UNIVERSITY OF TROMSØ UIT



FACULTY OF HEALTH SCIENCES
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Physical activity, osteoporosis and fracture risk

Long-Term Associations In A General Population

in bilde her... sett inn bilde her... sett i

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A dissertation for the degree of Philosophiae Doctor June 2011



Physical activity, osteoporosis, and fracture risk

Long-term associations in a general population



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Acknowledgements

This project was carried out at the Department of Community Medicine (ISM) with funding from the Research Council of Norway. In 2008, I was fortunate to be offered a position at ISM so that I could work with this project and proceed toward a PhD, and for that I am sincerely grateful. During my three years as a PhD candidate, I have enjoyed the inspiring work environment at ISM, and I greatly appreciate the support, input, and feedback from so many nice and competent co-workers.

I want to express my gratitude to my main supervisor, Lone Jørgensen, for all your input, feedback, clear answers and guidance. You are honest and supportive, your door is always open, and you always take the time needed to guide me. I am inspired by your work and knowledge, and your instant feedback and continuous support has been essential to me.

My warmest thanks to co-supervisor Nina Emaus for all the professional and social input throughout these years. Your enthusiasm and drive are truly inspiring, and your sincere interest has been of great importance to me. Your knowledge, contribution and commitment to osteoporosis are invaluable to me and others.

I am also sincerely grateful for the all the input and feedback from my other co-supervisor, Tom Wilsgaard – I greatly appreciate your always useful and reliable advice, not only on statistics, but on any subject. You have patiently guided me through the statistic and answered my novice statistical questions, even when you were really busy.

Bjarne K. Jacobsen, you were never formally my supervisor, but you have been there all the way as a 4th supervisor, with enthusiasm and vast knowledge, always giving more of your time than needed. Your eye for details, while at the same time keeping the general view, is impressing. I am sincerely grateful for your time, input, feedback and humorous reflections ©.

Svanhild, I am grateful that I you have become my friend. We have had many interesting conversations and some exciting trips - there have been both serious times and a lot of fun! Jan-Magnus, thank you for creating a great work environment in the small office that we shared these three years, for useful discussions, but also good, quiet moments. Sanda, thank you for being my friend and for the nice evenings with food and work and long conversations about EPINOR stuff and everything else. Marit, I am grateful for the friendship that we have developed, for all your caring support and help, for being our dog radiologist, and for all the teamwork throughout the PhD courses. Anna-Sofia, we have shared good moments, fun moments – and some more difficult statistical moments, too!

Kjell-Arne, Marthe, Unni, Haakon, Nadine, and Morten, thank you for a pleasant time together in EPINOR. Thanks to Laila, Anita, Guri, Kristin, and my other colleagues at the Department of Community Medicine

for helpful discussions and for sharing your knowledge. I would particularly like to thank my other coauthors, Ragnar Joakimsen, Luai Ahmed, Åshild Bjørnerem, and Jan Størmer for useful input and valuable hints. A special thanks to Luai for providing me with information whenever needed, for knowledgeable input, and for your goodwill at any time. I would also like to thank Aina Emaus at Oslo University Hospital for your kindness to provide necessary information whenever needed.

I am also grateful for all the instant help that I have received from the technical and administrative support team at ISM, a special thanks to Mona Ingebrigtsen, Jarle Mathiassen, and Merete Albertsen – you really know how to get things done! I want to thank the Research Council of Norway for funding this project. Of course, this work could not be done without all of you who took the time to participate in the Tromsø Study.

Finally, I want to express my gratitude to my family. My mother, who introduced me to sport and physical activity when I was very young and provided me with a lifelong commitment to physical activity in many ways. My dear dad, who died from me so suddenly halfway through my PhD. Our loving dog Mumigrisen who we also lost. We miss you both deeply. Luckily, I am still greeted by two joyful dogs every time I return back home to Bodø. Håvard, my life companion, you made this possible by taking care of everything in my life so that I could concentrate on the PhD. You have made me food, taken care of the dogs, the house, the car, the bills – I am truly grateful for your selfless support and for always wanting the best for me.

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Summary

Osteoporosis and related fractures are a major health problem among elderly people, and Norway has reportedly one of the highest fracture rates in the world. Many factors contribute to osteoporosis and fractures. One highly relevant protective factor is physical activity, which is a major mechanical determinant of the properties of the skeleton. Physical activity may postpone the age-related bone loss and decrease the risk of falling, and thereby reduce the risk of osteoporotic fractures.

Because osteoporosis and fractures primarily occur in the elderly, it is of interest to observe the long-term benefits of physical activity. The Tromsø Study, which is a population study with recurrent surveys, provides an excellent opportunity to follow people throughout adulthood into older age. Thus, the aim of this thesis was to examine the long-term associations between physical activity and outcomes such as bone mineral density (BMD) (paper II) and risk of non-vertebral fracture (paper III) in adults. Moreover, to form a basis for these associations, the stability (i.e. tracking) of physical activity habits over three decades was investigated (paper I). In all three papers, longitudinal data were derived from the surveys in the Tromsø Study. Adult women and men were followed throughout adulthood into older age.

Analyses of tracking of physical activity indicated that physical activity habits during adulthood are relatively stable (i.e. track) over time (paper I). Sedentary adults have markedly higher odds of being sedentary later in life than active adults. The same were true for the other physical activity levels, i.e. being physically active in adulthood is a strong predictor of being active later in life. The results from this study have implications for the subsequent studies in this thesis.

In paper II, examination of the associations between physical activity and BMD showed a positive linear trend in BMD across physical activity levels. The differences in BMD between physical activity groups were rather small, but consistent over different sites of the hip and forearm, and even small differences in BMD can have relatively large effects on fracture risk.

The results from paper III showed that moderate and high physical activity appeared protective against fractures in the weight-bearing (lower) skeleton, whereas the risk of fracture in the non-weight-bearing skeleton was not related to physical activity level, indicating that effects of physical activity on fracture risk are site-specific.

These population studies suggest that physical activity can prevent or delay osteoporosis and age-related fractures, and that the mechanisms partly involve bone mineral density, as physical activity was related to BMD in a dose-response pattern. Moreover, there is a tendency that physical activity habits in adults are fairly stable over a long time. This implies that adults who are sedentary tend to stay sedentary later in life, which may be worrying considering the many health benefits of physical activity.

Sammendrag

Osteoporose og osteoporotiske brudd utgjør et stort helseproblem blant eldre, og Norge har den høyeste forekomsten av hofte- og underarmsbrudd som er rapportert. Mange faktorer bidrar til osteoporose og brudd, deriblant lav fysisk aktivitet. Fysisk aktivitet er en viktig faktor for skjelettets mekaniske egenskaper og kan utsette det aldersrelaterte tapet av benmasse og redusere risikoen for å falle.

Osteoporotiske brudd oppstår hovedsakelig hos eldre, derfor er det av interesse å undersøke de langsiktige gevinstene av fysisk aktivitet. Tromsøundersøkelsen, som er en gjentatt helserelatert befolkningsundersøkelse, gjør det mulig å følge mennesker fra voksen til eldre alder. Målet med denne avhandlingen var å undersøke sammenhenger mellom fysisk aktivitet og bentetthet (artikkel II) og risiko for ikke-vertebrale brudd (artikkel III) over tid hos voksne. For å danne et grunnlag for analyse av disse sammenhengene, ble stabiliteten (dvs. "tracking") av fysiske aktivitetsvaner gjennom tre tiår utredet (artikkel I). I alle tre artiklene ble voksne kvinner og menn ble fulgt fra voksen til eldre alder, gjennom analyser av longitudinelle data fra Tromsøundersøkelsene.

Resultatene fra artikkel I viste at det fysiske aktivitetsnivået i voksen alder holder seg relativt stabilt over lang tid, inn i eldre år. Vi fant at voksne kvinner og menn som er fysisk aktive, har betydelig større sannsynlighet for å være aktive senere i livet enn de inaktive. På samme vis har de som er inaktive høy sannsynlighet for å være inaktive flere tiår senere. Resultatene fra denne studien dannet et grunnlag for de påfølgende studiene i denne avhandlingen.

Analysene i artikkel II viste at høy bentetthet var tydelig assosiert med høyt fysisk aktivitetsnivå. Den positive sammenhengen mellom fysisk aktivitet og bentetthet var konsekvent i hofte og underarm. Selv om forskjellene i bentetthet mellom ulike nivåer av fysisk aktivitet var relativt små, var de statistisk signifikante, og selv små forskjeller i bentetthet kan ha store effekter på risiko for benbrudd.

Analyser av bruddrisiko (artikkel III) viste at fysisk aktivitet beskytter mot brudd i det vektbærende skjelettet. Derimot var risiko for brudd i det ikke-vektbærende skjelett ikke relatert til fysisk aktivitetsnivå. Dette indikerer at effektene av fysisk aktivitet på bruddrisiko varierer med bruddsted.

Resultatene fra studiene i avhandlingen tyder på at fysisk aktivitet kan bidra til å forebygge osteoporose og aldersrelaterte brudd, og at dette delvis skjer via mekanismer som inkluderer bentetthet, ettersom vi har vist at fysisk aktivitet er positivt assosiert med bentetthet. Videre er det indikasjoner på at aktivitetsvaner i voksen alder har en tendens til å holde seg stabile over flere tiår. Dette medfører at voksne som er inaktive, har en tendens til å være inaktive også senere i livet, noe som er bekymringsfullt med tanke på at fysisk aktivitet har en rekke positive helseeffekter.

List of papers

The following papers are part of this thesis:

Paper I:

Morseth B, Jørgensen L, Emaus N, Jacobsen BK, Wilsgaard T. Tracking of leisure time physical activity during 28 yr in adults: The Tromsø Study. *Med Sci Sports Exerc* 2011;43(7):1229-1234.

Paper II:

Morseth B, Emaus N, Wilsgaard T, Jacobsen BK, Jørgensen L. Leisure time physical activity in adulthood is positively associated with bone mineral density 22 years later. The Tromsø study. *Eur J Epidemiol* 2010;25(5):325-331.

Paper III:

Morseth B, Ahmed LA, Bjørnerem Å, Emaus N, Jacobsen BK, Joakimsen R, Størmer J, Wilsgaard T, Jørgensen L. Leisure time physical activity and risk of non-vertebral fracture in women and men aged 55 years and older: The Tromsø Study. [Submitted]

Abbreviations

BMD: bone mineral density

BMI: body mass index CI: confidence interval

DXA: dual-energy X-ray absorptiometry GEE: generalized estimating equations

HR: hazard ratio

IPAQ: international physical activity questionnaire

MET: metabolic equivalent

MRI: magnetic resonance imaging

NHANES: National Health and Nutrition Examination Survey

OR: odds ratio

pQCT: peripheral quantitative computed tomography

RCT: randomized controlled trial

RR: relative risk

SD: standard deviation

SPSS: Statistical Package for Social Sciences

SXA: single-energy X-ray absorptiometry

UNN: University Hospital of North Norway (Universitetssykehuset Nord-Norge)

VO_{2max}: maximal oxygen uptake WHO: World Health Organization

1 Background

1.1 Epidemiology of osteoporosis and fractures

1.1.1 The burden of osteoporosis and related fractures

Osteoporosis is defined as "a systemic skeletal disease characterized by low bone mass and microarchitectural deterioration of bone tissue, with a consequent increase in bone fragility and susceptibility to fracture" Osteoporosis constitutes a considerable public health concern, estimated to affect 75 million people in the United States, Europe and Japan together. Although osteoporosis traditionally has been considered a female disorder, approximately one in four individuals with osteoporosis is a man¹²⁰. Bone loss increases with advancing age^{60, 63, 71}, and the prevalence of osteoporosis measured at the femoral neck has been shown to increase from 20% at the age of 65 to more than 40% at the age of 80 years in women⁶³. An even higher increase has been measured at the forearm, resulting in a prevalence of osteoporosis of 66% in women and 31% in men after the age of 70⁷¹. Several estimates indicate a rapid increasing prevalence of osteoporosis⁵⁵, and the increasing elderly population²⁷⁸ will further augment the number of people with low bone mass or osteoporosis in the future.

Accordingly, osteoporotic fractures, the clinical outcome of osteoporosis, arise as one of the major health care problems, particularly among elderly people¹⁰⁸, and Norway has the highest reported fracture incidence in the world¹⁶⁶. Fractures lead to substantial disability, morbidity, and reduced quality of life, as well as increased mortality, in the elderly^{39,70,108,265,269}. According to a recent meta-analysis, excess mortality (over and above mortality rates in control populations) the first year after a hip fracture ranges from 8% to 36%¹. In a Swedish study²²⁸, 50% of the hip fracture patients never recovered to their prefracture health status regarding ability to walk and home care needs. The high burden of fracture generates tremendous medical costs for society, illustrated by various estimates, particularly associated with hip fractures^{35,39,211}. Recent estimates from 2011 indicate that the costs of fragility fractures in six European countries amount to 31 billion Euro²³⁹.

1.1.2 Fracture incidence and lifetime risk

In 2000, the total number of new fractures worldwide was estimated to 9.0 million, including 1.6 million hip fractures, 1.7 million forearm fractures, and 1.4 million clinical vertebral fractures 108 . However, fracture incidences vary up to tenfold between populations 120 . The incidence is higher in Scandinavia than in North America, while fracture rates are lower in Asia and Latin America 39,108,269 . In Oslo, Norway, the annual age-adjusted incidence of hip fracture in the age group >50 years has been estimated to 12

per 1000 inhabitants for women and 4.5 in men during the 1980's and 90's^{65, 166}. Recent estimates from Harstad, Northern Norway, are somewhat lower⁶². The reason for the high incidences of hip and forearm fractures in Norway is not clear, and research reports have failed to link the incidence differences to cold climate¹⁶⁶. Moreover, the incidence of fracture is generally higher in urban than in rural areas^{39, 65, 182, 203, 240}

The absolute risk for an osteoporotic fracture, in terms of lifetime risk at age 50 years, is estimated to 39-53% in women and 13-22% in men in UK, Sweden, Australia, and US¹⁰⁷. In the Tromsø population, the comparable lifetime risk was recently reported to be 55% in women and 25% in men². Thus, in Tromsø more than one of two women and one of four men aged 50 years are expected to experience a fracture during their remaining lifetime. The lifetime risk for wrist fracture is lower; in UK women 16%, however declining with age, whereas the lifetime risk in men is low (3%)²⁶². Recent research indicates that the increasing trend in hip fractures observed in the past decades may recently have leveled off, of reasons still not known^{39, 124}.

Box 1: Epidemiology of hip and wrist fractures

Hip fractures

- Hip fractures are more severe than other fractures and lead to mortality, more severe disability and consequently higher costs⁴³
- The majority of all hip fractures are the result of a simple fall from standing position⁴³
- The majority of hip fractures are osteoporotic²⁶⁸
- 30% of all hip fractures occur in men²⁰²

Wrist fractures

- Wrist fractures occur mainly in women³⁹
- Whereas the incidences of hip fracture increase with age⁸⁵, wrist fracture incidence in women increase from 45 to 60 years, then levels off^{39, 107}
- The lifetime risk of wrist fracture in women declines from age 50 to 70 years²⁶²
- The incidence in men continues to stay low with advancing age²⁶²

1.2 Bone strength

Whole-bone strength, which determines the ability for a bone to bear load and resist fracture, is affected by biological mechanisms, which produce changes in bone properties (remodeling), as well as physical aspects^{32,78}.

Physical bone strength depends on the structural and material properties of bone^{4, 29, 31, 33, 42, 78, 269}, including:

- Bone mass
- Bone mineral density (BMD)
- Bone size
- Geometry/shape/macroarchitecture of the bone (spatial distribution of the bone mass)
- Microarchitecture of the bone, including
 - trabecular thickness, orientation, and connectivity
 - cortical thickness/mineral content and porosity
 - microcracks/microdamage
- The quality of bone matrix
- The degree of mineralization.

1.2.1 Bone mineral density (BMD)

There are various imaging techniques available for measuring bone strength, such as peripheral quantitative computed tomography (pQCT), high resolution magnetic resonance imaging (MRI), and finite element analysis^{30, 32}. However, the gold standard for diagnosis of osteoporosis is considered to be dualenergy X-ray absorptiometry (DXA)⁴².

DXA measures areal BMD (g/cm²), i.e. the ratio between bone mineral content and the scanned area⁴². DXA is based on quantification of the amount of X-ray energy that is absorbed by the mineralized bone mass (i.e. hydroxyapatite, which is the most important inorganic component of bone). Single-energy X-ray absorptiometry (SXA) is based on the same principles, although the measures must be done under water, thus it is only available for the forearm and heel. DXA and SXA are the most feasible and available instruments to express bone strength in humans, consequently the diagnosis of osteoporosis is based on areal BMD²⁷⁷.

1.2.2 The role of BMD in osteoporosis

The definition of osteoporosis incorporates both low bone mass and microarchitectural deterioration of the bone tissue⁴¹. As microarchitectural deterioration and other indicators of bone strength are not easily measureable with present non-invasive methods^{4, 29, 269}, the diagnosis of osteoporosis is based on BMD measurements. In 1994, WHO provided a diagnostic definition of osteoporosis in women as bone mineral density (BMD, g/cm²) more than 2.5 standard deviations (SD) below the young female adult mean BMD²⁷⁷ (table 1). Later, these criteria have been specified by introducing the femoral neck as the preferred reference site and by recommending the Third National Health and Nutrition Examination Survey (NHANES III) data for white women in the age range 20-29 years as the young normal reference range^{116, 122}. Diagnostic criteria for men have not been well established, as men were not included in the 1994 WHO criteria, but it is now recommended that the reference range for BMD in young adult women also be used for the diagnosis of osteoporosis in men^{119,122}. This view is based on results showing that the risk of hip fracture at a given absolute BMD value is independent of sex¹²².

Recently, there has been focus on incorporating other risk factors in addition to BMD, by expressing the absolute fracture risk (the probability of fracture within a given time period)¹²¹.

Table 1: Diagnostic thresholds for osteoporosis²⁷⁷

Definition	BMD values in relation to the mean value of peak bone mass in young normal women*	
Normal	Not more than 1 SD below the mean	
Osteopenia	Within -1 SD and -2.5 SD the mean	
Osteoporosis	More than 2.5 SD below the mean	
Severe osteoporosis	More than 2.5 SD below the mean and the presence of fractures the mean	

^{*}When BMD is measured in relation to the young female adult mean, one SD unit is equal to a T score of 1. When BMD is expressed in relation to the age- and sex-matched mean, one SD is equal to a Z score of 1^{271} .

1.2.3 BMD as a predictor of fracture risk

The use of BMD in diagnosing osteoporosis is based on the strong association between BMD and fracture risk^{192, 269}. Many studies have shown that risk of fracture increases with decreasing BMD, summarized in previous meta-analyses^{109, 171}. Laboratory studies have demonstrated a high correlation between BMD and the force that is required to break a bone⁴², and it is indicated that BMD predicts 50-85% of the variation in bone strength^{4, 29, 192}. The relationship between bone strength and BMD is non-linear, which means that small changes in BMD can lead to large changes in bone strength and fracture risk²⁹. Thus, BMD is one of the major predictors of fracture risk^{118, 171}.

Existing studies report fairly similar gradients of risk for fracture (i.e. the relative risk for each SD decrease in BMD)¹⁰⁹. The risk gradient varies with the site of BMD measurement and the fracture site at risk¹²². When BMD is measured at the hip, hip fracture risk generally increases with a relative risk (RR) of 2.6 per SD decrease in BMD, whereas RR of other fractures increases 1.6 times per SD^{109,171}. Although fractures are best predicted by site-specific BMD measurements¹²², BMD measured at other sites such as the spine, distal radius, or calcaneus indicate a RR of any fracture of 1.5 per SD decrease in BMD⁴². A Z-score of -2.5 thus means that the fracture risk is almost 9-fold higher (2.6^{2.5}) than compared with a Z score of 0¹²².

1.3 Pathophysiology of osteoporosis and fractures

1.3.1 Remodeling

Bone is a dynamic and highly metabolic tissue that is renewed during adulthood by continuous bone remodeling, so that in one year, 1-10% of the skeleton is exchanged. Remodeling involves bone resorption and formation, a continuous process by which bone cells remove and replace bone tissue in cycles of 3-5 months⁸⁸. The bone cells responsible are osteoblasts and osteoclasts, which together form the "basic multicellular unit"²¹⁷. Osteoclasts remove bone on the surface and create a cavity, and after a delay, osteoblasts produce new bone that fills the cavities²⁹. The net result of bone formation and resorption determines the mass, size, shape, and architecture of the bone²²⁶.

Cortical bone is the outer, dense part of bones, amounting to 80% of the bone mass, whereas trabecular bone is cancellous and fills the interior of the bone where it forms a net of trabeculae⁸⁸. The open net of trabeculae allows interaction with blood vessels, bone marrow, and connective tissue. Consequently the metabolic activity in trabecular bone is many times faster than in cortical bone. Remodeling can occur at different surfaces; the periosteum (the outer surface, covering cortical bone) and the endosteum (inner surface) which comprises the endocortical, trabecular, and intracortical (Haversian) surfaces^{217, 226}.

1.3.2 Pathophysiology of bone loss

Bone mass accumulates during childhood and adolescence, and peak bone mass is reached in the twenties at most sites⁹⁰. After bone mass has reached a peak in young adulthood, a gradual bone loss begins, possibly in the third or fourth decade^{61,274}. In women, bone loss accelerates during menopause, probably because of reduced estrogen levels (which lead to increased resorption and turnover), whereas men lose bone gradually^{226,227}. From the age of 20 to 70 years, both women and men may lose a considerable amount of bone mass. At the hip, as much as 25-40% in women and 20-35% in men of the peak bone mass may be lost^{41,178,274}. In elderly women and men, hip BMD may annually decrease 1.0-1.5% in women and 0.5-1.0% in men^{24,60,110,135}. At the forearm, it has been shown that BMD is stable up

to the age of 50 years in women, followed by a strong decline thereafter⁷¹. In men, BMD starts to decline at the age of 40, and after age 65, the decline in forearm BMD is similar in women and men.

