Physical activity, osteoporosis and fracture risk

Long-Term Associations In A General Population

Bente Morseth

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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 helselokalisert 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:**


**Paper II:**


**Paper III:**

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$_{2\text{max}}$: 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”\(^41\). Osteoporosis constitutes a considerable public health concern, estimated to affect 75 million people in the United States, Europe and Japan together\(^56\). Although osteoporosis traditionally has been considered a female disorder, approximately one in four individuals with osteoporosis is a man\(^120\). 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 women\(^61\). 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 70\(^71\). Several estimates indicate a rapid increasing prevalence of osteoporosis\(^55\), and the increasing elderly population\(^278\) 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 people\(^108\), and Norway has the highest reported fracture incidence in the world\(^166\). 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 study\(^228\), 50% of the hip fracture patients never recovered to their pre-fracture 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 Euro\(^239\).

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 \(\geq 50\) years has been estimated to 12
per 1000 inhabitants for women and 4.5 in men during the 1980’s and 90’s. Recent estimates from Harstad, Northern Norway, are somewhat lower. 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 climate. Moreover, the incidence of fracture is generally higher in urban than in rural areas.

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 US. In the Tromsø population, the comparable lifetime risk was recently reported to be 55% in women and 25% in men. 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.

Box 1: Epidemiology of hip and wrist fractures

<table>
<thead>
<tr>
<th>Hip fractures</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Hip fractures are more severe than other fractures and lead to mortality, more severe disability and consequently higher costs43</td>
</tr>
<tr>
<td>• The majority of all hip fractures are the result of a simple fall from standing position43</td>
</tr>
<tr>
<td>• The majority of hip fractures are osteoporotic268</td>
</tr>
<tr>
<td>• 30% of all hip fractures occur in men202</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Wrist fractures</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Wrist fractures occur mainly in women59</td>
</tr>
<tr>
<td>• Whereas the incidences of hip fracture increase with age, wrist fracture incidence in women increase from 45 to 60 years, then levels off59,107</td>
</tr>
<tr>
<td>• The lifetime risk of wrist fracture in women declines from age 50 to 70 years262</td>
</tr>
<tr>
<td>• The incidence in men continues to stay low with advancing age262</td>
</tr>
</tbody>
</table>
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.\textsuperscript{32, 78}

Physical bone strength depends on the structural and material properties of bone,\textsuperscript{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.\textsuperscript{30, 32} However, the gold standard for diagnosis of osteoporosis is considered to be dual-energy X-ray absorptiometry (DXA).\textsuperscript{42}

DXA measures areal BMD (g/cm\textsuperscript{2}), i.e. the ratio between bone mineral content and the scanned area.\textsuperscript{42} 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 BMD.\textsuperscript{277}
1.2.2 The role of BMD in osteoporosis

The definition of osteoporosis incorporates both low bone mass and microarchitectural deterioration of the bone tissue. As microarchitectural deterioration and other indicators of bone strength are not easily measureable with present non-invasive methods, 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 BMD (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. 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. This view is based on results showing that the risk of hip fracture at a given absolute BMD value is independent of sex.

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).

Table 1: Diagnostic thresholds for osteoporosis

<table>
<thead>
<tr>
<th>Definition</th>
<th>BMD values in relation to the mean value of peak bone mass in young normal women*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Normal</td>
<td>Not more than 1 SD below the mean</td>
</tr>
<tr>
<td>Osteopenia</td>
<td>Within -1 SD and -2.5 SD the mean</td>
</tr>
<tr>
<td>Osteoporosis</td>
<td>More than 2.5 SD below the mean</td>
</tr>
<tr>
<td>Severe osteoporosis</td>
<td>More than 2.5 SD below the mean and the presence of fractures the mean</td>
</tr>
</tbody>
</table>

*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.

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. Many studies have shown that risk of fracture increases with decreasing BMD, summarized in previous meta-analyses. Laboratory studies have demonstrated a high correlation between BMD and the force that is required to break a bone, and it is indicated that BMD predicts 50-85% of the variation in bone strength. 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 risk. Thus, BMD is one of the major predictors of fracture risk.
Existing studies report fairly similar gradients of risk for fracture (i.e. the relative risk for each SD decrease in BMD)\textsuperscript{109}. The risk gradient varies with the site of BMD measurement and the fracture site at risk\textsuperscript{122}. 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\textsuperscript{109, 171}. Although fractures are best predicted by site-specific BMD measurements\textsuperscript{122}, 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 BMD\textsuperscript{42}. A Z-score of -2.5 thus means that the fracture risk is almost 9-fold higher (2.6$^2$) than compared with a Z score of 0\textsuperscript{122}.

