44.2)	1
	p<0.001			p<0.001			
Cutting own toe nails							
- independent	193 (80.1)	269 (71.7)	462 (75.0)	110 (45.6)	148 (39.6)	258 (42.0)	
- difficulties	27 (11.2)	62 (16.5)	89 (14.4)	48 (19.9)	86 (23.0)	134 (21.8)	
- dependent	21 (8.7)	44 (11.7)	65 (10.6)	83 (34.4)	140 (37.4)	223 (36.3)	1
	p=0.063			p=0.319			

‡ All IADL task together include ability to prepare meals, do light housework, do heavy housework and carry a 5-kg load and the sum variable was classified into three categories: 1) independent and no difficulties in any of the included tasks, 2) able to carry out the tasks independently but having difficulties at least in one task and 3) dependent on assistance at least in one task.

P-values are calculated with two-sided Chi-Square or Fisher's Exact Tests and represents differences between genders at time of the examination.

IADL= Instrumental activities of daily living, mis=missing.