Osteoporosis may be a consequence of low bone mass gain during growth (resulting in low peak bone mass), insufficient maintenance of bone mass in adulthood, or excessive bone loss during late adulthood. The relative importance of bone mass increase during growth and peak bone mass in osteoporosis prevention at old ages is not yet thoroughly known. Some studies have indicated that bone mass gain in early years may not persist⁷⁹, emphasizing the role of preservation of bone mass during adulthood and elderly years.

As mentioned, an imbalance in the remodeling process during adulthood may lead to osteoporosis²¹⁷. During adulthood, bone formation and resorption should ideally be in balance, preserving net bone mass. With advancing age and in situations with abnormal remodeling, bone resorption exceeds bone formation, creating a surplus of resorption cavities and net bone loss²⁹. The net bone loss is a result of the trabeculae becoming thinner and detached, and cortical bone becoming thinner and porous, even though the periosteal bone formation increases with aging²²⁶.

1.3.3 Biomechanics of bone loading

Bones are built to be both strong and lightweight, which is accomplished by specific material and structural properties. Bone consists of organic material (mainly collagen) and inorganic matrix (mainly hydroxyapatite which is a mineral composed of calcium and phosphate)⁸⁸. Due to the flexible collagen, bone can allow elastic deformation of the bone (strain) during loading by storing energy²²⁶. A load that is applied to bone is called stress, defined as force divided by area²⁵¹. The applied load causes a mechanical deformation of bone tissue, and this deformation can be measured as strain^{113, 235}. Strain is the ratio of the amount of shortening divided by the original length, typically expressed as microstrain, 10⁻⁶ (i.e. a bone of length 500 mm experiencing 0.5 mm deformation gives a strain of 0.001 or 0.1%, equal to 1000 microstrain)²³⁵. Strains may be compressive, tensile (when the bone stretched), or torsional (shear) (when the bone is twisted), and in most situations, they affect bone in a combined way^{235, 251}, i.e. a deformation can create 2500 microstrain in compression on the concave side of a bending diaphysis, while creating 2000 microstrain in tension on the other side¹¹³.

At whole bone level, the relationship between load and deformation is represented by the stress-strain curve. The slope of the stress-strain curve is called Young's modulus (strain = stress/Young's modulus)¹⁴³. The yield point is the point on the slope where the deformation is beyond its elasticity. Deformation beyond the yield point will therefore lead to permanent deformation and eventually fracture.

1.3.4 Pathophysiology of fractures

When the energy from the applied load exceeds the capacity of the bone to absorb that energy, a fracture occurs. Thus, both extrinsic and intrinsic factors affect the occurrence of a fracture²³¹. For hip fractures, extrinsic factors that affect the applied load are primarily falls, as in the elderly, more than 90% of all hip fractures are caused by a fall, and magnitude and direction of applied load may be crucial. Intrinsic factors that affect bone strength are described in chapter 1.2.

1.4 Risk factors for osteoporosis and fracture

In elderly people, low BMD (osteoporosis) and falling are the two main risk factors of fracture¹²⁵. Genetic factors explain 50%-80% of the variation in BMD²¹⁵. However, fracture risk is also affected by many other factors, as shown in table 2.

Table 2: Risk factors for osteoporotic fractures

Clinical characteristics and medical history	Bone strength related	
Genetic factors ²⁶⁹	Low BMD ^{117, 269}	
Advancing age ^{39, 83, 117, 269}	Bone architecture and geometry ²⁶⁹	
Female gender ¹¹⁷	High bone turnover ^{117, 269}	
Asian or Caucasian ^{55, 83, 117}	Microdamage accumulation in bone ²⁶⁹	
Low weight/body mass index (BMI <18.5 kg/m²) ^{83,120}	Degree of mineralization of bone ²⁶⁹	
Weight loss (>10%) ^{202, 269}		
Height ²⁶⁹	Fall related	
Family history of hip fracture ^{39, 83, 117, 120}	Muscular weakness ²⁶⁹	
Prior fragility fracture ^{39, 83, 117, 269}	Impaired functional mobility ²⁶⁹	
Low dietary calcium intake/absorption55,83,117	Neuromuscular disorders ^{117, 269}	
Vitamin D deficiency ^{55, 83, 117}	Visual impairment ^{117, 269}	
Medications ^{83, 269}	Cognitive impairment ²⁶⁹	
Estrogen exposure ²⁶⁹	Impaired proprioception ²⁶⁹	
Premature menopause ^{39, 83, 117}	Increased postural sway ²⁶⁹	
Amenorrhea ¹¹⁷	Season ²⁶⁹	
Hyperparathyroidism ^{55,83}		
Low serum testosterone levels ^{55, 202}	Lifestyle related	
Poor health/comorbidity ⁸³	Cigarette smoking ^{83,117,120}	
	Physical inactivity ^{55, 83, 117, 269}	
	Excessive alcohol consumption ^{83, 117}	

1.5 Prevention of osteoporosis and fractures: Physical activity

The high fracture incidences and the serious outcomes of fractures call for knowledge about effective preventive strategies that are feasible for most people¹³⁴. The main non-pharmacological interventions for fracture reduction include prevention of osteoporosis and prevention of falling¹²⁵, accentuating physical activity as an important key factor. Physical activity may increase peak bone mass and postpone the age-related bone loss through mechanical mechanisms, and also increase muscle strength, neuromuscular functions and balance, and thus reduce the risk of falling^{17, 134}.

1.5.1 Physical activity

The Norwegian recommendations for physical activity aimed at health promotion state that adults *should* be physically active at least 30 minutes, preferably every day. The intensity should be at least moderate, as in fast walk. By increasing the duration or intensity, additional health benefits can be gained¹⁴. These recommendations are based on research of associations between physical activity and morbidity and mortality¹⁴. Physical inactivity is a known risk factor for many diseases, such as cardiovascular diseases¹⁴⁷. type 2 diabetes mellitus³, obesity⁵¹, and some types of cancer²⁴⁶. Physical inactivity also affects bone mass. This became apparent in the 1960's when space flight studies found loss of BMD in astronauts²⁶³. Because astronauts in space are subject to weightlessness due to microgravity, the loads on bone from gravitation and muscle contractions are minimal. Bone loss during microgravity has been confirmed in many studies, showing severe loss of both trabecular and cortical bone mass in astronauts attending long-duration space flights^{142,154,155}. These findings agree with studies of long-term bed rest^{159,160,282}. Since then, a vast number of studies have examined the association between physical activity and bone health. Yet, there are many contradictory findings and unsolved issues²², partially because of the challenges associated with assessment of physical activity and the diversity of physical activity behavior.

1.5.2 Mechanical loading

According to the prevailing theory, the effects of physical activity on BMD are linked to the mechanisms of mechanical loading^{230, 281}. In 1892, Wolff⁷⁷ stated that bone tissue accommodates to stress that is imposed on it, and later research on the topic has been founded on this contention. Several theories have been proposed to explain the loading mechanism, and one of the most recognized is the "Mechanostat theory" by Harold Frost^{75, 76}.

The mechanostat theory. Frost proposed that local deformation from mechanical loading stimulates bone cells, resulting in bone adaptation^{75, 76}. The mechanostat theory indicates that there is a lower and an upper strain threshold, creating a range where strain stimuli maintains homeostasis of the remodeling process and bone mass, called the physiological loading zone. Below the lower threshold (<200 microstrain), called the "minimum effective strain for remodeling", the stimuli is insufficient to maintain

formation, and resorption will be the overriding process, resulting in bone loss. Above the upper threshold (2000 microstrain, the "minimum effective strain for modeling"), formation is dominant, resulting in bone gain. These thresholds may be relative to the individual's habitual loads²³⁵. Systemic and local biochemical factors, age, sex, and genes probably influence the bone cells' sensitivity to mechanical stimuli²³⁴. Hormones influencing remodeling are mainly vitamin D, parathyroid hormone, estrogen, and calcitonin⁸⁸.

The mechanostat theory relies mainly on the *magnitude* of the strain as the important driving force for bone remodeling¹¹³. However, an increase in *frequency*, not only magnitude, may represent overload and bone formation^{113, 235}. Moreover, several animal studies have demonstrated that *dynamic*, but not static strains (whereby strain rate = 0), induce bone formation^{157, 222, 253}, implying that the activity should be dynamic, not static. *Uneven distribution* of the strain seems to have a higher potential for increasing osteogenesis than the habitual loading pattern^{67, 114}, indicating that the intensity of the activity should be increased or changed beyond the habitual level. Moreover, after *a few loading cycles*, the adaptive response decreases ^{222, 256}, indicating that duration is of less importance. Finally, inserting a *rest period* after each loading cycle can increase the osteogenic response ²¹⁸.

Box 2: Osteogenic activities

Mechanical characteristics of osteogenic activities

- + High-impact
- + Dynamic
- + Varying and increasing loads
- A few loading cycles seem sufficient

Mechanotransduction. The cellular mechanism responsible for conversion of a mechanical force into a cellular response is called mechanotransduction²²⁵. In recent years, animal studies have been focusing on osteocytes as mechanosensors, because of their suitable location^{27, 235, 279}. Osteocytes constitute the majority of bone cells and are scattered throughout the bone matrix where they are found in lacunae, connected to each other and to lining cells at the trabecular surface by a network of canaliculi^{36, 156}. Osteocytes are assumed to detect load applied by external forces (mechanical strain) and to transduce signals to the cells on the surface, where remodeling (resorption and formation) occurs²⁵⁴. Several mechanisms have been proposed for the activation of osteocytes²⁴³, and recently, fluid flow-induced shear stress has been acknowledged as the most essential mechanism^{212, 252}. The molecular mechanisms within osteocytes that transduce the mechanical signal into a biochemical signal are not fully understood, but may include ion channels, integrins, and the cytoskeleton^{38, 254}. The communication

between the sensor cells (osteocytes) and the effector cells (osteoblasts and osteoclasts) involve direct cell-to-cell contact and autocrine and paracrine signals³⁸. Within 48 hours, osteoblasts respond with bone formation and new osteoblasts and osteoclasts are recruited to the bone surface^{38, 235, 254}.

1.5.3 Fall prevention

Falling is very common among the elderly and the tendency to fall increases with age. A fall seems to be the strongest single risk factor for a fracture, as 90% of all hip fractures occur from a fall; moreover, the nature of the fall is a critical determinant for fracture^{37, 125}. Thus, in order to prevent fractures, it is important to prevent falls. The risk of falling is affected by age-related changes in muscle strength, which declines up to 50% from the age of 30 to 80 years⁴⁵, and impaired balance and gait pattern⁴⁵. Physical activity may improve physiological skills and thereby reduce the risk of falling¹³³. Muscle strength has been shown to increase up to 200% even in old people, and the skeletal muscles seem very adaptive to training even at old ages⁴⁵. Balance may also be improved by balance and strength training, although not consistently.

1.6 Rationale for the thesis

Because a fracture often has serious consequences, it would be favorable to call attention to preventive efforts. Physical activity is a feasible non-pharmacological approach that may delay bone loss and prevent falls. Nevertheless, a limited number of studies has examined physical activity and fracture incidence¹⁸⁵, and recent studies substantiate inconsistent findings^{9,195}.

Because BMD is a central component of osteoporosis, bone strength, and fracture risk, the association with physical activity is of great interest. Although a large number of short-term studies demonstrate a positive association between physical activity and BMD^{17,84}, fragility fractures are far more common in the elderly, whereas the bone mass benefits of physical activity seem more pronounced and consistent at younger age¹²⁶. Therefore, the long-term associations between physical activity and BMD at older ages are of interest.

Epidemiological studies typically assess physical activity with a single or few questions and the ability to assess changes in physical activity habits is often limited. Physical activity levels will most likely change during the follow-up period, while at the same time, most epidemiological studies are restricted to one measurement of physical activity, usually at baseline. Changes may affect the outcome of epidemiological studies; therefore, it is essential to gain knowledge about physical activity habits throughout the adult life.

2 Aims

The general objective of these cohort studies was to examine the associations between physical activity in adulthood and BMD and non-vertebral fractures at older age. When studying long-term associations, an important factor to consider is changes in physical activity level over time. Therefore, an additional aim was to describe the degree of stability (tracking) of physical activity in the population over the last three decades.

The specific aims were to examine:

- 1. Tracking of physical activity in adult women and men over three decades.
- 2. Associations between leisure time physical activity and BMD later in life in adult women and men.
- 3. Associations between leisure time physical activity levels in adulthood and risk of non-vertebral fracture in women and men.

3 Knowledge status

This chapter presents the knowledge status prior to each of the three studies, which were submitted in February 2010 (Paper II), July 2010 (Paper I), and March 2011 (Paper III).

3.1 Tracking of physical activity

Nordic Health Authorities recommend at least 30 minutes physical activity with moderate intensity most days of the week, and similar recommendations are given in other countries⁸⁹. Yet, in most countries, less than 50% of the population meet the national recommendations^{100, 232}. Development of targeted strategies that encourage physical activity necessitates knowledge of stability, or tracking, of physical activity over time, but the degree of stability of long-term physical activity habits is not very well known. Furthermore, in most epidemiological health studies, assessment of physical activity has to be confined, due to competing resources.

Stability, or tracking, of a characteristic is commonly defined as 1) maintenance of relative rank or position over time or 2) predictability of later values from earlier measurements^{13, 255, 275}. To estimate tracking or stability, correlation between repeated measures is the most frequent effect measure²⁷³. Only a few research groups have examined tracking of physical activity through adulthood. Studies from the United States^{5, 162, 223}, Belgium^{48, 163}, Canada⁷² and Finland^{144, 242} report low to moderate tracking of physical activity, with correlation coefficients approximate to 0.30 in most studies. Few studies have examined prediction of physical activity from earlier measurements^{144, 177, 242, 249}, and the majority of these investigated the time span from adolescence to adulthood^{177, 242, 249}. Kirjonen et al.¹⁴⁴ found that level of physical activity in adulthood was a strong predictor of physical activity level 5-28 years later.

3.2 Long-term associations between physical activity and BMD

Physical activity may prevent or delay osteoporosis by increasing peak bone mass during growth and early adulthood and reduce bone loss later in life, as shown i Figure 1.

Timing of exercise to reduce osteoporosis and related fractures:

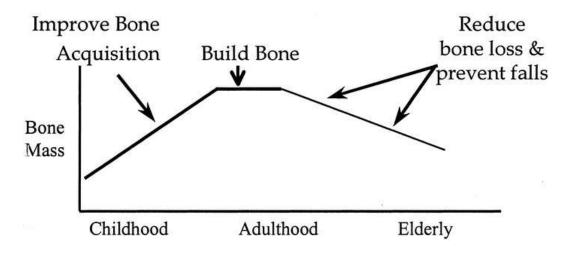


Figure 1. Exercise effects to reduce osteoporosis and fractures during life. Reprinted with permission ©Wolters Kluwer/Lippincott, Williams & Wilkins. Beck BR, Snow CM. Bone health across the lifespan--exercising our options. Exerc. Sport Sci. Rev. 2003;31(3):117-122.²²

3.2.1 General effects of physical activity on BMD

Unilateral and cross-sectional studies. Data from numerous cross-sectional studies have demonstrated a positive association between physical activity and BMD^{17, 22, 146}. Cross-sectional studies have typically compared athletes in various sports with sedentary controls. They report that athletes in a large range of high-impact sports have higher BMD than sedentary controls^{23, 53, 67, 92, 129, 189, 197, 280}. Endurance activities seem to be beneficial to a certain degree, whereas low-impact activities such as swimming and cycling are associated with similar or lower BMD than controls. For example Nikander et al.¹⁹⁷ compared femoral neck BMD in premenopausal female athletes who competed in sports with different types of load. Athletes competing in high-impact sports (volleyball, hurdling, squash-playing, soccer, speed skating, step-aerobics) had the highest femoral neck BMD, followed by weight-lifters, thereafter orienteering and skiing athletes, while swimmers and cyclists had BMD similar to the non-athletes¹⁹⁷.

However, cross-sectional studies mainly include young, athletic participants, and genetics cannot be ruled out as an explanation. Studies of the effect of unilateral loading on bone mass allow for control of the role of genetics, and these studies consistently show that in tennis players, the dominant arm has thicker cortices and up to 22% higher BMD than the non-dominant arm^{18, 96, 98, 99, 111, 123}.

Children/adolescence. The most consistent evidence of the effects of physical activity and exercise on BMD is found in intervention studies of pre- and peripubertal children. Both high-impact physical activity^{73, 169, 179, 187, 201, 260} and regular physical activity^{86, 164, 165} during growth has been shown to increase BMD in active boys and girls compared with more sedentary children. A review of randomized controlled trials (RCTs) showed that BMD after 6 months increased 1-5% prepubertal and early pubertal children, and 0-2% in pubertal adolescents, compared with controls⁹⁴.

Premenopausal women. In adults, the effects of physical activity on BMD are smaller and less consistent. Findings from intervention studies indicate that exercising premenopausal women continue to increase bone mass compared to non-exercising controls^{19, 20, 52, 74, 91, 167, 236, 259, 266, 276}. A review of intervention studies including premenopausal women concluded that impact activity may increase site-specific BMD by 1-3% compared with controls²⁴⁷.

Postmenopausal women. In postmenopausal women, many intervention studies have been undertaken, in addition to several meta-analyses and systematic reviews. Two reviews indicate that aerobic and impact physical activity may slow down the rate of bone loss at the femoral neck by approximately 1 % per year^{266, 276}. Other reviews confirm that aerobic exercise may slow down the loss of bone mass^{136, 137}. Moreover, there is evidence of an effect of walking on the femoral neck BMD in postmenopausal women^{26, 174, 229}. A recent review showed that both low-impact activity (including jogging) and high-impact combined with resistance training may reduce bone loss at the hip¹⁷⁵. In contrast, one review failed to show any effects of various exercise on femoral neck BMD¹³⁸.

Elderly men. The results seen in women are also present in men^{139,191}, although fewer studies have been conducted.

Type of activity. During physical activity, mechanical forces that act on bone are generated from two sources; loads from impact with the ground due to gravity (ground-reaction forces or impact forces) and loads from skeletal muscle contractions (muscle forces or no-impact forces)^{112,145,250}. *Impact activities* are weight-bearing (e.g. jumping)¹⁴⁵. However, most impact activities also involve muscle forces, and the individual effect of the ground-reaction forces can be difficult to separate^{112,145}. Impact activities primarily involve the lower skeleton. In contrast, *no-impact activities* influence bone mostly through muscle loading. No-impact activities can be weight-bearing (e.g. weight lifting) or weight-supported (e.g. swimming, cycling)^{112,145}. A few studies, mainly of post-menopausal women, have examined the effects of the type of activity in relation to BMD and very few studies in relation to fracture. Recent meta-analyses by Martyn-St James and Carroll^{172,173,174,175,176} studied the effect of different exercise types on BMD in pre- and postmenopausal women. Resistance training alone increased lumbar spine BMD, but not femoral neck BMD^{172,173,176}, whereas combining impact activities with resistance training significantly increased BMD at both sites^{175,176}. In postmenopausal women, low-impact exercise (jogging combined with stair climbing and walking) also increased BMD at the lumbar spine and femoral neck¹⁷⁵, but not

walking alone¹⁷⁴. These meta-analyses suggest that impact forces of a certain magnitude and rate, but not resistance training, were sufficient to increase femoral neck BMD, and that resistance training has strongest effect on lumbar spine BMD. However, in other studies, no-impact resistance training have been found to increase or preserve femoral neck BMD in postmenopausal women¹⁹³ and elderly men¹⁸¹, emphasizing the inconsistency of the findings.

3.2.2 Long-term effects of physical activity

Although data from numerous cross-sectional and short-term prospective studies have shown a positive effect of physical activity on BMD at all ages, benefits of physical activity on BMD seem to be more pronounced and consistent during growth than in adulthood^{17, 22, 146}, whereas risk of fracture is substantially higher in old age²⁷¹. Therefore, any long-term influence of lifetime physical activity on BMD at ages when osteoporotic fractures are more frequent would be of interest.

Sustained benefits of physical activity on BMD from childhood into young adulthood could result in a higher peak bone mass. Some studies have demonstrated that physical activity in childhood and adolescence predicts BMD levels in young adulthood, but the results are somewhat inconsistent^{16, 50, 69, 141, 180, 199, 261}. Whether these BMD benefits are sustained to older ages is unknown. A high peak BMD may be beneficial later in life, but the effect of a high BMD in young adulthood is not yet clarified, and some evidence suggest that peak bone mass does not determine bone mass later in life⁷⁹. The homeostatic system controlling bone mass is influenced by genetics, mechanical loading, and other lifestyle factors⁷⁹, and physical activity and mechanical loading during adulthood may be important factors determining bone mass later in life. Although the magnitude of the BMD benefits of physical activity in adults seems to be small, if bone loss could be reduced over a long time, this may be favorable for fracture risk at older ages.

Intervention studies and observational studies of physical activity effects are typically small and short-term, and only a few prospective, population-based studies can give insight to this issue^{12, 46}. Thus, most studies that could give insight to long-term effects of physical activity are cross-sectional and case-control (retrospective), asking about past physical activity or comparing former athletes with controls^{54, 64, 81, 101, 127, 130, 131, 148, 150, 198, 213, 258}. Former athletes seem to maintain higher BMD for 10-20 years after cessation compared to controls^{54, 64, 127, 130, 131, 209, 258}, and even up to 40 years after retirement¹⁶⁸, although most studies indicate that the benefits are lost after 30-40 years^{127, 128, 129, 130}. Retrospective studies of lifetime physical activity have shown significant associations^{101, 198} or no association between adulthood physical activity and BMD at older ages^{34, 81, 150, 213}.

3.3 Physical activity and risk of fracture

Physical activity may postpone the age-related decline in BMD and increase muscle strength and balance^{17, 132}, and thereby reduce the risk of fracture, but existing knowledge is limited by inconsistent results, few studies of fractures other than hip, and an almost complete lack of RCTs.