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 months\textsuperscript{88}. The bone cells responsible are osteoblasts and osteoclasts, which together form the "basic multicellular unit"\textsuperscript{217}. Osteoclasts remove bone on the surface and create a cavity, and after a delay, osteoblasts produce new bone that fills the cavities\textsuperscript{29}. The net result of bone formation and resorption determines the mass, size, shape, and architecture of the bone\textsuperscript{226}.

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 trabeculae\textsuperscript{88}. 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\textsuperscript{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 sites\textsuperscript{90}. After bone mass has reached a peak in young adulthood, a gradual bone loss begins, possibly in the third or fourth decade\textsuperscript{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\textsuperscript{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\textsuperscript{61, 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\textsuperscript{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 thereafter. 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 persist, 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 osteoporosis. 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 loss. 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 aging.

### 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). Due to the flexible collagen, bone can allow elastic deformation of the bone (strain) during loading by storing energy. A load that is applied to bone is called stress, defined as force divided by area. The applied load causes a mechanical deformation of bone tissue, and this deformation can be measured as strain. 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). 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, 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 side.

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). 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 fracture. 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 fracture. Genetic factors explain 50%-80% of the variation in BMD. However, fracture risk is also affected by many other factors, as shown in table 2.

<table>
<thead>
<tr>
<th>Table 2: Risk factors for osteoporotic fractures</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Clinical characteristics and medical history</strong></td>
</tr>
<tr>
<td>Genetic factors(^{269})</td>
</tr>
<tr>
<td>Advancing age(^{19, 83, 117, 269})</td>
</tr>
<tr>
<td>Female gender(^{117})</td>
</tr>
<tr>
<td>Asian or Caucasian(^{15, 83, 117})</td>
</tr>
<tr>
<td>Low weight/body mass index (BMI &lt;18.5 kg/m(^2))(^{83, 120})</td>
</tr>
<tr>
<td>Weight loss (&gt;10%)(^{202, 269})</td>
</tr>
<tr>
<td>Height(^{269})</td>
</tr>
<tr>
<td>Family history of hip fracture(^{19, 83, 117, 120})</td>
</tr>
<tr>
<td>Prior fragility fracture(^{19, 83, 117, 269})</td>
</tr>
<tr>
<td>Low dietary calcium intake/absorption(^{55, 83, 117})</td>
</tr>
<tr>
<td>Vitamin D deficiency(^{55, 83, 117})</td>
</tr>
<tr>
<td>Medications(^{83, 269})</td>
</tr>
<tr>
<td>Estrogen exposure(^{269})</td>
</tr>
<tr>
<td>Premature menopause(^{19, 83, 117})</td>
</tr>
<tr>
<td>Amenorrhea(^{117})</td>
</tr>
<tr>
<td>Hyperparathyroidism(^{55, 83})</td>
</tr>
<tr>
<td>Low serum testosterone levels(^{55, 202})</td>
</tr>
<tr>
<td>Poor health/comorbidity(^{83})</td>
</tr>
<tr>
<td><strong>Bone strength related</strong></td>
</tr>
<tr>
<td>Low BMD(^{117, 269})</td>
</tr>
<tr>
<td>Bone architecture and geometry(^{269})</td>
</tr>
<tr>
<td>High bone turnover(^{117, 269})</td>
</tr>
<tr>
<td>Microdamage accumulation in bone(^{269})</td>
</tr>
<tr>
<td>Degree of mineralization of bone(^{269})</td>
</tr>
<tr>
<td><strong>Fall related</strong></td>
</tr>
<tr>
<td>Muscular weakness(^{269})</td>
</tr>
<tr>
<td>Impaired functional mobility(^{269})</td>
</tr>
<tr>
<td>Neuromuscular disorders(^{117, 269})</td>
</tr>
<tr>
<td>Visual impairment(^{117, 269})</td>
</tr>
<tr>
<td>Cognitive impairment(^{269})</td>
</tr>
<tr>
<td>Impaired proprioception(^{269})</td>
</tr>
<tr>
<td>Increased postural sway(^{269})</td>
</tr>
<tr>
<td>Season(^{269})</td>
</tr>
<tr>
<td><strong>Lifestyle related</strong></td>
</tr>
<tr>
<td>Cigarette smoking(^{83, 117, 120})</td>
</tr>
<tr>
<td>Physical inactivity(^{55, 83, 117, 269})</td>
</tr>
<tr>
<td>Excessive alcohol consumption(^{83, 117})</td>
</tr>
</tbody>
</table>
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 people\textsuperscript{134}. The main non-pharmacological interventions for fracture reduction include prevention of osteoporosis and prevention of falling\textsuperscript{125}, 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\textsuperscript{17,134}.