The observational studies have mainly examined hip fractures, mostly reporting that physical activity is associated with a lower risk of hip fracture^{11, 44, 66, 68, 82, 151, 183, 184, 206, 216, 248}, although in men, some studies report a non-significant lower fracture risk^{97, 170, 190, 272}. Most case-control studies support an association between past physical activity and hip fracture incidence. Fewer studies include forearm fractures, and some studies report a higher risk of forearm fracture with higher physical activity^{102, 140, 214}, although other studies have found lower²⁴⁴ or no significant fracture risk^{82, 95, 194} with higher physical activity levels. A recent study of any osteoporotic fracture showed that leisure time physical activity was non-significantly inversely associated with overall fracture risk¹⁸⁶. In contrast, results from two studies including all fracture types indicate that physical activity⁹ and walking¹⁹⁵ can increase the fracture risk.

There are very few RCTs of exercise and non-vertebral fracture incidence²⁶⁴. One RCT lasting 30 months, examining the effects of jumping and balance exercises in elderly women, reported a reduced risk of fracture (any) in the exercise group compared with controls, but as the authors recognize, the sample size was too small to draw conclusions about fractures¹⁴⁹.

In a recent review, Moayyeri¹⁸⁵ suggests that physical activity may have different effects on different sites of fracture. However, very few studies of physical activity and fracture have focused on effects at various fractures sites. In 1998, Joakimsen et al.¹⁰⁵ examined physical activity in the second and third Tromsø Study in relation to non-vertebral fracture risk at various skeletal sites. In physically active women and men >45 years, the risk of fracture in the weight-bearing skeleton was lower (women non-significantly) than in sedentary subjects. In contrast, there was no reduction in risk of fracture in the non-weight-bearing skeleton among physically active compared with sedentary subjects.

4 Study population and methods

4.1 The Tromsø Study cohort

The Tromsø Study is a population-based health study, conducted in the municipality of Tromsø¹⁰³. Presently, the study design encompasses six periodic health surveys, starting in 1974, followed by repeated surveys in 1979–80, 1986–87, 1994–95, 2001-02, and 2007–08. Total birth cohorts and additional random samples of inhabitants of the municipality of Tromsø, Norway, were invited to the surveys by written invitations sent by mail. The participation rate ranged from 65% to 77% (Table 3, chapter 6.2). All three papers are based on data from the Tromsø Study as shown in Figure 2. The Tromsø 1 population was not included in any of the three studies in this thesis because only men were invited.

Ethics

The Tromsø Study was approved by the Norwegian Data Inspectorate and recommended by the Regional Committee of Research Ethics. In Tromsø 4, 5, and 6, each participant signed a written informed consent.

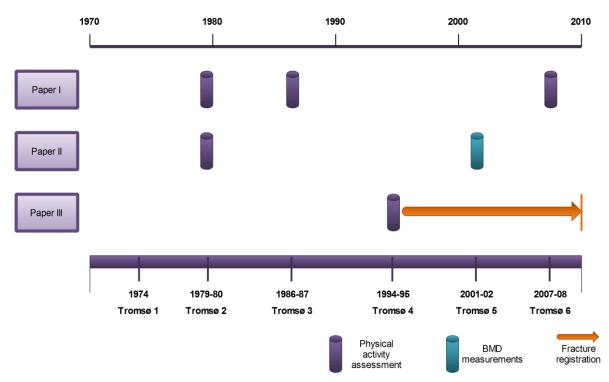


Figure 2. Design of the studies in the thesis.

Paper I study population

Paper I is a longitudinal tracking study of a cohort of men and women who participated in three of the six surveys in the Tromsø Study during the last three decades. We included subjects from the second survey in 1979–80 who had repeated measures in the third survey in 1986–87 and the sixth survey in 2007–08, as these surveys included the same question about leisure time physical activity. All men in the municipality aged 20–54 and all women aged 20–49, totally 21 439 persons, were invited to the Tromsø Study in 1979–80, and the participation rate was 77.5%. Of the 16 620 participants, 5432 persons also participated in the Tromsø 3 and Tromsø 6 surveys with valid information on physical activity.

Paper II study population

In paper II, we included participants from the second Tromsø Study in 1979–80 who also attended BMD measurements in the fifth Tromsø Study in 2001–02. The baseline source population comprised total birth cohorts of men aged 20–54 years (born between 1925 and 1959) and women aged 20–49 years (born between 1930 and 1959) who were living in the municipality of Tromsø, totally 21 439 persons. Of those invited, 16,546 persons (77%) attended and answered the question on leisure time physical activity in Tromsø 2. Of the baseline cohort in Tromsø 2, 4443 persons were invited to participate in the DXA measurements in follow-up survey in Tromsø 5 in 2001–02. Altogether 3217 subjects (72%, 1766 women and 1451 men) attended the DXA measurements at follow-up.

Paper III study population

In paper III, the subjects were participants in the fourth Tromsø Study in 1994–95, to which all inhabitants in Tromsø, aged 25 years or older (born before 1970), were invited (n=37 558). A total of 27 158 persons (12 865 men and 14 293 women) aged 25-97 years attended, which corresponds to a participation rate of 75% in women and 70% in men. In our study, subjects aged 55 years and older (n=7582) were included. We excluded subjects with pathological fractures (n=12) and subjects with missing data on smoking (n=20), height (n=27), and body mass index (n=1), leaving 7522 subjects (3450 men and 4072 women) in the study cohort.

4.2 Assessment of physical activity

The participants in the Tromsø Study responded to a self-administered questionnaire concerning several life style and health related topics, including physical activity in leisure time and at work. Table 4 shows the questions about physical activity and exercise that are used in the thesis.

Table 4: Questions regarding physical activity in the Tromsø Study

Tromsø Study	Question	Answer options
Tromsø 1, 1974 Tromsø 2, 1979-80 Tromsø 3, 1986-87 Tromsø 5, 2001-02 <70 years Tromsø 6, 2007-08	State your bodily movement and physical exertion in leisure time. If your activity varies much, for example between summer and winter, then give an average. The question refers only to the last twelve months.	 Reading, watching TV or other sedentary activity Walking, cycling or other forms of exercise at least 4 hours a week (including walking or cycling to place of work, Sunday walking, etc.) Participation in recreational sports, heavy gardening, etc. Note: Duration of activity at least 4 hours a week Participation in hard training or sports competitions regularly several times a week
Tromsø 4, 1994-95 Tromsø 5, 2001-02	How has your leisure time physical activity been the last year? Think of a weekly average for the year. The way to work is counted as leisure time.	Light activity (not sweating or out of breath): None <1 hour 1-2 hours 3 or more hours pr. week
		Hard activity (sweating/out of breath): None 1-2 hour 3 or more hours pr. week

4.3 Measurement of covariates

Adjustments for possible confounders were primarily done by baseline covariates. In paper I, possible confounders at follow-up in Tromsø 5 was also included. The Tromsø Study included self-administered questionnaire including numerous questions about lifestyle, and a physical examination, blood and urine samples¹⁰³. The covariates are described in the papers.

4.4 Measurement of BMD

In Tromsø 5, BMD was measured at the distal and ultradistal forearm in 5771 subjects, in the non-dominant arm when eligible. Two different single X-ray absorptiometric (SXA) devices (DTX-100, Osteometer MediTech, Inc., Hawthorne, CA, USA) were used to measure BMD. In addition, BMD was measured at the hip in 4938 subjects. Dual-energy X-ray absorptiometry (DXA) (GE Lunar Prodigy, LUNAR Corporation, Madison, WI, USA) was used to measure BMD of the total hip, femoral neck, and trochanter area in the left hip when eligible. Technically incorrect scans, scans with metal in the region of interest and scans of hips with severe deformities were excluded. Specially trained technicians performed all scans according to the protocol provided by the manufacturer and reviewed and reanalyzed the scans if necessary. All densitometers underwent daily phantom measurements to secure stability⁵⁹.

4.5 Fracture registration

The radiographic archives of the University Hospital of North Norway in Tromsø comprise all non-vertebral fractures occurring in the municipality and thus in the study population, as there is no other radiography service in the city or within 250 kilometers. The only exception would be fractures occurring while travelling with no control radiograph after returning home or fractures never radiographically examined. Registered fractures are linked to the subjects in the Tromsø Study by use of the national personal identification number and time of investigation.

All radiographic examinations of participants in the fourth survey of the Tromsø Study were inspected to verify the fracture code. In subjects with fractures, the exact anatomical location of the fracture was identified and the trauma mechanism was categorized into high-energetic (fall from a height or traffic accident), low energetic (fall from same level, non-traffic accident), or pathologic (tumor or metastasis), and consecutive fracture events were distinguished from one another. The fracture registration at the University Hospital of North Norway (UNN) has been validated by Joakimsen et al.¹⁰⁵, as discussed in chapter 6.3.3.

4.6 Statistical analyses

All analyses were performed using SPSS (Statistical Package for Social Sciences, Chicago, IL, USA), version 16 and 18. Two-sided *P* values <0.05 were considered statistically significant. Most analyses were performed using sex stratification, although a few associations were analyzed in women and men combined to gain sufficient statistical power to be able to demonstrate a real association. Multiple analysis models included relevant and available confounders. Testing for interactions was

not done extensively, but confined to a few interaction terms, primarily the cross product of physical activity and sex or age, to examine possible effect modifications by sex or age. Subjects with missing values for exposure, outcome, or confounders were excluded from the analyses.

Descriptive characteristics of the study population were presented as mean (SD) or frequency (%), and differences between physical activity groups were tested (paper II and III). In all three papers, leisure time physical activity was the exposure, and in paper II also changes in physical activity from baseline to follow-up in a set of sub-analyses. The participants were divided into groups based on the answer options from the questionnaires. Outcomes were BMD, fracture risk, and osteoporosis. In the tracking study, physical activity level at follow-up was the outcome. BMD was assessed at the hip (total hip, femoral neck, trochanter) and forearm (distal and ultradistal). Fractures were divided into the first non-vertebral fracture, weight-bearing fractures, non-weight-bearing fractures, and hip and forearm fractures.

Follow-up time in paper III was assigned from the date of the screening to the date of the first fracture, migration from Tromsø, death, or end of follow-up (December 31, 2009), whichever came first. The date of the first fracture was used for the analyses of non-vertebral fractures and weight-bearing/non-weight-bearing fracture (disregarding subsequent fractures). In the analyses of relationships with hip and forearm fractures, the date of the first hip fracture, respectively forearm fracture, was used.

The associations between physical activity and BMD, osteoporosis, and fracture risk were analyzed using linear and Cox proportional hazards regression models (paper II and III). In paper I, we analyzed tracking of physical activity using three different measures. We first calculated the proportion of subjects who maintained their physical activity level from examination I to examination II and III, compared with the expected proportions. In order to compare the observed proportions of agreement with the proportions expected by chance, we used Cohen's weighted kappa. Because weighted kappa analysis is not available in SPSS, we used a syntax available on http://support.spss.com²³⁷, using data generated from crosstabulation of physical activity levels. Furthermore, the degree of tracking of physical activity was assessed by Spearman's correlation coefficients for physical activity between pairwise examinations. Finally, we used generalized estimating equations (GEE) models to measure tracking in terms of predictability of later values from earlier measurements, using physical activity in examination I as independent variable and physical activity in examination II and III as dependent variable. Tracking was estimated by the odds ratio (OR) of being at a specific physical activity level at later examinations, given belonging to the same level at examination I, relative to any other baseline physical activity level. Furthermore, we estimated the OR of being non-sedentary at later examinations according to physical activity level at examination I, with the dependent variable dichotomized into sedentary/non-sedentary.

5 Results – summary of papers

Paper I

The aim of this study was to examine tracking of leisure time physical activity in adults in Northern Norway over three decades. We followed 5432 women and men who attended the Tromsø Study in 1979-80 and repeated surveys after 7 and 28 years.

We found that a higher than expected proportion of subjects maintained their physical activity level from examination I to II (58%) and III (53%). Kappa statistics showed moderate agreement of 0.41 and 0.29, respectively. Furthermore, we found that being physically active in young adulthood increased the odds of being physically active later in life (moderately active OR 3.4, 95% Confidence Interval (CI): 3.0-3.9), active OR 5.4 (95% CI: 4.6-6.4), and highly active OR 13.0 (95% CI: 7.4-22.8) compared with being sedentary. Those who were sedentary as adults had higher odds of being sedentary later in life than those who were active (OR 3.9, 95% CI: 3.5-4.4).

In conclusion, this study demonstrated tracking of leisure time physical activity during 28 years in a cohort of adults, substantiated by physical activity levels in early adulthood being a strong predictor of an active lifestyle later in life and by moderate agreement between repeated measurements.

Paper II

In this population-based study, the aim was to examine the association between leisure time physical activity in adulthood and areal BMD 22 years later in 3217 women and men aged 20-54 years at baseline.

We observed a positive linear trend in BMD across physical activity levels in both women and men, after adjustments for baseline age, height, weight, and smoking status (P < 0.05). The relationship between BMD and leisure time physical activity was consistent over different sites of the hip (total hip, femoral neck and trochanter area) and forearm (distal and ultradistal area). In a subsample of 2436 men and women under 70 years, those who were sedentary at both baseline and follow-up had lower BMD than those who were physically active at either baseline and follow-up, or both ($P \le 0.01$).

This study suggests that leisure time physical activity in adulthood is associated with higher BMD and reduced risk of osteoporosis later in life.

Paper III

The aim of this longitudinal cohort study was to examine the association between leisure time physical activity and the risk of non-vertebral fractures in 7522 women and men aged 55 years and older during a follow-up period of median 11 years.

A total of 1693 non-vertebral fractures were identified. Adjusted risk of any non-vertebral fracture decreased with increasing physical activity level in men (P_{trend} =0.005) and non-significantly in women (P_{trend} =0.2). The reduced fracture risk was mainly due to a reduced risk in the weight-bearing skeleton, whereas risk of fracture in the non-weight-bearing skeleton was not related to physical activity levels. At weight-bearing sites, an inverse relationship between physical activity and fracture risk was present in both sexes (P_{trend} <0.02). Compared with the sedentary subjects, the most active men and women had a 65% (HR=0.35, 95% CI: 0.16-0.75) and 55% (HR=0.45, 95% CI: 0.21-0.97) reduced fracture risk, whereas moderately active men and women had a 35% and 20% reduced fracture risk (HR=0.65, 95% CI: 0.46-0.92 in men and HR=0.80, 95% CI: 0.65-1.00 in women).

We concluded that in middle-aged and aged women and men, physical activity was protective against fractures at weight-bearing sites, but not at non-weight-bearing sites, indicating that effects of physical activity on fracture risk may be site-specific. Habitual physical activity seems to be an important non-pharmacological approach to prevent hip fracture, which is the most detrimental fracture.

6 Discussion of methodology

6.1 Internal and external validity

The validity of a study can be *internal*, i.e. refer to the inference drawn from the sample to the source population, or *external*, i.e. refer to the generalizability beyond the source population, to one or more target populations^{10, 28}.

Internal validity may be defined as "a measure of how confident we can be that a difference in outcome between groups can be attributed to the effects of the exposure"^{57 p.80}. An observed association between the exposure and the outcome may be real (causal or non-causal) or have three other possible explanations, which are threats to the internal validity^{25,57}:

- 1. Chance
- 2. Bias (systematic errors)
- 3. Confounders

Bias can occur at every step of the research process and may be classified into various categories, though selection bias, measurement (or information) bias, and confounding are the most common categories.

6.2 Selection bias

Rothman^{221 p.96} defines selection bias as "a systematic error that results from procedures used to select subjects and from factors that influence study participation". In causal association studies, selection bias may threaten the internal validity when the association between exposure (physical activity) and outcome (BMD and fractures) is different for the participants and non-participants^{80, 221}. Selection bias may occur in the sampling process (due to selection procedures) or during follow-up (due to loss of participants)²²¹. If the characteristics of the study participants differ systematically from those who were not selected, the external validity may be affected, without large impact on the internal validity.

In general, selection bias is not regarded a large problem in prospective cohort studies, because at the time of selection, the outcome is not known⁹³. In our studies, any difference in non-response or withdrawal between physical activity groups is not likely related to fractures that occur many years later. Moreover, in a cohort study, a participation rate >80% is generally considered to be less likely to produce considerable selection bias^{28, 93}. As shown in Table 3, the participation rates in the Tromsø Study surveys were close to or higher than 80%, and all residents of the municipality of Tromsø or a selected cohort among the inhabitants were invited to each survey. The participation rate for each of the papers is more

complex, as the inclusion of subjects required that participants were invited and attended repeated surveys, but in general, the participation rate relative to those who were eligible was high.

In conclusion, selection bias cannot be ruled out, but it seems reasonable to assume that it did not have a large impact on the results.

Table 3: Participation in the Tromsø Study surveys

Survey	Invited	Age (years)	Attended (n)	Participation rate* (% of invited)	
				Men	Women
Tromsø 2 1979-80	All women 20-49 years, all men 20-54 years	20-54	16 620	74	82
Tromsø 3 1986-87	All women 20-56 years, all men 20-61 years, and some younger and older subjects	12-67	21 826	72	79
Tromsø 4 1994-95	All inhabitants above the age of 25 years	25-97	27 158	70	75
Tromsø 5 2001-02	All inhabitants that attended the Tromsø 4 visit 2 survey and all residents aged 30, 40, 45, 60 or 75 years	30-89	8 130	76	81
Tromsø 6 2007-08	All participants in Tromsø 4 visit 2, a 10% random sample among inhabitants aged 30-39 years, a 40 % random sample among inhabitants aged 43-59 years, all inhabitants aged 40-42 years and 60-87 years	30-87	12 984	63	68

^{*}Percentages are adjusted for those who had died, migrated or who were temporarily absent (travel etc.) on the time of the survey.

6.3 Measurement bias

Measurement errors may lead to bias. When the measurement error occurs with discrete variables, it is commonly referred to as misclassification ¹⁰. Misclassification is an important issue, particularly when assessing behavior, such as physical activity. Misclassification can be non-differential or differential (bias). For a misclassification to be non-differential, the misclassification of physical activity must be unrelated to the outcome (BMD, fracture) and conversely²⁰⁷. Non-differential errors are less serious and will mostly weaken the real association, although with more than two groups, the directions may be more difficult to interpret^{57,80}. Differential misclassification is more serious and may distort the results in any direction⁵⁷.

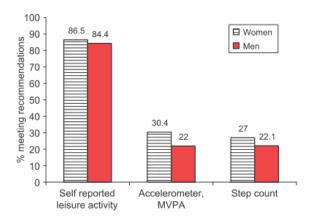
Some measurement biases are most common in case-control studies, such as recall bias²⁸, but in the three papers, there is one other bias that may particularly threaten the validity; reporting bias¹⁰ may arise if the participants report incorrect information, consciously or unconsciously, and with physical activity, overestimation must be expected.

6.3.1 Validity of physical activity assessment methods

Physical activity is a complex behavior to assess, and assessment of physical activity can be done in several ways. Objective measures include measurement of energy expenditure (double labeled water, calorimeter or similar techniques) and movement monitors like accelerometer and pedometer¹⁶¹. Subjective assessments of physical activity include self-reporting methods by questionnaire, interview or diary^{143,161}. To measure targeted bone loading or force-generation activity, motion sensors and ground reaction forces together with questionnaire may be the most ideal method today¹⁴³. Most epidemiological studies assessing physical activity, including the Tromsø Study, have to rely on questionnaires and do rarely have capacity to assess bone loading specifically. Self-administered questionnaires are very common because of low costs, feasibility, ability to reach large samples, and low burden for the participants. However, questionnaires have some disadvantages, which in the case of physical activity may relate to recall problems, misinterpretation, and the incapacity to assess different components of physical activity, possibly undermining reliability and validity²⁷⁰.

In Tromsø 2, 3, and 6 physical activity was assessed by a single questionnaire (table 4). This question was originally initiated by Saltin and Grimby²²⁴ 40 years ago and further developed for self-reporting by Wilhelmsen et al.¹⁵⁸. The question has been widely used in population studies^{7, 15, 152, 219}.

To obtain criterion-based validity, validation of assessment instruments should primarily be performed based on correlation with direct, objective instruments that are considered as the gold standard¹⁶¹. However, such instruments are often too expensive and not feasible. During this thesis, a study of the physical activity question in Tromsø 6 (which was also used in Tromsø 2 and 3) validated against objectively measured physical activity was published⁵⁸. In women and men aged 40-44 years, selfreported physical activity was positively associated with physical activity measured by accelerometer and steps/day in a dose-response relationship. There was also a positive association with maximal oxygen uptake (VO_{2max}) and an inverse association with resting heart rate. The study also utilized the same instruments to measure the proportion of subjects that met the national recommendations for physical activity. As shown i Figure 3, the proportion according to self-reported physical activity (the Tromsø Study question) was much higher than the proportion according to accelerometer and step count, indicating that self-reported physical activity may overestimate the real physical activity level. However, overestimation of physical activity level will probably underestimate the real effects of physical activity on the outcome. The study concluded that adult men and women estimate their physical activity level in accordance with objective measures of their physical activity level, and that this question has satisfactory validity to be used in epidemiological studies of physical activity and disease.



Percentage of adults meeting physical activity guidelines: self-reported leisure time activity, level 2–4; accelerometer, accumulation 30 min/day or more of moderate to vigorous physical activity (MVPA), in either one continuous bout, or several shorter bouts lasting i.e. 10 minutes; step count, minimum 10 000 steps per day; the Tromsø activity study (n=270).