1.5.1 Physical activity

The Norwegian recommendations for physical activity aimed at health promotion state that adults \textit{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 gained}\textsuperscript{14}. These recommendations are based on research of associations between physical activity and morbidity and mortality\textsuperscript{144}. Physical inactivity is a known risk factor for many diseases, such as cardiovascular diseases\textsuperscript{147,205}, type 2 diabetes mellitus\textsuperscript{1}, obesity\textsuperscript{51}, and some types of cancer\textsuperscript{246}. Physical inactivity also affects bone mass. This became apparent in the 1960's when space flight studies found loss of BMD in astronauts\textsuperscript{263}. 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\textsuperscript{142,154,155}. These findings agree with studies of long-term bed rest\textsuperscript{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 issues\textsuperscript{22}, 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\textsuperscript{230,281}. In 1892, Wolff\textsuperscript{77} 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\textsuperscript{75,76}.

The mechanostat theory. Frost proposed that local deformation from mechanical loading stimulates bone cells, resulting in bone adaptation\textsuperscript{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 loads. Systemic and local biochemical factors, age, sex, and genes probably influence the bone cells' sensitivity to mechanical stimuli. Hormones influencing remodeling are mainly vitamin D, parathyroid hormone, estrogen, and calcitonin.

The mechanostat theory relies mainly on the magnitude of the strain as the important driving force for bone remodeling. However, an increase in frequency, not only magnitude, may represent overload and bone formation. Moreover, several animal studies have demonstrated that dynamic, but not static strains (whereby strain rate = 0), induce bone formation, 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, 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, indicating that duration is of less importance. Finally, inserting a rest period after each loading cycle can increase the osteogenic response.

Box 2: Osteogenic activities

<table>
<thead>
<tr>
<th>Mechanical characteristics of osteogenic activities</th>
</tr>
</thead>
<tbody>
<tr>
<td>+ High-impact</td>
</tr>
<tr>
<td>+ Dynamic</td>
</tr>
<tr>
<td>+ Varying and increasing loads</td>
</tr>
<tr>
<td>+ A few loading cycles seem sufficient</td>
</tr>
</tbody>
</table>

Mechanotransduction. The cellular mechanism responsible for conversion of a mechanical force into a cellular response is called mechanotransduction. In recent years, animal studies have been focusing on osteocytes as mechanosensors, because of their suitable location. 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. 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) occurs. Several mechanisms have been proposed for the activation of osteocytes, and recently, fluid flow-induced shear stress has been acknowledged as the most essential mechanism. 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. The communication
between the sensor cells (osteocytes) and the effector cells (osteoblasts and osteoclasts) involve direct cell–to-cell contact and autocrine and paracrine signals. Within 48 hours, osteoblasts respond with bone formation and new osteoblasts and osteoclasts are recruited to the bone surface.

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. 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 years, and impaired balance and gait pattern. Physical activity may improve physiological skills and thereby reduce the risk of falling. 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 ages. 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 incidence, and recent studies substantiate inconsistent findings.

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, fragility fractures are far more common in the elderly, whereas the bone mass benefits of physical activity seem more pronounced and consistent at younger age. 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 countries. Yet, in most countries, less than 50% of the population meet the national recommendations. 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. To estimate tracking or stability, correlation between repeated measures is the most frequent effect measure. Only a few research groups have examined tracking of physical activity through adulthood. Studies from the United States, Belgium, Canada and Finland 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, and the majority of these investigated the time span from adolescence to adulthood. Kirjonen et al. 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 in Figure 1.
Timing of exercise to reduce osteoporosis and related fractures:

![Graph showing timing of exercise effects](image)

**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.

### 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-athletes\(^{197}\).

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 and regular physical activity 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% in prepubertal and early pubertal children, and 0–2% in pubertal adolescents, compared with controls.

**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. A review of intervention studies including premenopausal women concluded that impact activity may increase site-specific BMD by 1–3% compared with controls.