Figure 3. Proportion of adults meeting physical activity guidelines. Reprinted with permissions from Scand J Public Health and the authors. *Emaus A et al. Does a variation in self-reported physical activity reflect variation in objectively measured physical activity, resting heart rate, and physical fitness? Results from the Tromsø study. Scand J Public Health 2010;38(5 Suppl):105-118⁵⁸.*

According to Anderssen et al.⁷, there is evidence for acceptable construct validity for using this question in health surveys. In a study including 2860 women and men¹¹⁵, physical activity in leisure time according to the question in the Tromsø Study was positively associated with metabolic equivalents (MET). Aadahl et al.²⁸³ also found a linear trend for MET across levels of physical activity in leisure time in adult men and women. However, the validity may relate to studies of cardiovascular disease more than bone disease. Because the Tromsø Study and other large cohort studies originally focused primarily on cardiovascular disease, they mainly focused on physical activity that was beneficial to the heart. For bone disease, other aspects of physical activity may be beneficial than for aerobic fitness. Several studies have demonstrated that type of physical activity and partly intensity is more important to bone loading than frequency and duration. However, many activities that are beneficial to aerobic capacity are also beneficial to bone strength, by exerting external forces or muscle force on the bone.

Reliability of this question measured by test-retest administration after 4-6 weeks showed substantial reliability, with a Kappa value of 0.69^{21} and 86% agreement²³³.

Tromsø 4 used a different question regarding physical activity (Table 4). The question in Tromsø 2, 3, and 6 was not comparable with the Tromsø 4 questions, so we chose to exclude the Tromsø 4 population in the tracking paper (paper I). The two original physical activity questions in Tromsø 4 have been used in several large population studies^{200, 241, 245}, but we have found only one validation study of a small group

of men aged 20-39 years¹⁵³. By comparing the characteristics of the physical activity groups, we found inverse dose-response relationships between physical activity and characteristics that are shown to be associated, for example BMI, smoking, and cardiovascular diseases.

6.3.2 Validity of BMD measurements

In paper II, BMD of the total hip, femoral neck, and trochanter area was measured by DXA (GE Lunar Prodigy, LUNAR Corporation, Madison, WI, USA). Two different SXA devices (DTX-100, Osteometer MediTech, Inc., Hawthorne, CA, USA) were used to measure areal BMD of the distal and ultradistal forearm. As presented in the introduction, DXA measured areal BMD is currently considered the gold standard for diagnosis of osteoporosis⁴². Furthermore, DXA and SXA densitometers are very practicable in use, with low costs, low radiation, and they are quick and easy to operate³².

Generally, DXA and SXA measurements have excellent precision³². The Lunar Prodigy DXA densitometer was validated in a recent study²⁰⁴ showing good agreement between the various Lunar Prodigy densitometers. Moreover, phantom measurements confirmed the in vivo measurements. The SXA method has also been shown sufficiently precise to establish BMD²²⁰. However, we believe that the precision errors that may occur during DXA and SXA measurements are probably random.

Although BMD is a strong predictor of fracture risk, there are some issues to consider. DXA and SXA measurements produce two-dimensional BMD and cannot assess three-dimensional size, structure and geometry, or microarchitecture of bone, nor separate between cortical and trabecular bone^{32,40}. However, because other indicators than areal BMD can influence bone strength, DXA measurements may actually underestimate the effects of physical activity on bone strength. Although there is a strong gradient between BMD and fracture risk, fractures often occur in individuals with BMD values in the normal range, and even low BMD values does not necessarily lead to fracture¹¹⁸.

6.3.3 Validity of fracture registration

Misclassification in fracture registration may occur if patients are readmitted or transferred, or due to erroneous coding or punching¹⁰⁶. The fracture registration at the University Hospital of Northern Norway (UNN) has been validated by Joakimsen et al.¹⁰⁵. In a random sample of 1000 subjects from the Tromsø Study, one out of 68 fractures was not initially identified. This method, i.e. the use of a radiology database that was linked to the Tromsø Study database, was validated again by Joakimsen et al. in 2001¹⁰⁶, who concluded that the sensitivity of this method is very good and that the radiographic archive at UNN is accurate, as almost all fractures are coded correctly.

6.4 Confounding

"Confounding" originates from Latin, meaning "mix up" ²⁵. Confounding may be defined as "distortion of an exposure-outcome association brought about by the association of another factor with both outcome and exposure" ⁵⁷ p.158, and may distort the real association in any direction ⁵⁷. The common strategies to control confounders are randomization, matching of subjects, restriction of selection criteria, stratification by certain characteristics, and statistical adjustments for potential confounders by use of multivariable models ^{25,57}. However, in observational studies, it is impossible to control all other factors so that the groups only differ regarding the exposure, mostly due to ethical or logistic reasons ⁵⁷.

Because this work includes all observational studies in which data were already collected, matching and randomization were not options. We therefore had to attempt to control confounders in the analyses. Our strategy was a combination of stratification, which was done by sex, and adjustments for confounders. Stratification may not be an option for every relevant confounder because it creates small subgroups, resulting in insufficient statistical power to do the statistical analyses²⁵. We chose to stratify by sex in most analyses because sex is a common confounder, but also because we wanted to assess separate associations in women and men. Although the Tromsø Study has information on a large number of characteristics, the potential confounders were of course limited by the data material already collected. Potential confounders were chosen by comparing the characteristics of the population, and by selecting the most important factors that could be associated with both the exposure and the outcome. Still, there were probably unmeasured confounders in our studies, and there could also be residual confounding. Therefore, we cannot completely rule out confounding as an alternative explanation of the observed associations between physical activity and BMD and risk of fracture.

6.5 Generalizability (external validity)

External validity depends on internal validity, so if the results are not valid for the eligible subjects, judgment of the validity for other populations is irrelevant⁵⁷. We have previously addressed internal validity and concluded that although errors may have occurred, there are probably no major distortions of the associations.

To obtain external validity, epidemiologists want to be able to generalize from the source population to a larger target population. Generalization may be viewed as whether the *sample (study population)* is representative for other populations, or whether the observed *associations* can be applied to other populations^{10,57}. In order to assess causality, as opposed to descriptive research, some epidemiologists argue that the subjects do not need to be a representative sample of larger populations, and this is often not feasible^{10,57}. The important issue is whether the *associations* between outcome and exposure can be

applied to a general population. This means generalizing from specific observations in the source population to a more universal hypothesis applicable to a nonspecific target population¹⁰.

Even though the Tromsø population may not be entirely representative for Norway, the Nordic countries, Europe, or other geographic areas with regard to all aspects, for instance exposure to sun, snow and ice conditions, topography etc., the physiological associations between physical activity and BMD or fracture in adults are likely to apply to other populations than the Tromsø population. This is supported by the fact that results from physiological and genetic studies tend to have high external validity⁵⁷.

6.6 Causality

Ever since David Hume in the 18th Century characterized a causal relationship, researchers have developed criteria for determining whether a relationship is causal. Examples are "Mills canons" in the 19th Century, Hills criteria for a causal association²²¹, and Alfred Evan's postulates²¹⁰. More recently, Bhopal²⁵ published a modification of these criteria for epidemiology:

- 1. Strength of association
- 2. Consistency of evidence
- 3. Specificity of relationship
- 4. Temporality
- 5. Dose-response
- 6. Biological plausibility
- 7. Experimental confirmation

Some epidemiologists have criticized the use of such criteria in establishing a causal relationship, claiming that they are vague or not applicable to all associations^{25,80,221}. Furthermore, according to induction and refutationism, causality never can be proved, despite all these criteria. Nevertheless, examining causal relationships is crucial to medicine and public health⁵⁷. Many epidemiologists emphasize that such criteria should create a framework for judgment of causality, based on evidence from all disciplines, and that common sense should be used in the evaluation; moreover, the conclusion about causality should not be finite²⁵. Bhopal²⁵ argues that the criteria could be particularly useful in revealing lack of causality and for suggestions about further research.

Osteoporosis, like many other chronic diseases, has a complex etiology, and physical inactivity is one of many factors that may contribute to the development of osteoporosis. Although we found a beneficial association between physical activity and BMD, respectively fracture risk, in general most observed associations are actually not causal²⁵. As shown in the previous chapters, bias and confounding must be examined and should be ruled out as explanations for the observed associations. We have concluded that

selection bias may have occurred, but due to the population based design and the high attendance rate, there are reasons to believe that selection bias may not have had a large impact on the result. Measurement of BMD and fracture registration are thoroughly validated and not likely encumbered with differential errors of importance. However, misclassification of physical activity could be considerable, but this misclassification is probably non-differential. A recent validation study⁵⁸ indicates that this single physical activity question seems to have satisfactory validity to be used in epidemiological studies of physical activity and disease, although self-reported physical activity may overestimate the real physical activity level and thus weaken the real associations. Although we adjusted for the assumed relevant confounders that were available, we cannot completely rule out unmeasured confounders as an explanation. Still, we conclude that the associations we observed were only modestly affected by bias and confounding, and by using P values <0.05 and 95% confidence intervals in the statistical analyses, the possibility that chance was an explanation for the results was weakened.

Inferring about causality from a single study is generally not recommended. Therefore, in this thesis we will not aim at drawing final conclusions about causality, but rather use some of the criteria as a basis for a discussion of some issues related to the results. Besides temporality, which is necessary for a causal relationship (the cause must precede the effect)^{25, 221}, the plausibility of the results, as well as the strength and consistence with previous research, are central principles when evaluating epidemiological research.

7 Discussion of results - interpretation and context

7.1 Strength of the association and dose-response relationship

A dose-response relationship between exposure and outcome is an indicator of the strength of the observed associations²⁸. Additionally, the dose-response relationship may also have implications for public health advice about physical activity^{80,161}. Because a large proportion of individuals does not meet the recommendations for physical activity, health authorities commonly advice the minimum of activity needed for health benefits¹⁶¹.

Physical activity can be explained by intensity, frequency, duration, type, or total volume (intensity, frequency, and duration), and may have different effects depending on these aspects, as well as the goal of the activity (endurance or resistance skills, lower body weight etc.)¹⁶¹. The physical activity question in paper II partly covers duration (more or less than 4 hours per week) and is a crude measure of intensity, but does not cover type or frequency of the activity. Therefore, we have used the answer as an estimate of the volume of activity. The dose-response relationship between volume of physical activity and BMD (paper II) and fracture (paper III) strengthens the observed associations in the thesis.

Generally, total volume is regarded sufficient to show a dose-response relationship, although too inaccurate to find the exact level of physical activity to prevent disease¹⁶¹. Still, in paper II there is a cut-off point at 4 hours a week between the sedentary and moderate categories, which means that physical activity in paper II, defined as activity more than four hours per week with moderate or high intensity, is in accordance with the Nordic Health Authorities' recommendations, which is 30 minutes physical activity with moderate intensity most days of the week⁸. The physical activity questions in paper III are less suited to measure physical activity in relation to the national physical activity recommendations.

Aiming at describing a dose-response relationship has consequences for the choice of statistical methods. In the statistical analysis, physical activity can be treated as a categorical or continuous variable. In the present work, physical activity was modeled as both as a categorical and as a continuous variable; one reason for this choice is obviously that we wanted to describe a kind of dose-response relationship, as well as detect differences between high and low physical activity levels.

The strength of the associations may also be evaluated based on the effect size²⁵. In this work, the associations were not very strong, as HRs and BMD differences were mostly small or moderate. This is however expected in studies of physical activity, as the physical activity level in a general population is rather low. Furthermore, physical activity is one of many risk factors that may explain or predict BMD and fracture.

7.2 Biological plausibility

There are some well-grounded theories behind the biological mechanisms explaining associations between physical activity and fracture, as described in the introduction (mechanical loading and mechanotransduction, improved muscle strength, balance, and neuromuscular control). Low BMD is a risk factor for fracture, and physical activity may reduce the incidence of fractures by the mechanisms of mechanical loading. Our results cannot directly identify the biological mechanisms responsible for lower fracture risk associated with physical activity, but the observed association between both physical activity and fracture at the hip, and also between physical activity and BMD, could imply that BMD is partly involved in these mechanisms.

Although the subjects in paper II and III were from different Tromsø Study surveys, they have probably been engaged in the same type of activities (some of the subjects may have been included in both studies). Although we do not have information about the type of activity, it seems reasonable to assume that habitual physical activity primarily involves the lower skeleton, as walking is the decidedly most common activity among Norwegians⁶. However, we found that both hip and forearm BMD were positively associated with physical activity in a linear trend, and the same trend was found between physical activity and fractures at the hip, but not the forearm. The reason for this is not clear, but higher BMD in the forearm does not seem to protect against forearm fracture. This could indicate that other skeletal mechanisms are involved, or that falls are a stronger determinant for fracture than BMD, as suggested by Järvinen et al.¹⁰⁴.

Not all fractures occur in osteoporotic patients²³⁸, and physical activity may also prevent fracture through improved muscle strength and balance. Several observational studies have shown that physical activity (particularly resistance and balance training) reduces the incidence of falls^{37, 125, 133}, also in people with low BMD⁴⁹. Most, but not all RCTs support these results¹³³. Unfortunately, we did not have data on falls in relation to fractures.

Physical activity may also reduce fracture risk through other mechanisms than BMD, by positively affecting structural properties of the bone^{47, 257}. Some animal studies have shown that exercise induces positive changes in bone strength and structure, but not BMD²⁶⁷, demonstrating the limitations of DXA BMD measurements in giving information about cortical and trabecular structure, size, shape, and bone mass distribution¹⁹⁶. Recently, advances in imaging techniques (pQCT, MRI) have made it possible to assess bone strength more properly. pQCT can be used to assess macroarchitecture, and trabecular and cortical bone density as volumetric BMD (g/cm³), and MRI can assess trabecular microarchitecture, however at peripheral sites³⁰. More recently developed techniques include high-resolution microcomputed tomography and finite element analysis³⁰. Quantitative ultrasound can also be used to measure bone mineral and architecture⁸⁸. These instruments can measure other aspects of bone strength,

including bone strength index (BSI), stress-strain index (SSI), cross-sectional moment of inertia (CSMI) and section moduli (Z), and maximal moment of inertia (Imax)¹⁹⁶. We did however not have access to such instruments in this work. A review of RCTs measuring exercise effects on bone strength mostly showed no significant effects in adolescence, middle-aged, and older individuals, but a small effect in young boys¹⁹⁶. However, the studies are few and short-term, and no RCTs including men were found. The review revealed that the instruments for measuring bone strength still are subject to technical challenges. A review of all types of studies in older women⁸⁷ showed a little more promising results with positive but modest exercise effects on bone geometry at loaded sites. Similarly, Daly and Bass⁴⁷ reported that lifetime and mid-adulthood physical activity was associated with 6-15% higher mid-femur total and cortical areas measured by quantitative computed tomography (QCT), while there was no observed association between areal BMD and lifetime physical activity. As suggested by Daly and Bass, because of the two-dimensional nature of areal BMD measures, DXA may actually underestimate the effect of physical activity on bone strength.

7.3 Consistency with previous research

In this section, the results from each paper will be commented and placed in the context of other results in this thesis, as well as in a larger context, and the results will be discussed in general. The results are compared with previous results in more detail in the enclosed papers I-III.

Causality between physical activity and BMD needs to be demonstrated in experiments (RCTs) or laboratory studies, to control the factors that may bias or confound the results, but such intervention studies are not well suited for exploration of long-term effects of physical activity, because of their short duration and limited number of participants. Therefore, investigations of long-term effects of physical activity on BMD are usually based on epidemiological studies, either prospective or case-control (retrospective) studies. Epidemiological observation studies are important in order to confirm findings from RCTs in studies that assemble real-life in large populations²⁵, and repeated population studies, such as the Tromsø Study, are suited for long-term analyses.

7.3.1 Tracking of physical activity

Tracking of physical activity habits during adulthood has not been object of many studies. Moreover, the existing studies have been performed with different physical activity categories and cut-offs, and with varying time span and methods; therefore, comparison with previous research is problematic. Yet, in paper I, we made an effort to compare our results with previous studies. In terms of correlation between repeated measurements, which is the most commonly used measure for tracking, our results are in agreement with previous studies^{48,72,144,162,163,223,242}, showing moderate tracking. Several methods are available for analyses of tracking, and we furthermore examined prediction of physical activity levels

from earlier measurements of physical activity. By using GEE models, we added a new procedure to the literature of physical activity tracking. We found that physical activity in adulthood was a strong predictor of later physical activity levels, with high ORs. The only other study we found that was comparable with this method reported similar results¹⁴⁴.

Finally, we calculated the proportion who maintained their physical activity level after 28 years. Our results indicated that 58% and 53% of the participants remained at their baseline physical activity level after 7 and 28 years, respectively. These results are not easily comparable with similar studies (which, again, are few) because physical activity is categorized differently. Consequently, these results seem difficult to interpret; is 58% an adequate proportion for the study of associations between physical activity and BMD or fracture incidence? What is the signification of these results for health outcomes?

In terms of health benefits, high levels of tracking can be interpreted as both advantageous and unfortunate, since habitual physical activity is beneficial to health, while inactivity is undesirable. Our findings that more than 25% decreased their physical activity level over time indicate that effort should be directed at continuing an active lifestyle. In terms of relevance for epidemiological studies, the proportion of participants that did not change their physical activity level (between 50% and 60%) was statistically higher than expected, but the relevance must be based on subjective opinions. If we add those who decreased their physical activity level (26%-27%), which may have attenuated the associations, it seems reasonable that an observed association in paper II and III rest on the assumption that physical activity levels were relatively stable throughout the follow-up period. Furthermore, it is evident that physical activity level is strongly associated with later physical activity levels.

After the submission of this paper, a new study¹⁸⁸ using internet tracking of self-reported physical activity was published. The study is interesting because it follows community-living women in real-time weekly for 2.5 years, and the results show that physical activity habits are very stable across long periods, which support the assumption that physical activity habits in adults are rather stable. Another new study of tracking of physical activity in adults was published in 2011²⁰⁸. Tracking of physical activity over 10 years was studied in 3258 Dutch adult men and women, showing that 31.4% of the populations were active throughout the time period. Once again, the methods used differed slightly between our study and this Dutch study, so most numbers are not directly comparable. They reported that 45% changed their physical activity habits, which is comparable and similar to our numbers. The authors highlight an essential argument; with these individual changes in physical activity habits over time, the strong and consistent effects of physical activity that are found in many health studies are striking and could actually be much higher²⁰⁸.

7.3.2 Long-term associations between physical activity and BMD

Retrospective studies, which are susceptible to recall bias, have reported inconsistent results, and only a few prospective studies have examined the long-term association between physical activity during adulthood and BMD at older ages. Augestad et al.¹² reported that physical activity was protective against low forearm BMD 11 years later in 2924 Norwegian postmenopausal women in Trøndelag (the HUNT study). Daly et al.⁴⁶ examined forearm BMD in 358 elderly women and men with repeated measurements 10 years apart. They found a lower bone loss in individuals who were physically active over 10 years than in those who were sedentary over the period. In our study (paper II), we were able to examine hip BMD as well. We observed that higher levels of physical activity were associated with higher BMD 22 years later, both in forearm, as did the Daly et al.⁴⁶ and Augestad et al.¹², and also at the hip. Our study thus extends the existing knowledge about long-term benefits of physical activity into middle age and old age. However, in contrast to Daly et al.⁴⁶, we did not have baseline measurements of BMD, which may impede the ability to show a causal relationship.

With only one measure of physical activity in our study, it is uncertain whether the higher BMD in active vs. sedentary participants is a result of continued physical activity in the active subjects or prolonged effects of physical activity 20 years earlier. Paper I examined the stability of physical activity over 28 years, showing that the proportion of participants who maintained their physical activity level was 50% to 60%. Adding those who decreased their physical activity level (26%-27%), which may have attenuated the associations, it seems reasonable to assume a fairly stable physical activity level over decades.

We did however have follow-up assessment of physical activity among a subsample of the participants in Tromsø 2 (those aged < 70 years at follow-up in 2001). The sub-analyses showed that 71% of the paper II population were active and 6% were sedentary at both examinations, thus an even higher proportion of participants than found in paper I maintained their physical activity level. Interestingly, those who were sedentary at both surveys had lower BMD than those who were moderately active or active at one or both surveys. These results indicate that any activity is better than being sedentary, and that not only past, but also recent activity may influence BMD. However, the subgroup excluded all subjects older than 70 years and the results may thus not relate to older people.

The positive trends in BMD across physical activity levels in paper II were consistent across all measured sites, implying an association between physical activity and fracture risk as well. This provided the basis for paper III, in which the aim was to study physical activity in relation to fracture risk. Unfortunately, we could not assess fracture risk in paper II, because we analyzed the Tromsø 2 population which was examined in 1979-80, whereas the fracture registry started in 1988. Thus, we chose the large Tromsø 4 population (1994-95) as study population for paper III.

7.3.3 Physical activity and fracture risk

There is no uniform definition of an osteoporotic fracture^{107, 120}. Historically, fractures of the hip, spine, and distal forearm have been considered the main osteoporotic fractures³⁹. Another approach has been to define low-energy fractures (i.e. falling from the same level) as osteoporotic, but patients with low BMD are probably more likely to suffer a fracture from a high-energy trauma as well, compared with non-osteoporotic patients¹⁰⁷. Kanis¹²⁰ discusses yet another definition of osteoporotic fracture as "sustained in an individual over the age of 50 years at a site that increases in frequency the lower the BMD, increases in incidence with age, and provides a risk indicator for future osteoporotic fracture"¹²⁰ p.92. Our definition of an osteoporotic fracture is largely in accordance with this definition, as we chose to exclude only clearly high trauma fracture sites. However, because most studies have focused on hip and forearm fractures, we also did sub-analyses of these two fracture sites, in order to be able to compare our results with the previous studies.

Our results of the associations between physical activity and risk of fracture in the hip and forearm were generally in accordance with previous studies, although studies of physical activity in relation to forearm fractures are few and inconsistent. The main objective of paper III was to examine fracture risk at weight-bearing versus non-weight-bearing sites, which was possible because of the large cohort with a large number of fractures. Paper III can be viewed as a continuation of a previous study of the Tromsø cohort by Joakimsen et al.¹⁰⁵, who examined physical activity in relation to fractures at weight-bearing and non-weight-bearing sites in the cohorts of Tromsø 2 and 3. Joakimsen et al.¹⁰⁵ found that high physical activity was associated with a significantly lower risk of fracture in the lower (weight-bearing) extremities, although non-significant in women. Our study analyzed data from the fourth Tromsø Study survey, which is partly a different cohort, still the results were similar to the previous study by Joakimsen et al.¹⁰⁵. Similarly, none of these two studies found associations between physical activity and risk of fracture at non-weight-bearing sites.

On the other hand, two recent studies report that higher physical activity levels may actually increase the risk of fracture in elderly individuals^{9, 195}. These results indicate that physical activity also may represent an increased risk of fracture, and although our study may have pointed to an important issue regarding the different benefits in the weight-bearing and non-weight-bearing skeleton, more research is needed to clarify the role of physical activity in fracture prevention.

8 Conclusions, implications and future research

8.1 Conclusions

Main conclusion 1: Physical activity habits in adulthood are a strong determinant of physical activity habits later in life.

- 53% of the subjects maintained their physical activity over 28 years. 27% decreased and 20% increased their level of physical activity.
- Sedentary adults have higher odds of being sedentary later in life than active adults.
- Being physically active in adulthood is a strong predictor of being active later in life.

Main conclusion 2: Being physically active in adulthood seems to reduce the risk of osteoporosis later in life, at ages when individuals are more prone to fragility fractures.

- There is a positive dose-response relationship between physical activity in adulthood and BMD measured later in life.
- Being physically active in early or late adulthood, or both, is beneficial to BMD compared with being sedentary throughout adulthood.

Main conclusion 3: Physical activity seems to protect against fractures in the weight-bearing skeleton in subsequent years in middle-aged and aged women and men.

- Being highly active in adulthood reduces the risk of fracture in the weight-bearing skeleton by
 55-65% compared with being sedentary.
- In non-weight-bearing skeleton, risk of fracture is not related to physical activity. Thus, effects of physical activity on fracture risk seem to be site-specific.

8.2 Implications for public health

- Many individuals maintain their sedentary lifestyle or decrease their activity level from early or
 middle adulthood into older age, which implies that adults and elderly should be considered as
 target groups for public health interventions that promote physical activity.
- It is important that physical activity habits during childhood and adolescence are carried forward
 into adulthood, as being active in early or middle adulthood increases the odds of being active at
 older ages.
- Physical activity during adulthood should be encouraged as part of the prevention of osteoporosis
 and preservation of bone mass. Physical activity in the prevention of osteoporosis should be
 encouraged among older people as well, as being active in early or late adulthood, or both, is more
 beneficial to BMD than being sedentary throughout adulthood.
- Following the recommendations from the Norwegian health authorities about exertion of physical
 activity may be sufficient for significant BMD preservation later in life. Higher activity levels may
 further escalate the BMD benefits.
- In order to prevent hip fractures, which are the most serious fracture, weight-bearing physical activity should be recommended.

8.3 Future research

The association between physical activity and BMD has been studied extensively for 30 years, both in cross-sectional studies, longitudinal observation studies, and RCTs. Yet, there are some unsolved questions.

- 1. Because most studies are short-term, long-term changes in physical activity should be assessed in relation to long-term changes in BMD, as one remodeling cycle takes up to 5 months.
- 2. Assessment of physical activity is often based on subjective measurements, thus objective measurement of physical activity should be performed when possible, and assessment of physical activity should include the specific components of physical activity (frequency, intensity, type, and duration).
- 3. Assessing type of activity is crucial because of the mechanical loading theory. Many different types of activity seem to be beneficial, and future research should focus on which types of activity (weight-bearing, resistance, walking etc.) are most useful for osteoporosis prevention.

4. Because BMD measures only one aspect of bone strength, measurements of bone structure in relation to physical activity should be encouraged, along with development of methods and instruments to assess bone structure.

The association between physical activity and fractures has been much less examined, and there are many uncertain areas. Long-term RCTs are not likely to be performed on physical activity and fracture. There are too many restraining aspects, such as the long time period needed, expensiveness, the number of subjects needed, and the ethics of requesting people to be more or less sedentary for a long time. Most suggestions above also relate to physical activity and fracture risk, though there are some additional aspects of interest:

- 5. Most studies involve hip, but the effects of physical activity at other fracture sites should also be examined.
- 6. Falls are a very important aspect when studying fracture. Thus, physical activity and fracture studies should include data on fall incidence.

Regarding habits of physical activity, future studies may examine determinants or predictors of physical activity and secular trends in physical activity over decades. Moreover, more comprehensive and standardized questionnaires are needed for a better foundation for comparison between populations in epidemiological studies when objective assessment of physical activity is not possible.

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Paper I

Paper II

Paper III

Appendix A

Questionnaire 1, the 2nd Tromsø Study 1979-80

Norwegian version

JA NE	D JA NEI
Har De, eller har De hatt:	Røyker De daglig for tiden? 52
Hjerteinfarkt? 33	Hvis svaret var "JA" på forrige spørsmål,
Angina pectoris (hjertekrampe)? 34	
Annen hjertesykdom?ss	Røyker De sigaretter daglig ?
Åreforkalkning i bena?	Hvis De ikke røyker sigaretter nå, besvar da
Hjerneslag?	Har De røykt sigaretter daglig tidligere? . 54
Sukkersyke?	Hyis De svarte "JA", hvor lenge er det siden De sluttet?
Er De under behandling for:	The state of the s
Høyt blodtrykk?	1 Mindre enn 3 måneder?
Bruker De :	2 3 måneder - 1år?
Nitroglycerin? 40	3 1 - 5 år?
Får De smerter eller ubehag i brystet når De:	
Går i bakker, trapper eller fort på flat mark? 4	Antall &c:
Går i vanlig takt på flat mark?	reykt daglig?
Hvis De får smerter eller ubehag i brystet ved gange, pleier De da å:	Hvor mange sigaretter røyker eller røykte De daglig ? Oppgi antall pr. dag ** (handrullede + fabrikkframstilte)
1 Stanse?	Royker De noe annet enn sigaretter daglig?
2 Saktne farten?	Sigarer eller serutter/cigarillos? 62
3 Fortsette i samme takt?	Pipe ?
Hvis De stanser eller saktner farten, forsvinner smertene da:	Hvis De røyker pipe, hvor mange pakker tobakk (50 gram) bruker De i pipa pr. uke?
1 Etter mindre enn 10 minutter? 4	Oppgi gjennomsnittlig antall pakker pr.uke. ""
2 Etter mer enn 10 minutter?	E LA NEI
Får De smerter i tykkleggen når De :	Har De vanligvis skiftarbeid eller nattarbeid? 67
Går?	Kan De vanligvis komme hjem fra arbeidet:
Eriro? 46	Hver dag?
Hvis De får leggsmerter, besvar da : Forverres smertene ved raskere	Hver helg?
tempo eller i bakker?	Har De i perioder lengre arbeidsdager enn vanlig?
Gir smertene seg når De stopper ? 48	(f.eks. under sesongfiske, onnearbeid)
Har De vanligvis:	Har De i løpet av siste året hatt:
Hoste om morgenen?	Sett kryss i den ruten hvor "JA" passer best.
Oppspytt fra brystet om morgenen? so	1 Overveiende stillesittende arbeid? 71 (f.eks. skrivebordsarb., urmakerarb., montering)
Bevegelse og kroppslig anstrengelse i	2 Arbeid som krever at De går mye? (f.eks. ekspeditorarb, lett industriarb, undervisn.)
Hvis aktiviteten varierer meget f.eks.	3 Arbeid hvor De går og løfter mye? (f.eks. postbud, tyngre industriarb., bygningsarb.)
mellom sommer og vinter så ta et gjennomenitt.	4 Tungt kroppsarbeid?
Spørsmålet gjelder bare det siste året.	(f.eks. skogsarbeid, tungt jordbruksarb., tungt bygningsarb.)
Sett kryss i den ruten hvor "JA" passer best.	Har De i løpet av de siste 12 mnd måttet flytte fra hjemstedet på grunn av
Leser, ser på fjernsyn eller annen stillesittende beskjeftigelse?	forandring i arbeidssituasjonen?
2 Spaserer, sykler eller beveger Dem på annen måte minst 4 timer i uken? (Hari medregnes også gang eller sykling)	Har De i løpet av de siste 12 mnd fått arbeidsledighetstrygd?
Ini arbeidestedet, søndagsturer m.m.	Er De for tiden sykmeldt, eller får De
3 Driver mosjonsidrett, tyngre hage- arbeid e.L.?	attioring spenger! 75
(Merk at yirksomheten skal vare minst)	Har De full eller delvis uførepensjon? 76
4 Trener hardt eller driver konkurranse-	JA NEI NO
idrett regelmessig og flere ganger i uken!	Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)? . 77
	Er to eller flere av Deres besteforeldre av finsk ætt?
, -4	Er to eller flere av Deres hesteforelde
	av samisk ætt?

Do you have, or have you had:	No Do you smoke daily at present?
A heart attack?	If the answer was "Yes" in the previous question,
Angina pectoris (heart cramp)?	then:
Any other heart disease?	Do you smoke cigarettes daily? 53
Hardened arteries in the legs?	(hand-rolled or factory made)
A cerebral stroke?	If you do not smoke cigarettes at present, then:
Diabetes?	Have you previously smoked cigarettes daily? 4 If "Yes", how long is it since you stopped:
Are you being treated for:	
High blood pressure?	1 Less than 3 months?
Do you use:	2 3 months to 1 year?
Nitroglycerine?	3 1 to 5 years?
B	More than 5 years?
Do you have get or discomfort in the chest when:	For those who smoke or have smoked previously:
Walking up hills or stairs, or walking fast on level ground?	How many years altogether have you smoked daily?
Walking at normal pace at level ground? 42	How many cigarettes do you smoke, or did you. No of cigarettes
If you get pain or discomfort in the chest when walking, do you usually:	smoke daily? Give number of cigarettes per day (hand-rolled or factory made)
1 Stop?	Do you smoke tobacco products other than cigarettes daily?
2 Slow down?	Cigars or cigarillos?
3 Carry on at the same pace?	A pipe?
If you stop or slow down, does the pain disappear:	If you smoke a pipe, how many packs of tobacco
Within 10 minutes?	(50 grams) do you smoke per week? No. of tobacco
² After more than 10 minutes?	Give the average number of packs per week.
	Yes No
Do you get pain in the calf while: Walking?45	Do you usually work shifts or at nights?
Resting?	Can you usually come home from work: Every day?
If you get pain in the calf, then:	Every weekend?
Does the pain increase when you walk	Are there periods during which your working
faster or uphill?	days are longer than usual?
Does the pain disappear when you stop?*	(e.g. fishing season, harvest)
Do you usually have:	During the last year, have you had:
Cough in the morning?	Tick "Yes" beside description that fits best
Phlegm chest in the morning?	1 Mostly sedentary work?
Exercise and physical exertion in leisure time.	Work that requires a lot of walking
If your activity varies much, for example	³ Work that requires a lot of walking and lifting?
between summer and winter, then give an average.	(e.g. postman, heavy industrial work, construction)
The question refers only to the last twelve months:	4 Heavy manual labour?
Tisk W/ // Last at a start of the start	(e.g. forestry, heavy farm-work, heavy construction)
Tick "Yes" beside the description that fits best: 1 Reading, watching TV, or other sedentary	During the last 12 months, have you had
Activity?	to move for work reasons?
² Walking, cycling, or other forms of	Is housekeeping your main occupation? **
exercise at least 4 hours a week?	Have you within the last 12 months received unemployment benefit?
Sunday walk/stroll, etc.) 3 Participation in recreational sports,	Are you at present on sick leave, or receiving
heavy gardening, etc.?	renabilitation allowance?
(note: duration of activity at least 4 hours a week)	Do you receive a complete or partial disability pension?
4 Participation in hard training or sports	Ves No know
competitions, regularly several times a week?	Have one or more of your parents or sisters or brothers had a heart attack (heart wound), or angina pectoris (heart cramp)?
	Are two or more of your grandparents of Finnish origin?
	Are two or more of your grandparents of Sami origin?

Appendix B

Questionnaire 1, the 3rd Tromsø Study 1986-87

Norwegian version

we En TOMSO III **HELSEUNDERSØKELSEN I TROMSØ** Helseundersøkelsen kommer nå til Deres distrikt. (Gjelder bare den person som brevet er adressert til.) Tid og sted for frammøte vil De finne nedenfor. De finner en orientering om undersøkelsen i den vedlagte brosjyren. Vi ber Dem vennligst fylle ut spørreskjemaet på baksiden og ta med dette til undersøkelsen. Vi ber Dem eventuelt melde fra om fravær på den vedlagte fraværsmeldingen. Kuinner 1930-66 Menn 1925-66 Med hilsen KOMMUNEHELSETJENESTEN I TROMSØ FYLKESLEGEN I TROMS UNIVERSITETET I TROMSØ

Kretsnr.

STATENS HELSEUNDERSØKELSER

Første bokstav i

Møtested Kjønn etternavn Dag og dato Klokkeslett

Kommune

Født dato

Personnr.

HØYDE TSM 82 ANM 70 KODE 75 MÅLING 2 MÅLING 3 MÅLING 1 MAR MAR MAR S S 85 94 100 HR D HR D HR D 118 109

FAMILIE		F RØYKING	JA NEI
Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina	JA NEI VET	Røyker De daglig for tida?	10
pectoris (hjertekrampe)?12		Røyker De sigaretter daglig? 31	
B EGEN SYKDOM		(håndrullede eller fabrikkfremstilte) Dersom De ikke røyker sigaretter nå,	
Har De, eller har De hatt:	JA NEI	svar da på dette: Har De røykt sigaretter daglig tidligere?32	
Hjerteinfarkt? 13		Dersom De svarte «JA», hvor lenge er det	
Angina pectoris (hjertekrampe)?		da siden De sluttet? Mindre enn 3 måneder?	1
Sukkersyke? 16		3 måneder – 1 år?	2
Er De under behandling for:		1–5 år?	3 4
Høyt blodtrykk? 17	324	Skal besvares av de som røyker nå eller som har røykt tidligere:	
Bruker De:		Hvor mange år til sammen har	
Nitroglycerin?		De røykt daglig?34 Hvor mange sigaretter røyker eller	År
SYMPTOMER		røykte De daglig?	
Får De smerter eller ubehag i brystet når De:	JA NEI	Gi opp antallet sigaretter daglig	Sigarette
Går i bakker, trapper eller fort på flat mark?19		Røyker De noe annet enn sigaretter daglig?	
Går i vanlig takt på flat mark? 20		Sigarer eller serutter/sigarillos?	
Dersom De får smerter eller vondt i brystet ved gange, pleier De da:		Dersom De røyker pipe, hvor mange pakker tobakk (50 gram) bruker De i pipen	
Stoppe? 21	1 2	på en uke?	
Fortsette i samme takt?	3	Gi opp gjennomsnittlig tall på pakker i uken42	
Dersom De stopper eller saktner farten, går da smertene bort:		G KAFFE	Tobakksp
Etter mindre enn 10 minutter?	1 2	Hvor mange kopper kaffe drikker De	
Har De vanligvis:	JA NEI	vanligvis hver dag? Sett kryss i den ruten som passer best.	
Hoste om morgenen?		Drikker ikke kaffe, eller mindre	
Oppspytt fra brystet om morgenen?24 MOSJON	E135	enn en kopp	
Bevegelse og kroppslig aktivitet i Deres fritid.		5 – 8 kopper	3
Dersom aktiviteten varierer mye, f.eks. mellom		9 eller flere kopper Hva slags kaffe drikker De vanligvis hver dag?	
sommer og vinter, så ta ett gjennomsnitt. Spørsmålet gjelder bare det siste året.		Kokekaffe	
Sett kryss i den ruten som passer best. Leser, ser på fjernsyn eller annen		Pulverkaffe 48	
stillesittende beskjeftigelse?25	1	Koffeinfri kaffe49 Drikker ikke kaffe50	
Spaserer, sykler eller beveger Dem på annen måte minst 4 timer i uken?	2	H ARBEID	JA NE
(Her skal De også regne med gang eller		Har De i de siste 12 månedene	
sykling til arbeidsstedet, søndagsturer m.m.) Driver mosjonsidrett, tyngre hagearbeid e.l.?		fått arbeidsledighetstrygd?51	T T
(Merk at aktiviteten skal vare i minst 4 timer i uken.)		Er De for tiden sykemeldt, eller får De attføringspenger?52	<u> </u>
Trener hardt eller driver konkurranseidrett regelmessig og flere ganger i uken?	4	Har De full eller delvis uførepensjon?53	
SALT/FETT		Har De vanligvis skiftarbeid eller nattarbeid54	
Hvor ofte bruker De salt kjøtt eller salt fisk til middag?		Har De i det siste året hatt:	
Sett kryss i den ruten som passer best.		Sett kryss i den ruten som passer best. For det meste stillesittende arbeid? 55	
Aldri eller sjeldnere enn en gang i måneden26		(f.eks. skrivebordsarb., urmakerarb., montering)	
Inntil en gang i uken	2	Arbeide som krever at De går mye? (f.eks. ekspeditørarb., lett industriarb., undervisn.)	H
Inntil to ganger i uken	3 4	Arbeide der De går og løfter mye? (f.eks. postbud, tyngre industriarb., bygningsarb.)	
Hvor ofte pleier De å strø ekstra salt på middagsmaten?		Tungt kroppsarbeid? (f.eks. skogsarb., tungt jordbruksarb., tungt bygningarb.)	
Sett kryss i den ruten som passer best.			JA N
Sjelden eller aldri	1 2	Er husmorarbeid hovedyrket Deres? 56	
Alltid eller nesten alltid	3	I ETTERUNDERSØKELSE	
Hva slags margarin eller smør bruker De vanligvis på brødet?		Har noen i husstanden Deres (utenom Dem selv) vært innkalt til nærmere under-	
Sett kryss i den ruten som passer best.		søkelse hos lege etter den siste hjerte-	
Bruker ikke smør eller margarin på brød28	1	karundersøkelsen?	
Smør	2 3	Dersom denne helseundersøkelsen viser at De bør undersøkes nærmere: Hvilken almen-	
Myk (Soft) margarin	4 5	praktiserende lege ønsker De da å bli henvist til?	100
Hva slags fett blir vanligvis brukt til	5	Skriv navnet på legen her	
matlaging i husholdningen Deres?	202	*	Ikke skriv
Sett kryss i den ruten som passer best. Smør eller hard margarin	1	58	
Myk (Soft) margarin eller olje	2	Ingen spesiell lege	

THE TROMSØ HEALTH SURVEY (Applies only to the person to whom the letter is addressed.) The health so You find the You will find enclosed broadlessed.

The health survey is coming now to your district.

You find the time and place for attendance below.

You will find an orientation on the survey in the enclosed brochure.

We would like you to fill in the form on the back and take it with you to the survey.

We ask those possibly not attending to report their absence in the attached absence report.

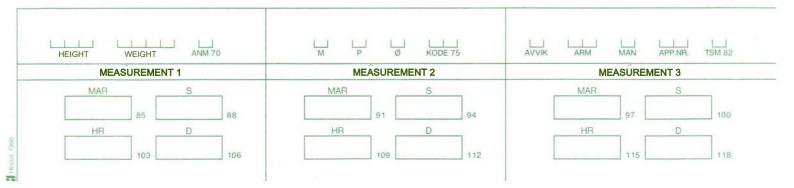
Yours sincerely

MUNICIPAL HEALTH AUTHORITY OF TROMSØ
COUNTY DOCTOR OF TROMS UNIVERSITY OF TROMSØ
NATIONAL HEALTH SCREENING SERVICE

Birth date Personal number Municipality Circuit number

First
letter of

Meeting place Gender last name Day and date Time



FAMILY	9 3 6 9 5 9	F SMOKING	Yes
Have one or more of your parents or siblings	Yes No Don't	Do you smoke daily at present?30	
had a heart attack (heart wound) or angina	know	If the answer is "YES", then:	
pectoris (heart cramp)?12		Do you smoke cigarettes daily?31	
OWN II I NEGGEO	11223	(hand-rolled or factory made)	
OWN ILLNESSES		If you do not smoke cigarettes at present,	
De very house, on house you had.	Yes No	then:	
Do you have, or have you had:		Have you previously smoked cigarettes daily?32	
A heart attack?		If you answered "Yes", how long is it since	
Angina pectoris (heart cramp)?		you stopped:	
Diabetes?		Less than 3 months?	
A TOTAL STREET, STREET		1 -5 years?	
Are you been treated for:		More than 5 years?	
High blood pressure? 17		To be answered by those who smoke or	
Do you use:		who have smoked previously:	
Do you use.		How many years altogether have you	
Nitroglycerine? 18		smoked daily?34	V
CVMPTOMO	APY TO	How many cigarettes do you smoke or	Y
SYMPTOMS		did you smoke daily?	
Do you get pain or discomfort in the chest when	n: Yes No	Give number of cigarettes per day	Ciga
Walking up hills or stairs, or walking		Do you smoke anything else other than cigarettes daily?	
fast on level ground?19		Cigars or cigarillos/cheroots?	
Walking at normal pace at level ground?20		A pipe?40	
If you get pain or discomfort in the chest when			
walking, do you usually:		If you smoke a pipe, how many packs of	
Stop?21		tobacco (50 grams) do you smoke per week?	
Slow down?	2	Give the average number of packs per	
Carry on at the same pace?	3	week42	_
If you stop or slow down, does the pain disappear:		G COFFEE	Tob pa
After less than 10 minutes?	, 1		
After more than 10 minutes?	2	How many cups of coffee do you usually drink daily?	
Do you usually have:	Yes No	-	
Cough in the morning?23	1	Tick the most appropriate box.	
Phlegm chest in the morning?24		Do not drink coffee, or less than one cup45	
EXERCISE	2 (1) (1) A	1 -4 cups	
	100	5 -8 cups	
Exercise and physical exertion in leisure time.		9 or more cups	
If your activity varies much, for example between summer and winter, then give an average.		What type of coffee do you usually drink daily?	
The question refers only to the last year:		Coarsely ground coffee for brewing (boiled)46	
Tick the most appropriate box.		Finely ground filter coffee	
Reading, watching TV, or other sedentary		Caffeine free coffee	
activity?25	, 1	Do not drink coffee	
Walking, cycling or other forms of		H EMPLOYMENT	
exercise at least 4 hours a week?	2	H LIMI EOTHIEIT	Yes
(include walking or cycling to place of work, Sunday walk/stroll, etc.)		Have you within the last 12 months received	
Participation in recreational sports, heavy		unemployment benefits?51	
gardening, etc.?	3	Are you at present on sick lease, or	= 4
(note: duration of activity at least 4 hours a week)		receiving rehabilitation allowance? 52	
,			
Participation in hard training or sports competitions, regularly several times a week?		Do you receive a complete or partial disability pension? 53	
		Do you usually work shifts or at	
SALT/ FAT	a la el cuist	night?54	
How often do you use salted meat		During the last year, have you had:	- 12
or salted fish for dinner?	6		
Tick the most appropriate box.		Tick the most appropriate box. Mostly sedentary work?55	
The tite meet appropriate box.		(e.g. office work, watchmaker, light manual work)	
Never or less than once a month		Work that requires a lot of walking?	
Once a week or less	2	(e.g. shop assistant, light industrial work, teaching)	
Twice a week or less	3	Work that requires a lot of walking and lifting?	
More than twice a week	4	(e.g. postman, heavy industrial work, construction) Heavy manual labour?	
How often do you add extra salt to		(e.g. forestry, heavy farm-work, heavy construction)	
your dinner?		(c.g. lorostry, licary lattirwork, ficary constituction)	Yes
Tick the most appropriate box.		ii promoterante de constitución de constitució	108
Rarely or never2	7 2	Is house-keeping your main occupation? 56	
Sometimes or often	3	I FOLLOW-UP EXAMINATION	
Always or nearly always			
What type of margarine or butter do you		Has any one in your household (other than	1000
usually use on your bread?		yourself) been called in to a doctor for further medical examination after the	2 8
Tight the most appropriate to be		previous cardiovascular disease survey? 57	
Tick the most appropriate box.		p	
Do not use margarine or butter on bread2			
Do not use margarine or butter on bread 2 Butter	2	If this survey suggests that you need a further	-
Do not use margarine or butter on bread 2 Butter Hard Margarine	2 3	If this survey suggests that you need a further medical examination, which general	
Do not use margarine or butter on bread 2 Butter Hard Margarine Soft (soya) margarine spread	2 3 4		
Do not use margarine or butter on bread 2 Butter	2 3	medical examination, which general practitioner do you wish to be referred to?	
Do not use margarine or butter on bread	2 3 4	medical examination, which general	Don't
Do not use margarine or butter on bread	2 3 4	medical examination, which general practitioner do you wish to be referred to?	Don't v
Do not use margarine or butter on bread	2 3 4 5	medical examination, which general practitioner do you wish to be referred to?	Don't
Do not use margarine or butter on bread	2 3 4 5	medical examination, which general practitioner do you wish to be referred to? Write the doctor's name here?	Don't v

Appendix C

Questionnaire 1, the 4th Tromsø Study 1994-95

Norwegian version

Innbydelse til HELSEUNDERSØKELSEN



Fødselsdato

Personnr.