**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. Other reviews confirm that aerobic exercise may slow down the loss of bone mass. Moreover, there is evidence of an effect of walking on the femoral neck BMD in postmenopausal women. A recent review showed that both low-impact activity (including jogging) and high-impact combined with resistance training may reduce bone loss at the hip. In contrast, one review failed to show any effects of various exercise on femoral neck BMD.

**Elderly men.** The results seen in women are also present in men, 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). Impact activities are weight-bearing (e.g. jumping). However, most impact activities also involve muscle forces, and the individual effect of the ground-reaction forces can be difficult to separate. 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). 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 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, whereas combining impact activities with resistance training significantly increased BMD at both sites. In postmenopausal women, low-impact exercise (jogging combined with stair climbing and walking) also increased BMD at the lumbar spine and femoral neck, but not
walking alone\textsuperscript{174}. 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 women\textsuperscript{193} and elderly men\textsuperscript{181}, 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\textsuperscript{17, 22, 146}, whereas risk of fracture is substantially higher in old age\textsuperscript{271}. 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\textsuperscript{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 life\textsuperscript{79}. The homeostatic system controlling bone mass is influenced by genetics, mechanical loading, and other lifestyle factors\textsuperscript{79}, 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\textsuperscript{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\textsuperscript{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\textsuperscript{54, 64, 127, 130, 131, 209, 258}, and even up to 40 years after retirement\textsuperscript{168}, although most studies indicate that the benefits are lost after 30-40 years\textsuperscript{127, 128, 129, 130}. Retrospective studies of lifetime physical activity have shown significant associations\textsuperscript{101, 198} or no association between adulthood physical activity and BMD at older ages\textsuperscript{34, 81, 150, 215}.
3.3 Physical activity and risk of fracture

Physical activity may postpone the age-related decline in BMD and increase muscle strength and balance\textsuperscript{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\textsuperscript{11, 44, 66, 68, 82, 151, 183, 184, 206, 216, 248}, although in men, some studies report a non-significant lower fracture risk\textsuperscript{97, 170, 190, 277}. 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\textsuperscript{102, 140, 214}, although other studies have found lower\textsuperscript{244} or no significant fracture risk\textsuperscript{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 risk\textsuperscript{186}. In contrast, results from two studies including all fracture types indicate that physical activity\textsuperscript{9} and walking\textsuperscript{195} can increase the fracture risk.

There are very few RCTs of exercise and non-vertebral fracture incidence\textsuperscript{244}. 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 fractures\textsuperscript{149}.

In a recent review, Moayyeri\textsuperscript{185} 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.\textsuperscript{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 Tromsø. 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, 5,432 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, 4,443 persons were invited to participate in the DXA measurements in follow-up survey in Tromsø 5 in 2001–02. Altogether 3,217 subjects (72%, 1,766 women and 1,451 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=7,582) 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 7,522 subjects (3,450 men and 4,072 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

<table>
<thead>
<tr>
<th>Tromsø Study</th>
<th>Question</th>
<th>Answer options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tromsø 1, 1974</td>
<td>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.</td>
<td>□ 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</td>
</tr>
<tr>
<td>Tromsø 2, 1979-80</td>
<td></td>
<td>□ If □ 1-2 hours □ 3 or more hours pr. week</td>
</tr>
<tr>
<td>Tromsø 3, 1986-87</td>
<td></td>
<td>□ Light activity (not sweating or out of breath):</td>
</tr>
<tr>
<td>Tromsø 5, 2001-02 &lt;70 years</td>
<td></td>
<td>□ None □ &lt;1 hour □ 1-2 hours □ 3 or more hours pr. week</td>
</tr>
<tr>
<td>Tromsø 6, 2007-08</td>
<td>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.</td>
<td>□ 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</td>
</tr>
<tr>
<td>Tromsø 4, 1994-95</td>
<td>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.</td>
<td>□ Light activity (not sweating or out of breath):</td>
</tr>
<tr>
<td>Tromsø 5, 2001-02</td>
<td></td>
<td>□ None □ 1-2 hours □ 3 or more hours pr. week</td>
</tr>
<tr>
<td>Tromsø 6, 2007-08</td>
<td>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.</td>
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<td>Tromsø 4, 1994-95</td>
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<td>□ Light activity (not sweating or out of breath):</td>
</tr>
<tr>
<td>Tromsø 5, 2001-02</td>
<td></td>
<td>□ None □ &lt;1 hour □ 1-2 hours □ 3 or more hours pr. week</td>
</tr>
</tbody>
</table>

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 samples. 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 stability.