Kommune

Kretsnr.

Velkommen til helseundersøkelsen i Tromsø!

Helseundersøkelsen kommer nå til Tromsø. Tid og sted for frammøte finner du nedenfor. Du finner også en orientering om undersøkelsen i den vedlagte brosjyren.

Vi ber deg fylle ut spørreskjemaet på baksiden og ta det med til undersøkelsen.

Undersøkelsen blir mest verdifull om frammøtet blir så fullstendig som mulig. Vi håper derfor at du har mulighet til å komme. Møt selv om du kjenner deg frisk, om du er under legebehandling, eller om du har fått målt kolesterol og blodtrykk i den senere tid.

> Vennlig hilsen Kommunehelsetjenesten Fagområdet medisin, Universitetet i Tromsø Statens helseundersøkelser



EGEN HELSE	MOSJON
Hvordan er helsen din nå? Sett bare ett kryss.	Hvordan har din fysiske aktivitet i fritiden vært det siste
Dårlig	året? Tenk deg et ukentlig gjennomsnitt for året.
Ikke helt god	Arbeidsvei regnes som fritid.
God	Timer pr. uke
Svært god 4	Lett aktivitet (ikke Ingen Under 1 1-2 3 og mer
	svett/andpusten)56
Har du, eller har du hatt: JA NEI Alder første gang	Hard fysisk aktivitet
Hjerteinfarkt	(svett/andpusten)57
And the state of t	(Svetvariapusteri)5/
Angina pectoris (hjertekrampe) 16	
njernesiag/njernebiodning	KAFFE
Astma	Hvor mange kopper kaffe drikker du daglig?
Diabetes (sukkersyke)25	Sett 0 hvis du ikke drikker kaffe daglig. Antall kopper
	Kokekaffe 58
Bruker du medisin mot høyt blodtrykk?	Annen kaffe 60
Nå 28 1	Airiteti kaire
Før, men ikke nå 2	ALKOHOL
Aldri brukt	Er du total avholdsmann/-kvinne? 62 JA NEI
7,001,010,010	Li da total avriologitati i kviitio i
Har du i løpet av det siste året vært plaget med	Hvor mange ganger i måneden drikker du vanlig-
smerter og/eller stivhet i muskler og ledd som JA NEI	vis alkohol? Regn ikke med lettøl. Antall ganger
har vart i minst 3 måneder sammenhengende? 29	Sett 0 hvis mindre enn 1 gang i mnd 63
	Hvor mange glass øl, vin eller brennevin drikker du
Max du do cieto to ulcano felt dos.	vanligvis i løpet av to uker? 65 Øl Vin Brennevin
Har du de siste to ukene følt deg:	Regn ikke med lettøl. glass glass glass
En god Svært Nei Litt del mye	Sett 0 hvis du ikke drikker alkohol.
Nei Litt dei Hiye	
Nervøs og urolig? 30	
Plaget av angst?31	Hva slags margarin eller smør bruker du vanligvis på
Trygg og rolig? 32	brødet? Sett ett kryss.
Irritabel?33	Bruker ikke smør/margarin 71 1 Meierismør
	Wielensmor
Glad og optimistisk? 34	
Glad og optimistisk? 34	Hard margarin
Nedfor/deprimert?35	Hard margarin 3 Bløt (soft) margarin 4
	Hard margarin 3 Bløt (soft) margarin 4 Smør/margarin blanding 5
Nedfor/deprimert?35	Hard margarin 3 Bløt (soft) margarin 4 Smør/margarin blanding 5 Lettmargarin 6
Nedfor/deprimert?35	Hard margarin 3 Bløt (soft) margarin 4 Smør/margarin blanding 5
Nedfor/deprimert?35	Hard margarin 3 Bløt (soft) margarin 4 Smør/margarin blanding 5 Lettmargarin 6
Nedfor/deprimert? 35	Hard margarin 3 Bløt (soft) margarin 4 Smør/margarin blanding 5 Lettmargarin 6 UTDANNING/ARBEID Hvilken utdanning er den høyeste du har fullført?
Nedfor/deprimert?35	Hard margarin 3 Bløt (soft) margarin 4 Smør/margarin blanding 5 Lettmargarin 6 UTDANNING/ARBEID
Nedfor/deprimert?35	Hard margarin 3 Bløt (soft) margarin 4 Smør/margarin blanding 5 Lettmargarin 6 UTDANNING/ARBEID Hvilken utdanning er den høyeste du har fullført? Grunnskole, 7-10 år, framhaldsskole, folkehøgskole 72 1 Realskole, middelskole, yrkesskole, 1-2-årig
Nedfor/deprimert?35	Hard margarin 3 Bløt (soft) margarin 4 Smør/margarin blanding 5 Lettmargarin 6 UTDANNING/ARBEID Hvilken utdanning er den høyeste du har fullført? Grunnskole, 7-10 år, framhaldsskole, folkehøgskole 72 1 Realskole, middelskole, yrkesskole, 1-2-årig videregående skole 2
Nedfor/deprimert?35	Hard margarin 3 Bløt (soft) margarin
Nedfor/deprimert?35	Hard margarin 3 Bløt (soft) margarin. 4 Smør/margarin blanding. 5 Lettmargarin 6 UTDANNING/ARBEID Hvilken utdanning er den høyeste du har fullført? Grunnskole, 7-10 år, framhaldsskole, folkehøgskole. 72 Realskole, middelskole, yrkesskole, 1-2-årig videregående skole. 2 Artium, øk.gymnas, allmennfaglig retning i videregående skole 3
Nedfor/deprimert?35 Ensom?36 1 2 3 4 RØYKING Røykte noen av de voksne hjemme da du vokste opp?37 Bor du, eller har du bodd, sammen med noen dagligrøykere etter at du fylte 20 år?38 Hvis "JA", hvor mange år tilsammen?39	Hard margarin 3 Bløt (soft) margarin
Nedfor/deprimert?35 Ensom?36 1 2 3 4 RØYKING Røykte noen av de voksne hjemme da du vokste opp?37 Bor du, eller har du bodd, sammen med noen dagligrøykere etter at du fylte 20 år?38 Hvis "JA", hvor mange år tilsammen?39 Hvor lenge er du vanligvis daglig	Hard margarin 3 Bløt (soft) margarin
Nedfor/deprimert?35 Ensom?36 1 2 3 4 RØYKING Røykte noen av de voksne hjemme da du vokste opp?37 Bor du, eller har du bodd, sammen med noen dagligrøykere etter at du fylte 20 år?38 Hvis "JA", hvor mange år tilsammen?39 Hvor lenge er du vanligvis daglig tilstede i røykfylt rom?41 Antall timer	Hard margarin 3 Bløt (soft) margarin
Nedfor/deprimert?35 Ensom?36 1 2 3 4 RØYKING Røykte noen av de voksne hjemme da du vokste opp?37 Bor du, eller har du bodd, sammen med noen dagligrøykere etter at du fylte 20 år?38 Hvis "JA", hvor mange år tilsammen?39 Hvor lenge er du vanligvis daglig	Hard margarin
Nedfor/deprimert?35 Ensom?36 1 2 3 4 RØYKING Røykte noen av de voksne hjemme da du vokste opp?37 Bor du, eller har du bodd, sammen med noen dagligrøykere etter at du fylte 20 år?38 Hvis "JA", hvor mange år tilsammen?39 Hvor lenge er du vanligvis daglig tilstede i røykfylt rom?41 Antall timer	Hard margarin 3 Bløt (soft) margarin
Nedfor/deprimert?35 Ensom?36 1 2 3 4 RØYKING Røykte noen av de voksne hjemme da du vokste opp?37 Bor du, eller har du bodd, sammen med noen dagligrøykere etter at du fylte 20 år?38 Hvis "JA", hvor mange år tilsammen?39 Hvor lenge er du vanligvis daglig tilstede i røykfylt rom?41 Sett 0 hvis du ikke oppholder deg i røykfylt rom. Røyker du selv:	Hard margarin
Nedfor/deprimert?35 Ensom?36 I 2 3 4 RØYKING Røykte noen av de voksne hjemme da du vokste opp?37 Bor du, eller har du bodd, sammen med noen dagligrøykere etter at du fylte 20 år?38 Hvis "JA", hvor mange år tilsammen?39 Hvor lenge er du vanligvis daglig tilstede i røykfylt rom?41 Sett 0 hvis du ikke oppholder deg i røykfylt rom. Røyker du selv: Sigaretter daglig?43	Hard margarin
RØYKING Røykte noen av de voksne hjemme da du vokste opp? Bor du, eller har du bodd, sammen med noen dagligrøykere etter at du fylte 20 år? 38 Hvis "JA", hvor mange år tilsammen? 39 Hvor lenge er du vanligvis daglig tilstede i røykfylt rom? 41 Sett 0 hvis du ikke oppholder deg i røykfylt rom. Røyker du selv: Sigaretter daglig? 43 Sigarer/sigarillos daglig? 44	Hard margarin
Nedfor/deprimert?35 Ensom?36 I 2 3 4 RØYKING Røykte noen av de voksne hjemme da du vokste opp?37 Bor du, eller har du bodd, sammen med noen dagligrøykere etter at du fylte 20 år?38 Hvis "JA", hvor mange år tilsammen?39 Hvor lenge er du vanligvis daglig tilstede i røykfylt rom?.41 Sett 0 hvis du ikke oppholder deg i røykfylt rom. Røyker du selv: Sigaretter daglig?43 Sigarer/sigarillos daglig?44 Pipe daglig?45	Hard margarin
RØYKING Røykte noen av de voksne hjemme da du vokste opp?	Hard margarin
RØYKING Røykte noen av de voksne hjemme da du vokste opp? Bor du, eller har du bodd, sammen med noen dagligrøykere etter at du fylte 20 år? 38 Hvis "JA", hvor mange år tilsammen? 39 Hvor lenge er du vanligvis daglig tilstede i røykfylt rom? 41 Sett 0 hvis du ikke oppholder deg i røykfylt rom. Røyker du selv: Sigaretter daglig? 43 Sigarer/sigarillos daglig? 44 Pipe daglig? 45	Hard margarin
RØYKING Røykte noen av de voksne hjemme da du vokste opp?	Hard margarin
RØYKING Røykte noen av de voksne hjemme da du vokste opp?	Hard margarin
RØYKING Røykte noen av de voksne hjemme da du vokste opp?	Hard margarin
RØYKING Røykte noen av de voksne hjemme da du vokste opp?	Hard margarin
RØYKING Røykte noen av de voksne hjemme da du vokste opp?	Hard margarin
Røykte noen av de voksne hjemme da du vokste opp?	Hard margarin
Røykte noen av de voksne hjemme da du vokste opp?	Hard margarin
Røykte noen av de voksne hjemme da du vokste opp?	Hard margarin

HEALTH SURVEYInvitation



Date of birth

Social security No.

Municipality

Electoral ward No.

Welcome to the Tromsø Health Survey!

The Health Survey is coming to Tromsø. This leaflet will tell you when and where. You will also find information about the survey in the enclosed brochure.

We would like you to fill in the form overleaf and take it with you to the examination.

The more people take part in the survey, the more valuable its results will be. We hope, therefore, that

you will be able to come. Attend even if you feel healthy, if you are currently receiving medical treatment, or if you have had your cholesterol and blood pressure measured recently.

Yours sincerely,

Municipal Health Authorities Faculty of Medicine - University of Tromsø National Health Screening Service



TOOK OWN HEALTH	EXERCISE
What is your current state of health? Tick one box only.	How has your physical activity in leisure time been during this
Poor 12 1	last year? Think of your weekly average for the year.
Not so good 2	Time spent going to work counts as leisure time.
Good	Hours per week
Very good 4	Light activity (not None Less than 1 1-2 3 or more
Do you have or have you had: Yes No Age first	sweating/out of breath) 56
bo you have, or have you had.	Hard activity (sweating/
A heart affack13	out of breath)57
Angina pectoris (heart cramp) 16	1 2 3 4
A cerebral stroke/ brain haemorrhage 19 years	COFFEE
Asthma 22 years	How many cups of coffee do you drink daily?
Diabetes	Put 0 if you do not drink coffee daily.
	Coarsely ground coffee for brewing 58
Do you take medications for high blood pressure?	Other coffee 60 Cups
Currently 28 1	
Previously, but not now 2	ALCOHOL
Never used	Are you a teetotaller? 62 Yes No
Have you during the last year suffered from pains	How many times a month do you normally drink alcohol? Do not count low-alcohol beer.
and/or stiffness in muscles and joints that have	Times
lasted continuously for at least 3 months?	Put 0 if less than once a month 63
	How many glasses of beer, wine or spirits do you
Have you in the last two weeks felt:	normally drink in a fortnight? 65 Beer Wine Spirits
Very	Do not count low-alcohol beer. Glasses Glasses Glasses
No A little A lot much	Put 0 if less than once a month.
Nervous or worried?, 30	FAT
Anxious?31	What type of margarine or butter do you usually use on
Confident and calm? 32	bread? Tick one box only.
Irritable? 33	Don't use butter/margarine 71
Happy and optimistic? 34	Butter2
Down/depressed? 35	Hard margarine 3
Lonely?36	Death and for a sum assistance of the sum of
1 2 3 4	Light warmaning
CMOKING	
SMOKING	EDUCATION/WORK
Did any of the adults at home smoke while you were growing up?	What is the highest level of education you have completed?
you were growing op:	7-10 years primary/secondary school,
Do you currently, or did you previously, live together Yes No	modern secondary school
with daily smokers after your 20 th birthday? ³⁸	school, 1-2 years senior high school
Years	High school diploma
If "YES", for how many years in all? 39	(3-4 years)3
How many hours a day do you normally spend	College/university, less than 4 years 4
in smoke-filled rooms? 41	College/university, 4 or more years
	What is your current work situation?
Put 0 if you do not spend time in smoke-filled rooms.	Paid work 73
Do you yourself smoke: Yes No	Full-time housework 74
Cigarettes daily? 43	Education, military service 75
Cigars/ cigarillos daily? 44	Unemployed, on leave without payment 76
A pipe daily? 45	How many hours of paid work do you have per 77 No. of hours
If you previously smoked daily, how long	week?
is it since you stopped?	Do you receive any of the following benefits? Sickness benefit (sick leave)
	Rehabilitation benefit 80
If you currently smoke, or have smoked before:	Disability pension
	Old-age pension 82
How many cigarettes do you or did you usually smoke per day?	Social welfare benefit 83
	Unemployment benefit 84
1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1. 1	
now old were you when you began	ILLNESS IN THE FAMILY
How old were you when you began smoking daily?	Have one or more of your parents or
now old were you when you began	Have one or more of your parents or siblings had a heart attack or had angina (heart cramp)?

Appendix D

Questionnaire 1 (<70 years), the 5th Tromsø Study 2001-02

Norwegian version

<u>.</u>	MOSJON OG FYSISK AKTIVITET	13. BRUK	K AV MEDISINER	H		
10.1	1 Hvordan har din fysiske aktivitet <u>i fritiden</u> vært det siste året?	Med n Kosttil	Med medisiner mener vi her medisiner kjøpt på apotek. Kosttilskudd og vitaminer regnes ikke med her	r medisiner k	jøpt på apo ed her	tek.
	i orsmålene.	13.1 Bruker du?	du?	» ⊢	. Na Si.≕	Før, men ikke nå
	Tim er pr. uke Lett aktivitet Ingen Under1 1-2 3 og mer (//kke svett/andpusten),	Medisi Kolest	Medisin mot høyt blodtrykk			
	(Svett/andpussen)	13,2 Hvor c følgen (Sett e	Hvor ofte har du i løpet av de <u>siste 4 ukene</u> brukt følgende medisiner? Ikke Sjeldnere Hver uke (Sett ett kryss pr. linje) huksisse em hver men Ikke (Sett ett kryss pr. linje)	r de <u>siste 4 u</u> Ikke brukt siste 4 uker	Sjeldnere Hver much uke	er uke, en ikke aglig
10.2	2 Angi bevegelse og kroppslig anstrengelse i <u>din fritid.</u> Hvis aktiviteten varlerer meget i eks. mellom sommer og vinter, så ta et gjennomsnitt. Sporsmålet gjelder bare <u>det siste året.</u> (Selt kryss i den rula som passer bes)	Smerte	Smertestillende uten resept Smertestillende på resept			
	Leser, ser på fjernsyn eller annen stillestitende beskjettigelse?	Sovem Berolig	Sovemedisin Beroligende medisin			
	Spaserer, sykler eller beveger deg på annen måte minst 4 timer i uka?	Medisi	Medisin mot depresjon Annen medisin på resept		~	
	uka) 🔲 3	13.3 For de og sor Angi na	For de medisinene som du har krysset av for i pkt. og som du har brukt i lopet av de <u>siste 4 ukene:</u> Angi navnet og hvilken grunn det er til at du tar/har tatt	u har krysse et av de <u>sist</u> m det er til at	krysset av for i pkt. 13. de <u>siste 4 ukene:</u> er til at du tar/har tatt	d. 13.
	Trener hardt eller driver konkurranseidrett regelmessig og <u>flere ganger i uka?</u>	disse ((Kryss	disse (sykdom eller symptom): (Kryss av for hvor lenge du har brukt medisinen)	m): har brukt me	disinen)	Hvor le brukt n
‡	. FAMILIE OG VENNER	Navn (ett në	Navn på medisinen: (ett navn pr. linje):	Grunn til bruk av medisinen:	uk en:	Inntil 1 år
#	1 Bor du sammen med: Ektefelle/samboer?					
11.2						
	Regn med de du kan snakke fortrolig med og som kan gi deg hipg dersom du trenger det. Ill kke med de du bor sammen med, men					
11.3						
É	(Sett bare ett kryss) Stor					
	Incresse interesse interes	(-			
11.4	Hvor mange foreninger, lag, grupper, kirkesamfunn e.l. deltar du i på fritiden? Antall (Skriv 0 hvis ingen)	14. RES	2	MAET SK	SKAL BARE	ш
11,5	Foler du at du kan pâvirke det som skjer i lokalsamfunmet der du bor? (Seit bare eit kryss) Har ikke Ja, i stor grad Ja, en del Ja, i liten grad Nei forsøkt	BES 14,1 Hvor g menst	BESVARES AV KVINNE Hvor gammel var du da du fikk menstruasion aller første gang?	AV KVINNEK du da du fikk er første gang?	Alder i år	
ţ	1	14.2 Hvis d hvor g	Hvis du ikke lenger får menstruasjon, hvor gammel var du da den sluttet?	enstruasjon, en sluttet?		IЩ
12.1	VET Har en eller flere av dine foreldre eller sosken JA NEI VET hatt hjerterfakt (sår på hjerte) eller annins annins annins annins annins annins annins i kiloterteramon?	14.3 Er du	Er du gravid nå? Ja Nei Usikker	Over fruktbar alder	bar	'
12.2	Kryss av for de slektningene som har eller har hatt noen av sykdommene: (Sett kryss for hver linje)	4.4 Hvor n	n har c		Antall barn	
	Hjerneslag eller Mor Far Bror Soster Barn av disse hjerneblødning	14.5 Bruke (Sett e	Bruker du, eller har du brukt? (Sett ett kryss for hver linje)	Z	Før, men ikke nå	nå
	Hjerteinfankt for 60 års alder	P-pille/ Hormo	P-pille/minipille/p-sprøyte Hormonspiral (ikke vanlig spiral)	oiral)		
	Astma	Østrog	Ostrogen (tabletter eller plaster) Ostrogen (krem eller stikkpiller)	ster)		
12.3	Diabetes (sukkersyke). Hvis noen slekthinger har diabetes, i hvilken alder fikk de diabetes franch dan som filt det dat diabetes far non dan som filt det	14.6 Hvis d Hvor le	H vis du bruker/har brukt <u>reseptpliktig</u> østrogen: Hvor lenge har du brukt dette? Antall år	eseptpliktig te?	østrogen: Antall år	
	ars alder Brors alder Sosters alder Barns alder	4.7 Hvis d	14.7 Hvis du bruker p-pille, minipille, p-sprøyle, hormonspiral eller østrogen; hvilket merke bruker du?	nipille, p-spr en; hvilket n	øyte, nerke bruke	er du?