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., 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.com, using data generated from cross-tabulation 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% 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 <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 ($P_{\text{trend}}=0.005$) and non-significantly in women ($P_{\text{trend}}=0.2$). 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 ($P_{\text{trend}}\leq 0.02$). 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\textsuperscript{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”\textsuperscript{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\textsuperscript{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\textsuperscript{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\textsuperscript{50, 221}. Selection bias may occur in the sampling process (due to selection procedures) or during follow-up (due to loss of participants)\textsuperscript{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 known\textsuperscript{95}. 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\textsuperscript{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

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

*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 conversely\(^{20}\). 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 direction\(^{57}\).

Some measurement biases are most common in case-control studies, such as recall bias\(^{28}\), but in the three papers, there is one other bias that may particularly threaten the validity; reporting bias\(^{10}\) 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 pedometer. Subjective assessments of physical activity include self-reporting methods by questionnaire, interview or diary. To measure targeted bone loading or force-generation activity, motion sensors and ground reaction forces together with questionnaire may be the most ideal method today. 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 validity.

In Tromsø 2, 3, and 6 physical activity was assessed by a single questionnaire (table 4). This question was originally initiated by Saltin and Grimby 40 years ago and further developed for self-reporting by Wilhelmsen et al. The question has been widely used in population studies. 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 standard. 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 published. In women and men aged 40-44 years, self-reported 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 in 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).


According to Anderssen et al., there is evidence for acceptable construct validity for using this question in health surveys. In a study including 2860 women and men, physical activity in leisure time according to the question in the Tromsø Study was positively associated with metabolic equivalents (MET). Aadahl et al. 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 and 86% agreement.

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, but we have found only one validation study of a small group.
of men aged 20-39 years. 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 osteoporosis. Furthermore, DXA and SXA densitometers are very practicable in use, with low costs, low radiation, and they are quick and easy to operate.

Generally, DXA and SXA measurements have excellent precision. The Lunar Prodigy DXA densitometer was validated in a recent study 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 BMD. 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. 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 fracture.

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 punching. The fracture registration at the University Hospital of Northern Norway (UNN) has been validated by Joakimsen et al. 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 2001, 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". Confounding may be defined as "distortion of an exposure-outcome association brought about by the association of another factor with both outcome and exposure" and may distort the real association in any direction. 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. 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.

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 analyses. 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 irrelevant. 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. 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. 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 population\textsuperscript{10}.

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 validity\textsuperscript{17}.

### 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 association\textsuperscript{221}, and Alfred Evan's postulates\textsuperscript{210}. More recently, Bhopal\textsuperscript{25} 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\textsuperscript{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 health\textsuperscript{17}. 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 finite\textsuperscript{25}. Bhopal\textsuperscript{25} 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 causal\textsuperscript{25}. 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 study\textsuperscript{58} 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 $\leq 0.05$ 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)\textsuperscript{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 associations\textsuperscript{28}. Additionally, the dose-response relationship may also have implications for public health advice about physical activity\textsuperscript{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 benefits\textsuperscript{161}.

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.)\textsuperscript{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 disease\textsuperscript{161}. 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 week\textsuperscript{8}. 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 size\textsuperscript{25}. 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 Norwegians\(^6\). 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 patients\(^{238}\), 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 BMD\(^{49}\). Most, but not all RCTs support these results\(^{133}\). 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 BMD\(^{267}\), demonstrating the limitations of DXA BMD measurements in giving information about cortical and trabecular structure, size, shape, and bone mass distribution\(^{196}\). 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/cm\(^3\)), and MRI can assess trabecular microarchitecture, however at peripheral sites\(^{30}\). More recently developed techniques include high-resolution micro-computed tomography and finite element analysis\(^{30}\). Quantitative ultrasound can also be used to measure bone mineral and architecture\(^{88}\). 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). 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 boys. 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 women showed a little more promising results with positive but modest exercise effects on bone geometry at loaded sites. Similarly, Daly and Bass 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 populations, 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, 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 results\textsuperscript{144}.

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 study\textsuperscript{188} 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 2011\textsuperscript{208}. 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 higher\textsuperscript{208}. 

45
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.\textsuperscript{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.\textsuperscript{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.\textsuperscript{46} and Augestad et al.\textsuperscript{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.\textsuperscript{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\cite{107, 120}. Historically, fractures of the hip, spine, and distal forearm have been considered the main osteoporotic fractures\cite{39}. 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 patients\cite{107}. Kanis\cite{120} 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"\cite{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.\cite{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.\cite{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.\cite{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\cite{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.
References


47. Daly RM, and Bass SL. Lifetime sport and leisure activity participation is associated with greater bone size, quality and strength in older men. *Osteoporos Int* 2006;17(8):1258-1267.