- Aktri Brukt Daglig 1 og 13.2,

Helse-undersøkelsen

Personlig innbydelse

(Kryss av for nvor lenge du nar brukt medisinen)	tu nar brukt medisinen)	Hvor len brukt me	Hvor lenge har du brukt medisinen?
Navn på medisinen: (ett navn pr. linje):	Grunn til bruk av medisinen:	Inntil 1 år	Ett år eller mer

14.1	Hvor garr menstrua	imel var d isjon aller	14,1 Hvor gammel var du da du fikk menstruasjon aller første gang? 14.9 Hvis du ikke langer får manetruasion	ck 1g? Friesion	Alder i år	3	
	hvor gam	mel var d	hvor gammel var du da den sluttet?	luttet?	Alder i år		
5.	14.5 Er du gravid na ? Ja Nei	Nei	Usikker	Over fruktbar alder	ä	_	
	_	ο _γ		4			
14.4	Hvor man	ige barn h	14.4 Hvor mange barn har du født?		Antall barn		*0 00

 \dashv

8. RØYKING	Н	8.2 Røykte noen av de voksne hjemme JA NEI da du vokste opp?	8,3 Bor du, eller har du bodd, sammen med noen dadijerevkere etter at du fulte 20 år?	Ja, nà Ja, rà Ja, ràdigere Aldri	Hvis ALDRI: Hopp til spørsmål 9 (UTDAN)	8.5 Hvis du røyker daglig nå, røyker du: JA NEI	Sigaretter?		8.6 Hvis du har roykt daglig <u>tidligere,</u> hvor lenge er det siden du sluttet? Antall år	8.7 Hvis du røyker daglig nå eller har røykt tidligere:	Hvor mange sigaretter røyker eller røykte du vanligvis daglig? Antali sigaretter	Hvor gammel var du da du begynte â Alder i âr røyke daglig?	Hvor mange år til sammen har du røykt daglig?	9. UTDANNING OG ARBEID	9.1 Hvor mange års skolegang har du gjennomfort? Antall år	(Ta med alle år du har gått på skole eller studert)		 Beskriv virksomheten på det arbeidsstedet (avdelingen) der du utførte inntektsgivende arbeid i lengst tid de siste 12 mnd. (Feks. regnskapsbyrå, ungdomsskole, 	barneavd, på sykehus, snekkerverksted, bilverksted, bank, dagligvarehandel e.l.)	Virksamhet. Virksamhet. Hvis pensjonert, skriv tidligere hovedvirksomhet og yrke. Gjelder også 9.4	9.4 Hvilket yrkefrittel har eller hadde du på dette arbeidsstedet? (F.eks. sekretær, lærer, industriarbeider, barnepleier, myhalenakkar avidiannelader selnar elster els	Yrke:	9.5 Arbeider du i ditt hovedyrke som selvstendig, som ansatt eller som familiemedlem uten fast avtalt Jonn? Salvstendig Ansatt Familiemedlem		9.6 Mener du at du stàr i fare for à miste ditt JA NEI nàværende arbeid eller inntekt de nærmeste 2 årene?	9.7 Mottar du noen av følgende ytelser? JA NEI	Sykepenger (er sykmeldt)	Alderstrygd, fortidspensjon (AFP) eller ettertattepensjon.	Vierepensjon (net eller delvis)	Dagpenger under arbeidsledighet	Overgangsstønad for enslige forsørgere
7. MAT OG DRIKKE	7.1 Hvor ofte spiser du vanligvis disse matvarene? (Sett ett kryss pr. lirje) Sjeden 13.9, 1.3, 4.6, 1.2, 3.9 et mer (Sett ett kryss pr. lirje) Sjedin 13.9, 1.0, 1.0, 1.0, 1.0, 1.0, 1.0, 1.0, 1.0		Ost (alle typer)	Foteter	Rå grønnsaker/salat	Feit fisk (i.eks. laks,	er du oftest? (Sett ett kryss pr. linje) Bruker Meieri- Hard Myklett	margarin ma	matlagingen	7.3 Bruker du folgende kosttilskudd: Ja, dagig telant Nei Tran, trankapsler, fiskeoljekapsler?		7.4 Hvor mye drikker du vanligvis av folgende? (Sett eft kryss pr. Inje) Selden 1-6 1 glass 2-3 4 glass lating glass pridag glass et met		Lettmelk, cultura, lettyoghurt	Ekstra lettmelk	Fruktjuice	Vann		7.5 Drikker du vanligvis brus/cola: Med sukker 🗍 1 Uten sukker 🧾 2	7.6 Hvor mange kopper kaffe og te drikker du daglig? Antall kopper (Sett 0 for de typene du ikke drikler daglig)	Filterkaffe	Kokekaffe/frykkanne	Annen kalle	Те	7.7 Omtrent hvor ofte har du i løpet av det siste året drukket alkohol? (Lettlo og diskolvinitt di ergers kker med en det en det en det en her kieke drukket. Noen is annen 1 aana	alkohol siste år siste år	2-3 ganger ca.1 gang 2-3 ganger 47 ganger primaned luka luka luka luka	le glass	eller drinker har du vanligus drukket? 7.9 Ombrent hvor mange ganger i lopet av det siste året har du drukket så mye som minst 5 glass	eller drinker i lopet av ett dogn? Anfall ganger 7.10 När du drikker, drikker da avanligvis: (Sett ett eller flere kryss)	
3. ANDRE PLAGER	3.1 Under finner du en liste over uilke problemer. Har du opplevd noa av dette den <u>siste uken</u> (til og med i dag)?	(seu eu kryss lot inver plage) likke Litt Ganske Veldig plaget plaget mye mye	Plutselig frykt uten grunn	Matthet eller svimmelhet	Foler deg anspent eller oppjaget	Lett for å klandre deg selv 📗 📗 🛅	Søvnproblemer	Folelse av å være unyttig, lite verd	Følelse av at alt er et slit	Følelse av håploshet mht. framtida 1 2 3 4	4. BRUK AV HELSETJENESTER	4.1 Hvor mange ganger de siste 12 månedene har du selv brukt: (Sett ett kryss for hver linje)		Bedriftslege	(private eller på poliktinikk)	Annen spesialist (privat eller på poliktinikk)	Sykehusinnleggelse	Hjemmesykepleie	Kiropraktor	Alternativ behandler	5. OPPVEKST OG TILHØRIGHET	5.1 Hvor lenge har du samlet bodd i fylket? (Sett 0 hvis mindre enn et halvt ár)	5.2 Hvor lenge har du samlet bodd i kommunen? (Seit O hvis mindre enn et halvt dr)	 Hvor bodde du <u>det meste</u> av tiden før du fylte 16 år? (knyss av for <u>ett</u> allemativ og spesifiser) 		² □	Annet tylke i Norge 3 Hvilket: Utenfor Norge	5.4 Har du flyttet i lopet av de siste fem årene?	2	6. VEKT	6.1 Anslå din vekt da du var 25 år gammel:
. EGEN HELSE	Hvordan er helsen din nå? (Sett bare ett kryss) Dårlig Ikke helt god God Svært god	2 3	1.2 Har du, eller har du hatt?: Alder forste	JA NEI gang	Abula	Høysnue	Kronisk bronkit/emfysem	Diahotos (elikkoreuko)		Benskjørhet (osteoporose)	Fibromyalgi/kronisk smertesyndrom	Psykiske plager som du har sokt hjelp for 🔲 📗	Hjerteinfarkt	Angina pectoris (hjertekrampe)		rjernestag/njerneblødning	1.3 Har du merket anfall med plutselig endring i JA NEI nulsen eller hierberdmen eiste året?	Gâr i bakker, trapper eller fort på flat mark?	1.5 Hvis du fâr slike smerter, pleier du da â: Sloope? Sakhe farten? Fortsette i samme takt?	2 🔲 3	1.6 Dersom du stopper, forsvinner smertene da etter mindre enn 10 minutter?	A NEI 7.7 Kan slike smerter opptre selv om du er i ro?	. MUSKEL OG SKJELETTPLAGER1 Har du vært plaget med smerter og/eller stivhet	i muskler og ledd i løpet av de siste 4 <u>ukene?</u> (Varighet angis bare hvis du har hatt plagen) Varighet 2 uker like En del Sterk	plaget plaget	Armer, hender	Korsryggen	Hofter, ben, føter	1 2 3 1 2 Alder 2 Alder 2 1 Alder 2	Brudd i hândledd/underarm?	Lárhaisbrudd?

Γ



Personal Invitation

Don't write here	5.3 (Municipality)	(County)	(Country)			
9.3 (Business)		9.4 (Occupation)		14.7 (Mark)		

1. \	YOUR OWN HEALTH	3.	OTHER COMPLAINTS
1.1	What is your current state of health? (Tick one only) Poor Not so good Good Very good 1 2 3 4	3.1	Below is a list of various problems. Have you experienced any of this during the last week (including today)? (Tick once for each complaint) No Little Pretty Very
	_ 1 2 3 4		complaint complaint much
1.2	Do you have, or have you had?: Age first		Sudden fear without reason
	Yes No	Т	Feel afraid or anxious
	Asthma	1	Faintness or dizziness
	Hay fever		Feel tense or upset
	hay lever		Tend to blame yourself
	Chronic bronchitis/emphysema		Depressed, sad
	Diabetes		Feeling of being useless, worthless
	Diabetes		Feeling that everything is a struggle
	Osteoporosis		Feeling of hopelessness with regard to the future 1 2 3 4
	Fibromyalgia/chronic pain syndrome	4.	USE OF HEALTH SERVICES
	Psychological problems for which you have sought help	4.1	How many times in the <u>last 12 months</u> have you been to/used: (Tick once for each line) None 1-3 4 or times more
	A heart attack		A general medical practitioner (GP)
			Medical officer at work
	Angina pectoris (heart cramp)		Psychologist or psychiatrist
	Cerebral stroke/brain haemorrhage		Other specialist (private or out-patient clinic)
			Emergency GP (private or public)
1.3	Have you noticed attacks of sudden changes in Yes No		Hospital admission
	your pulse or heart rhythm in the last year? Yes No	Т	Home nursing care
1.4	Do you get pain or discomfort in the chest when: Walking up hills, stairs or walking fast on level ground?	'	Physiotherapist
15	If you get such pain, do you usually:		Chiropractor
	Stop? Slow down? Carry on at the same pace?		Dentist
	1 2 3		Alternative practitioner
1.6	If you stop, does the pain disappear within 10 minutes?	5.	CHILDHOOD/YOUTH AND AFFILIATION
	Yes No	5.1	How long altogether have you lived in the county?
1.7	Can such pain occur even if you are at rest?		(Put 0 if less than half a year)
2. I	MUSCULAR AND SKELETAL COMPLAINTS	5.2	How long altogether have you lived in the municipality?
2.1	Have you suffered from pain and/or stiffness in muscles and joints during the <u>last 4 weeks</u> ?		(Put 0 if less than half a year) Where did you live most of the time before the age of 16?
	(Give duration only if you have had problems) No Some Severe complaint comp	5.5	(Tick one option and specify)
	Neck/shoulders		Same municipality 🗀1
	Arms, hands		Another municipality in the county
	Upper part of your back		Another county in Norway 3 Which one:
	Lumbar region		Outside Norway 4 Country::
	Hips, legs, feet	5.4	Have you moved within the last five years?
	Other places		No Yes, one time Yes, more than once
	1 2 3 1 2 Age last time		
2.2	Have you ever had: Yes No		
	Fracture in the wrist/forearm	6.	BODY WEIGHT
	Hip fracture?	6.1	Estimate your body weight when you were 25 years old:

7.1 Now often do you usually eat these foods? First, berries	7. F	FOOD AND BEVERAGES	8. 9	SMOKING
Print_berries	7.1	(Tick once per line) Rarely 1-3 times 1-3 times 4-6 times 1-2 times 3 times or	8.1	
Potatoes		Fruit, berries	8.2	Did any of the adults smoke at nome
Solid vegetables Solid veget			8.3	together with a daily smoker after your
Faity fish (e.g. salmon.			8.4	Yes, now Yes, previously Neve
7.2 What type of fat do you usually use? (Tiek once per fire) What type of fat do you usually use? (Tiek once per fire) For cooking		Fatty fish (e.g. salmon,	8.5	
Cigarac(cigatilors?	7.2			Cigarettes?
For cooking		Don't Hard Soft/light use Butter margarine margarine Oils Other		
7.3 Do you use the following dictary supplements: Cod liver oil, fish oil capsules Cod liver yil capsules C				
supplements: Vitamins and/or mineral supplements?	7.3	1 2 3 4 5 6		long is it since you stopped? Number of years
7.4 How much of the following do you usually drink? (Tick once per fave) Review 1.6 Rev		supplements:	8.7	before:
Full milk, full-flat curded milk,	- 4	• •		
Semi-skimmed milk, semi-skimmed	7.4	(Tick once per line) Rarely 1-6 1 glass 2-3 4 glasses /never glasses /day glasses or more		
Skimmed milk		yoghurt		How many years in all have you smoked daily? Number of years
Subsective the second of the street of the		Skimmed milk, skimmed	9. E	EDUCATION AND WORK
Subsective that the years you have attended school or studied			9.1	
Mineral water (e.g. Farris,				(Include all the years you have attended school or studied)
Cola-containing soft drink				
Other soda/soft drink		Ramløsa etc)		
7.5 Do you usually drink soft drink: with sugar 1 without sugar 2 7.6 How many cups of coffee and tea do you drink daily? Number of cups (Put 0 for the types you don't drink daily) Filtered coffee Secretary, teacher, industrial worker, nurse, carpenter, manager, salesman, driver, etc.) Other type of coffee Secretary, teacher, industrial worker, nurse, carpenter, manager, salesman, driver, etc.) Occupation: 7.7 Approximately how often have you during the last year consumed alcohol? (Do not count low-alcohol and alcohol-free beer) Never Have not consumed Secretary Self-employee Family member 7.7 Approximately how often have you during the last year consumed alcohol? (Do not count low-alcohol and alcohol-free beer) Never Have not consumed Secretary Self-employee Family member 7.6 Do you believe that you are in danger of losing your current work or income within the next two years? 7.8 When you drink alcohol, how many glasses or drinks do you normally drink? number 7.9 Approximately how many times during the last year: 7.8 When you drink alcohol, how many glasses or drinks within 24 hours? Number of times 7.10 When you drink, do you normally drink? (Tick one or more) 8 Business: I' retired, enter the former business and occupation. Also applies to 9.4 9.4 Which occupation/title have or had you at this workplace? (e.g. Secretary, teacher, industrial worker, nurse, carpenter, manager, salesman, driver, etc.) Occupation: 9.5 In your main occupation, do you work as self-employed, as an employee or family member without regular salary? Self-employee 9.6 Do you believe that you are in danger of losing yes No your current work or income within the next two years? 9.6 Do you believe that you are in danger of losing yes No your current work or income within the next two years? 9.7 Do you receive any of the following benefits? 9.8 Vick years 9.9 Do you believe that you are in danger of losing yes No you greater the former business and occupation.		Other soda/soft drink	9.3	you had paid work for the longest period in the last 12 months. (e.g. Accountancy firm, school, paediatric department, carpentry workshop, garage, bank,
Also applies to 9.4				Business:
Boiled coffee/coarsely ground coffee for brewing Other type of coffee	7.6	(Put 0 for the types you don't drink daily)		
Occupation: Other type of coffee			9.4	(e.g. Secretary, teacher, industrial worker, nurse,
Tea		Boiled coffee/coarsely ground coffee for brewing		Occupation:
consumed alcohol? (Do not count low-alcohol and alcohol-free beer) Never consumed alcohol alcohol last year last year a month 1 2 3 times per month a week glasses or drinks do you normally drink? 7.8 When you drink alcohol, how many glasses or drinks do you normally drink? number 7.9 Approximately how many times during the last year have you consumed alcohol equivalent to 5 glasses or drinks within 24 hours? Number of times 7.10 When you drink, do you normally drink: (Tick one or more) Beer Wine Spirits About 1 time a month a mont			9.5	as an employee or family member without regular salary?
consumed alcohol? (Do not count low-alcohol and alcohol-free beer) Never consumed alcohol alcohol last year last year a month 1 2 3 times per month a week glasses or drinks do you normally drink? 7.8 When you drink alcohol, how many glasses or drinks do you normally drink? number 7.9 Approximately how many times during the last year have you consumed alcohol equivalent to 5 glasses or drinks within 24 hours? Number of times 7.10 When you drink, do you normally drink: (Tick one or more) Beer Wine Spirits About 1 time a month a mont	77	Approximately how often have you during the last year	9.6	Do you believe that you are in danger of losing Yes No
9.7 Do you receive any of the following benefits? Yes No 2-3 times About1 time a week a week a week 5 To those who have consumed the last year: 7.8 When you drink alcohol, how many glasses or drinks do you normally drink? 7.9 Approximately how many times during the last year have you consumed alcohol equivalent to 5 glasses or drinks within 24 hours? 7.10 When you drink, do you normally drink: (Tick one or more) Beer Wine Spirits 9.7 Do you receive any of the following benefits? Yes No Old age pension, early retirement (AFP) or survivor pension	1.1	Consumed alcohol? (Do not count low-alcohol and alcohol-free beer) Never Have not consumed A few times About 1 time	0.0	your current work or income within the next
per month a week a week a week a week a week a week Sickness benefit (are on sick leave) Cold age pension, early retirement (AFP) or survivor pension Cold age pension, early retirement Cold age pension, early retir			9.7	Do you receive any of the following benefits? Yes No
To those who have consumed the last year: 7.8 When you drink alcohol, how many glasses or drinks do you normally drink? number 7.9 Approximately how many times during the last year have you consumed alcohol equivalent to 5 glasses or drinks within 24 hours? Number of times 7.10 When you drink, do you normally drink: (Tick one or more) Beer Wine Spirits Old age pension, early retirement (AFP) or survivor pension		per month a week a week a week		
7.9 Approximately how many times during the last year have you consumed alcohol equivalent to 5 glasses or drinks within 24 hours? Number of times 7.10 When you drink, do you normally drink: (Tick one or more) Beer Wine Spirits Rehabilitation/reintegration benefit		To those who have consumed the last year:		Old age pension, early retirement (AFP) or survivor pension
year have you consumed alcohol equivalent to 5 glasses or drinks within 24 hours? Number of times 7.10 When you drink, do you normally drink: (Tick one or more) Beer Wine Spirits Disability peristor (tall of partial) Unemployment benefits during unemployment	7.8	glasses or drinks do you normally drink? number	\top	Rehabilitation/reintegration benefit
7.10 When you drink, do you normally drink: (Tick one or more) Beer Wine Spirits Social welfare benefits	7.9	year have you consumed alcohol equivalent to		
Beer Wine Spirits	7.10			

Don't know. not applicable Beyer Hecos

Appendix E

Questionnaire 1, the 6th Tromsø Study 2007-08

Norwegian version



	penn. Du kan ikke bruke komma, bruk b		
	2007 – 2008 KONFIDENSIELT		
1	HELSE OG SYKDOMMER Hvordan vurderer du din egen helse sånn i	6	Under finner du en liste over ulike problemer. Har du opplevd noe av dette <u>den siste uken</u> (til og med i dag)? (Sett ett kryss for hver plage)
	alminnelighet?		Ikke Litt Ganske Veldig plaget plaget mye mye
			Plutselig frykt uten grunn
	☐ Dårlig☐ Meget dårlig☐ ☐ Dårlig☐ ☐ Meget dårlig☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐		Matthet eller svimmelhet \square \square \square \square Føler deg anspent eller
2	Hvordan synes du at helsen din er sammenlignet med andre på din alder?		oppjaget
	☐ Mye bedre		Søvnproblemer
	 □ Litt bedre □ Omtrent lik □ Litt dårligere □ Mye dårligere 		Nedtrykt, tungsindig
3	Alder første Har du eller har du hatt? Alder første Ja Nei gang		Følelse av håpløshet mht. framtida
	Hjerteinfarkt	7	BRUK AV HELSETJENESTER Har du i løpet av de siste 12 måneder vært hos: Hvis JA; Hvor mange ganger? Ja Nei Ant ggr
	Hjerteflimmer (atrieflimmer)		Fastlege/allmennlege
	Astma		Legespesialist utenfor sykehus (utenom fastlege/allmennlege/psykiater)
	Psykiske plager (som du har søkt hjelp for)		Annen behandler (homøopat, akupunktør, fotsoneterapeut, naturmedisiner, håndspålegger, healer, synsk el.l)
	Nyresykdom, unntatt urinveisinfeksjon		Tannlege/tannpleier
4	Migrene	8	Har du i løpet av de siste 12 måneder vært på sykehus? Ja Nei Ant ggr
	smerter som har vart i <u>3 måneder eller mer</u> ? ☐ Ja ☐ Nei		Innlagt på sykehus 🗆 🗆 🗆
5	Hvor ofte har du vært plaget av søvnløshet de siste		Konsultasjon ved sykehus uten innleggelse;
J	12 måneder?		Ved psykiatrisk poliklinikk 🔲 🗀 📗
	Aldri, eller noen få ganger		Ved annen sykehuspoliklinikk \[\square \square \square \square \qq \qqq \qqq \qq
	☐ 1-3 ganger i måneden ☐ Omtrent 1 gang i uken ☐ Mer enn 1 gang i uken	9	Har du gjennomgått noen form for operasjon i løpet av de siste 3 årene? Ja Nei Heritage Her

BRUK AV MEDISINER FAMILIE OG VENNER 10 Bruker du, eller har du brukt, noen av følgende 13 Hvem bor du sammen med? (Sett kryss for hvert medisiner? (Sett ett kryss for hver linje) spørsmål og angi antall) Alder → Ja Nei Antall første Ektefelle/samboer...... brukt Nå Før gang Andre personer over 18 år...... Medisin mot høyt blodtrykk... Personer under 18 år..... Kolesterolsenkende medisin.... Medisin mot hjertesykdom.... 14 Kryss av for de slektninger som har eller har hatt Foreldre Søsken Vanndrivende medisin..... Medisin mot beinskjørhet Hjerteinfarkt..... (osteoporose) П Hjerteinfarkt før fylte 60 år..... Insulin..... Angina pectoris (hjertekrampe)..... Diabetesmedisin (tabletter)...... Hjerneslag/hjerneblødning..... Stoffskiftemedisinene Beinskjørhet (osteoporose) Thyroxin/levaxin..... Magesår/tolvfingertarmsår..... \Box Hvor ofte har du i løpet av de siste 4 ukene brukt følgende medisiner? (Sett ett kryss pr linje) Astma..... Diabetes Ikke brukt Sjeldnere Hver siste 4 enn hver uke, men Demens..... uker uke ikke daglig Daglig Psykiske plager..... Smertestillende Rusproblemer..... på resept..... Smertestillende 15 Har du nok venner som kan gi deg hjelp reseptfrie..... når du trenger det? Sovemidler..... ☐ Ja ☐ Nei Beroligende П medisiner..... 16 Har du nok venner som du kan snakke fortrolig med? Medisin mot ☐ Ja ☐ Nei depresjon..... 17 Hvor ofte tar du vanligvis del i foreningsvirksomhet 12 Skriv ned alle medisiner – både de med og uten som for eksempel syklubb, idrettslag, politiske lag, resept – som du har brukt regelmessig i siste 4 ukers religiøse eller andre foreninger? periode. (Ikke regn med vitaminer, mineraler, urter, Aldri, eller noen få ganger i året naturmedisin, andre kosttilskudd etc.) 1-2 ganger i måneden ☐ Omtrent 1 gang i uken ☐ Mer enn en gang i uken ARBEID, TRYGD OG INNTEKT 18 Hva er din høyeste fullførte utdanning? (Sett ett kryss) Grunnskole, framhaldsskole eller folkehøyskole Yrkesfaglig videregående, yrkesskole eller realskole Allmennfaglig videregående skole eller gymnas Høyskole eller universitet, mindre enn 4 år ☐ Høyskole eller universitet, 4 år eller mer Får du ikke plass til alle medisiner, bruk eget ark. 19 Hva er din hovedaktivitet? (Sett ett kryss) VED FRAMMØTE vil du bli spurt om du har brukt ☐ Yrkesaktiv heltid ☐ Hjemmeværende antibiotika eller smertestillende medisiner de siste 24 timene. Om du har det, vil vi be om at du oppgir ☐ Yrkesaktiv deltid Pensjonist/trygdet preparat, styrke, dose og tidspunkt Arbeidsledig Student/militærtjeneste

Hvor hardt mosjonerer du da i gjennomsnitt? ☐ Tar det rolig uten å bli andpusten eller svett. ☐ Tar det så hardt at jeg blir andpusten og svett ☐ Tar meg nesten helt ut Hvor lenge holder du på hver gang i gjennomsnitt? ☐ Mindre enn 15 minutter ☐ 30 minutter – 1 time ☐ 15-29 minutter ☐ Mer enn 1 time ALKOHOL OG TOBAKK
Hvor ofte drikker du alkohol? Aldri Månedlig eller sjeldnere 2-4 ganger hver måned 2-3 ganger pr. uke 4 eller flere ganger pr.uke Hvor mange enheter alkohol (en øl, et glass vin, eller
en drink) tar du vanligvis når du drikker? 1-2
Hvor ofte drikker du 6 eller flere enheter alkohol ved en anledning? aldri sjeldnere enn månedlig månedlig ukentlig daglig eller nesten daglig Røyker du av og til, men ikke daglig?
Ja

tuelt når og hvorfor.

-UNDBLAD MEDIA AS, TROMSØ, 77 75 32 50 - ONR 082222



The form will be read electronically. Please use a blue or black pen You can not use comas, use upper-case letters.

2007 2009 Confidential

	2007 - 2008 Confidential	
1	HEALTH AND DISEASES How do you in general consider your own health to be?	Below you find a list of different situations. Have you experienced some of them in the last weel (including today)? (Tick once for each complaint) No Little Pretty Very
	☐ Very good	complaint complaint much
	☐ Good	Sudden fear without reason \square \square \square
	☐ Neither good nor bad	You felt afraid or worried
	□ Bad	Faintness or dizziness
	□ Very bad +	You felt tense or
2	How is your health compared to others in	upset
	your age?	Easily blamed yourself
	Much better	Sleeping problems
	☐ A little better	Depressed, sad \square \square \square You felt useless,
	About the same	worthless
	☐ A little worse	Feeling that life is a struggle \Box \Box \Box
	☐ Much worse Age first	Feeling of hopelessness with
3	Do you have, or have you had? Yes No time	regard to the future
	A heart attack 📙 📗	USE OF HEALTH SERVICES
	Angina pectoris (heart cramp)	Have you during the last 12 months visited:
	Cerebral stroke/brain hemorrhage	If YES; how many times? Yes No No. of times
	High blood pressure	General practitioner (GP)
	Osteoporosis	Psychiatrist/psychologist
	Asthma	Medical specialist outside hospital
	Chronic bronchitis/Emphysyma/COPD	(other than general practitioner/psychiatrist)
	Diabetes mellitus	Physiotherapist
	Psychological problems (for which you have sought help)	Chiropractor
	Low metabolism	(homeopath, acupuncturist, foot zone therapist, herbal medical practitioner, laying on hands
	Kidney disease, not including urinary	practitioner, healer, clairvoyant, etc.)
	Migraine	Dentist/dental service 📙 🗀 🗀
4	Do you have persistent or constantly recurring	Have you during the last 12 months been to a hospital? Yes No No. of times
	pain that has lasted for 3 months or more?	
	☐ Yes ☐ No	Admitted to a hospital
5	How often have you suffered from sleeplessness during	At psychiatric out-patient clinic \(\square\)
	the last 12 months? Never, or just a few times	At another out-patient clinic
	☐ 1-3 times a month	•
	Approximately once a week	Have you undergone any surgery during the last 3 years? ☐ Yes ☐ No
	☐ More that once a week	+

FAMILY AND FRIENDS USE OF MEDICINE 10 Do you take, or have you taken some of the Who do you live with? (Tick for each question and give the number) following medications? (Tick once for each line) Yes No Number Never Spouse/partner used Now Earlier time Other people older than 18 years.. \Box Medications for high blood pressure People younger than 18 years Lipid lowering drugs Medications for heart disease Tick for the relatives who have or have had Parents Children Siblings Diuretics Medications for П A heart attack osteoporosis A heart attack before age 60 Insulin Angina pectoris (heart cramp) Tablets for diabetes Cerebral stroke/brain haemorrhage Metabolic disorder medications Thyroxine/levaxin Osteoporosis Stomach/duodenal ulcer How often have you during the last 4 weeks used the following medications?(Tick once for each line) Asthma Diabetes mellitus Not used Less than Every the last every week, but Dementia 4 weeks week Daily not daily Psychological problems Painkillers with prescription П П Problem with substance abuse .. \square Painkillers without 15 Do you have enough friends who can give you prescription help when you need it? Sleeping pills ☐ Yes Tranquillizers П Do you have enough friends whom you can talk confidentially with? Antidepressants .. П П How often do you normally take part in State the names of all medications -both those organised gatherings, e.g. sports clubs, political with or without prescription- which you have meetings, religious or other associations? used regularly during the last 4 weeks. Do not include vitamins, minerals, herbs, natural Never, or just a few times a year remedies, other nutritional supplements, etc. 1-2 times a month Approximately once a week **WORK, SOCIAL SECURITY AND INCOME** What is the highest level of education you have completed? (Tick once) Primary or secondary school Technical or vocational school High secondary school (A-level) College/university less than 4 years ☐ College/university 4 years or more If the space is not enough for all medications, use an additional paper of your own. 19 What is your main activity? (Tick once) When attending the survey centre you will be ☐ Full time work asked whether you have used antibiotics or ☐ Housekeeping painkillers the last 24 hours. If you have, you Part time work Retired/benefit recipient will be asked to provide the name of the drug, strength, dose and time of use. ☐ Unemployed Student/military service

20	Do you receive any of the following benefits? Old-age, early retirement or survivor pension Sickness benefit (sick leave) Rehabilitation benefit Full disability pension Partial disability pension Unemployment benefits Transition benefit for single parents Social welfare benefits	26	How hard do you exercise on average? Easy- do not become short-winded or sweaty You become short-winded and sweaty Hard- you become exhausted For how long time do you exercise every time on average Less than 15 minutes
21	What was the households total taxable income last year? Include income from work, social benefits and similar ☐ Less than 125 000 NOK ☐ 401 000-550 000 NOK ☐ 125 000-200 000 NOK ☐ 551 000-700 000 NOK ☐ 201 000-300 000 NOK ☐ 701 000 -850 000 NOK ☐ 301 000-400 000 NOK ☐ More than 850 000 NOK		How often do you drink alcohol? Never Monthly or more infrequently 2-4 times a month 2-3 times a week 4 or more times a week
22	Do you work outdoor at least 25% of the time, or in cold buildings (e.g. storehouse/industry buildings)? Yes No	29	How many units of alcohol (a beer, a glass of wine or a drink) do you usually drink when you drink alcohol? 1-2 5-6 10 or more 7-9
23	If you have paid or unpaid work, which statement describes your work best? Mostly sedentary work (e.g. office work, mounting) Work that requires a lot of walking (e.g. shop assistant, light industrial work, teaching) Work that requires a lot of walking and lifting (e.g. postman, nursing, construction) Heavy manual labour	30	in one occasion? Never Less frequently than monthly Monthly Weekly Daily or almost daily
24	Describe your exercise and physical exertion in leisure time. If you activity varies much, e.g. between summer and winter, then give an average. The question refers only to the last year. (Tick the one that fits best) Reading, watching TV, or other sedentary activity. Walking, cycling, or other forms of exercise at least 4 hours a week (here including walking or cycling to place of work, Sunday-walking, etc.) Participation in recreational sports, heavy gardening etc. (note:duration of activity at least 4 hours a week) Participation in hard training or sports competitions, regularly several times a week.	34	
25	How often do you exercise?(With exercise we mean for example walking, skiing, swimming or training/sports) Never Less than once a week Once a week 2-3 times a week Approximately every day		Number of years How many years in all have you smoked daily? Number of years Do you use or have you used snuff or chewing tobacco? No, never Yes, sometimes Yes, previously Yes, daily

	DIET		QUESTIONS FOR WOMEN		
38	Do you usually eat breakfast every day?	46	Are you pregnant at the moment?		
	☐ Yes ☐ No		☐ Yes ☐ No ☐ Uncertain		
	Harrison with a fig. 10 and a fig. 11		How many children have you given birth to?		
39	How many units of fruit or vegetables do you eat on average per day? (units means for example a fruit, a cup of juice, potatoes, vegetables)		Number +		
	Number of units	48	If you have given birth, fill in for each child:		
	Trainber of units		birth year, birth weight and months of breastfeeding (Fill in the best you can)		
40	How many times a week do you eat warm dinner?		Child Birth year Birth weight in grams breastfeeding		
	Number		1		
41	How often do you usually eat these food products? (Tick once for each line)		2		
			3		
	0-1 2-3 1-3 4-6 1-2 times/ times/ times/ times/ times mth mth week week day	5/	4		
	mth mth week week day Potatoes		5		
	Pasta/rice				
	Meat (not processed)		6		
	Processed meat	49	Have you during pregnancy had high blood		
	(sausages/meatloaf/meatballs)		pressure?		
	Fruits, vegetables, berries		☐ Yes ☐ No		
	Lean fish	50	If yes, during which pregnancy?		
	(e.g. salmon, trout, mackerel, herring, halibut, redfish)		☐ The first ☐ Second or later		
42			Have you during pregnancy had proteinuria?		
72			☐ Yes ☐ No		
	1-6 1 2-3 4 or more Rarely/ glasses glass glasses glasses				
	never /week /day /day /day	52	If yes, during which pregnancy?		
	Milk, curdled milk, yoghurt		☐ The first ☐ Second or later		
	Juice	53	Were any of your children delivered prematurely		
	Soft drinks		(a month or more before the due date) because of preeclampsia?		
	with sugar		☐ Yes ☐ No		
43	How many cups of coffee and tea do you drink				
	daily? (Put 0 for the types you do not drink daily) 54		If yes, which child?		
	Number of cups		1st child 2nd child 3rd child 4th child 5th child		
	Filtered coffee				
	Boiled coffee (coarsely ground coffee for brewing)	55	How old were you when you started menstruating?		
	Other types of coffee				
	Tea		Age		
44	How often do you usually eat cod liver and roe? (i.e. "mølje")	56	Do you currently use any prescribed drug influencing the menstruation?		
	\square Rarely/never \square 1-3 times/year \square 4-6 times/year		Oral contraceptives, hormonal intrautrine or similar Yes No		
	☐ 7-12 times/year ☐ More than 12 times/year		Hormone treatment for		
		menopausal problems Yes No			
45	Do you use the following supplements? Daily Sometimes No		When attending the survey centre you will get a		
+	Cod liver oil or fish oil capsules	questionnaire about menstruation and possible use of hormones. Write down on a paper the names of			
	Omega 3 capsules (fish oil, seal oil)		all the hormones you have used and bring the paper with you. You will also be asked whether your		
	Vitamins and/or mineral supplements		menstruation have ceased and possibly when and		
	vicaminis and/or ininieral supplements		why.		

Appendix F

Fracture registration protocol

Fracture registration protocol

by Luai A. Ahmed, UiT

Note: The registration process describes a registry in 2002 that covers the period 1994-2000. There has been two follow-up fracture registries since, in 2005 (covers 2001-2004) and in 2010 (covers 2005-2009). The newer registers (2001-2005 and 2005-2010) were performed using very similar protocols.

Fracture registration (protocol)

Information from the radiographic descriptions was registered in a Microsoft Access file.

Description of the variables used in the fracture registration process (2002):

Akt. Rekv.nr.: The referral number in the archive of the department of radiology.

Navn: The name of the patient.

Usdag: The date of examination.

Side: The side of the examination, right (Dex) or left (Sin).

Brudd side: The side of the fracture, Dex or Sin.

If it wasn't match with the fracture site in the X-ray report, that will be mentioned in the comment bar.

Lokal: Code for the location of the fracture. See codes below.

- -albue
- -Ankel
- -ansikt
- -bekken
- -cervicalcol.
- -clavikula
- -finger
- -fotrot
- -Håndledd
- -håndrot
- -hofte
- -kne
- -lårskaft
- -legg
- -lumbalcol.
- -nese
- -overarm
- -ribben
- -scapula
- -skulder
- -sternum
- -tær
- -thorocalcol.
- -underarm

Utvkl: Code for the x-ray picture purpose. See codes description below.

Forbedring: Forverring:

Gamle forandringer: Old changes.

Kontroll: Control picture.

Mistenkt:

Opr. Innlagt rtg. Tett mat.: Postop. Forandringer: Progresjon: Progression. Regresjon: Regression.

Repoert: Sekvele:

Brudd etter 94: If the fracture occurred after 1994 (ja/ yes) or before 1994 (nei/ no).

All fractures examined in 1994-95 with uncertain dates of fracture were reported as (Nei); not after 1994.

Sikkert Brudd:

Ja: the fracture was confirmed in the X-ray report.

Nei: No fracture in the X-ray report. The fracture was not certain, not confirmed in the X-ray report or been described as suspected, probable or possible fracture.

Brudd #: The number of fractures for the same person by the day of examination.

- Fractures of more than one bone at the same site or location (description of locations below) were counted as one fracture, for example Tib/Fib or Ulna/Rad.
- Refracture or a new fracture at the same site was counted as a new fracture when it occurred after the first one (not at the same day).
- If more than one fracture happened at the same time at different sites, for example in a car accident, the number of fractures at the time of examination was counted as the total number of fractures.

- If there was a fracture, which mentioned only in the X-ray report, it will be counted in

the total number of fractures and its site will be stated in the comment bar.

- Vertebral compression fractures were counted as one fracture if they were at the same

vertebral segment (ex. Lumber vertebrae). Each involved vertebra was mentioned in

the comment bar.

- If a new vertebra within the same vertebral segment developed compression for the

first time, it was counted as a new fracture in addition to the old compression counted

before.

Increase in the compression of one or more vertebrae wasn't counted as a new

fracture.

- (21-03-02) start mentioning which bones were involved in finger, toe, hand root, foot

root, carpal, tarsal and rib bones in the comment bar.

For finger and toe, we reported which digit and phalange were fractured

(ex. 1st, 3rd phal. = first digit, distal phalange).

For hand root, foot root, carpal, tarsal and rib, we reported the number of bones fractured.

Brudd lok. Describes the location of the fracture as one of the following sites:

Albu fx flere: Fracture of the elbow: involvement of more than two bones around the elbow.

Annet*: any other fracture not mentioned in the list below.

Ansikts fx: Fracture of the face: fracture of any bone of the face bones.

Bekken fx.: Fractures of the pelvis.

Cervicalcol: Fracture of the cervical vertebrae: wedge compression fracture of the vertebral

body, fracture of the atlas, fracture of the dens of the axis and fracture of a spinous process.

Clavicula fx: Fracture of the clavicle.

Coccyx fx: Fracture of the coccyx.

Femur dist: Fracture of the distal part of the femur: supracondylar fracture or fracture of the femoral condyles.

Femur skaft: Fracture of the shaft of the femur.

Femur trock : Fracture of the femoral trochanteric region: any fracture that lies approximately between the greater and the lesser trochanter.

Femurcollum: Fracture of the neck of the femur.

Fibula dist.: Fracture of the distal part of the fibula, isolated fracture of the lateral malleolus.

Fibula prox.: Fracture of the proximal part of the fibula.

Fibula skaft: Fracture of the shaft of the fibula

Finger fx.: Fracture of the phalanges of the fingers.

Håndrots fx.: Fracture of the carpal bones.

Humerus dist: Fracture of the distal part of the humerus: fracture of the epicondyle, the condyle or supracondylar fracture.

Humerus prox.: Fracture of the proximal part of the humerus: fracture of the neck or fracture of the greater tuberosity.

Humerus skaft: Fracture of the shaft of the humerus.

Kne fx flere: Fracture about the knee involving more than one bone, the femoral condyles, the patella or the tibial condyles.

Lumbalcol.: Fracture of the lumbar vertebrae: wedge fracture compression of the vertebral body

Metacarp. fx.: Fracture of the metacarpal bones.

Metatars. fx.: Fracture of the metatarsal bones.

Radius dist.: Fracture of the distal part of the radius: fracture of the lower end of the radius (Colles's fracture).

Radius prox.: Fracture of the proximal part of the radius: the head of the radius.

Radius skaft: Fracture of the shaft of the radius.

Ribben: Fracture of the ribs

Sacrum fx.: Fracture of the sacrum.

Skulderblad fx.: Fracture of the scapula.

Sternum: Fracture of the sternum.

Tå fx.: Fracture of the phalanges of the toes.

Thoracalcol.: Fracture of the thoracic vertebrae: wedge fracture compression of the vertebral body.

Tib/Fib skaft: Fracture of the shafts of the tibia and fibula.

Tibia dist: Fracture of the distal part of the tibia, isolated fracture of the medial malleolus.

Tibia prox.: Fracture of the proximal part of the tibia, the condyles of the tibia.

Tibia skaft: Fracture of the shaft of the tibia.

Ulna dist.: Fracture of the distal part of the ulna.

Ulna prox: Fracture of the proximal part of the ulna: fracture of the olecranon process, the coronoid process and the upper most third of ulna.

Ulna skaft: Fracture of the shaft of the ulna.

Ulna/Radius skaft: Fracture of the shafts of the forearm bones: both ulna and radius.

* Patella fractures were reported as (Annet); others, and explained in the comment bar.

Energi: Description of the energy (the causative injury) when the fracture has occurred.

Usikker: No description for the energy in the medical report: fall.

Lav: law-energy fracture, the causative injury was slight: stumble, slip. At the level of the ground, the standing height, with no additional force.

Hoy: high-energy fracture, the causative injury was strong: traffic accident, fall from the stairs or any level above the ground level.

Patologi: the cause of fracture was a pathological disease in the bone, metastasis.

Sportsulykke: the fracture happened while practicing any kind of sport.

Snø/is: Involvement of snow or ice in the fracture mechanism.

Ukjent: there was no mention of the fracture mechanism or there was snow or ice in it.

Ja: snow or ice was mentioned in the medical report in the description of the fracture; slippery surface, slid on ice, skiing, skating, shuffling snow, etc.

Nei: the medical report described the mechanism of fracture inside the house (bedroom, kitchen, bathroom, etc), on the floor, on the street.