Paper I
Paper II
Paper III
Appendix A

Questionnaire 1, the 2nd Tromsø Study 1979-80

Norwegian version

English version, preliminary translation
(the final version will be made available at www.tromsostudy.com)
**A**

**Do you have, or have you had:**
- A heart attack? [ ] Yes [ ] No
- Angina pectoris (heart cramp)? [ ] Yes [ ] No
- Any other heart disease? [ ] Yes [ ] No
- Hardened arteries in the legs? [ ] Yes [ ] No
- A cerebral stroke? [ ] Yes [ ] No
- Diabetes? [ ] Yes [ ] No

**Are you being treated for:**
- High blood pressure? [ ] Yes [ ] No
- Do you use: Nitroglycerine? [ ] Yes [ ] No

**B**

**Do you have get or discomfort in the chest when:**
- Walking up hills or stairs, or walking fast on level ground? [ ] Yes [ ] No
- Walking at normal pace at level ground? [ ] Yes [ ] No

**If you get pain or discomfort in the chest when walking, do you usually:**
- 1 Stop? [ ] Yes [ ] No
- 2 Slow down? [ ] Yes [ ] No
- 3 Carry on at the same pace? [ ] Yes [ ] No

**If you stop or slow down, does the pain disappear:**
- 1 Within 10 minutes? [ ] Yes [ ] No
- 2 After more than 10 minutes? [ ] Yes [ ] No

**Do you get pain in the calf while:**
- Walking? [ ] Yes [ ] No
- Resting? [ ] Yes [ ] No

**If you get pain in the calf, then:**
- Does the pain increase when you walk faster or uphill? [ ] Yes [ ] No
- Does the pain disappear when you stop? [ ] Yes [ ] No

**Do you usually have:**
- Cough in the morning? [ ] Yes [ ] No
- Phlegm chest in the morning? [ ] Yes [ ] No

---

**Exercise 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:

Tick "Yes" beside the description that fits best:

1. Reading, watching TV, or other sedentary activity? [ ] Yes [ ] No
2. Walking, cycling, or other forms of exercise at least 4 hours a week? (include walking or cycling to place of work, Sunday walk/stroll, etc.) [ ] Yes [ ] No
3. Participation in recreational sports, heavy gardening, etc.? (note: duration of activity at least 4 hours a week) [ ] Yes [ ] No
4. Participation in hard training or sports competitions, regularly several times a week? [ ] Yes [ ] No

---

**D**

**Do you smoke daily at present?**

If the answer was "Yes" in the previous question, then:

**Do you smoke cigarettes daily?**
- (hand-rolled or factory made)

**If you do not smoke cigarettes at present:**

**Have you previously smoked cigarettes daily?**

If "Yes", how long is it since you stopped:
- 1 Less than 3 months? [ ] Yes [ ] No
- 2 3 months to 1 year? [ ] Yes [ ] No
- 3 1 to 5 years? [ ] Yes [ ] No
- 4 More than 5 years? [ ] Yes [ ] No

For those who smoke or have smoked previously:

**How many years altogether have you smoked daily?**

**How many cigarettes do you smoke, or did you, smoke daily? Give number of cigarettes per day**
- (hand-rolled or factory made)

**Do you smoke tobacco products other than cigarettes daily?**
- Cigars or cigarillos? [ ] Yes [ ] No
- A pipe? [ ] Yes [ ] No

If you smoke a pipe, how many packs of tobacco (50 grams) do you smoke per week? Give the average number of packs per week:

---

**E**

**Do you usually work shifts or at nights?**

**Can you usually come home from work:**
- Every day? [ ] Yes [ ] No
- Every weekend? [ ] Yes [ ] No

**Are there periods during which your working days are longer than usual?**
- (e.g. fishing season, harvest)

During the last year, have you had:

Tick "Yes" beside description that fits best:

1. Mostly sedentary work? (e.g. office work, watchmaker, light manual work)
2. Work that requires a lot of walking (e.g. shop assistant, light industrial work, teaching)
3. Work that requires a lot of walking and lifting (e.g. postman, heavy industrial work, construction)
4. Heavy manual labour? (e.g. forestry, heavy farm-work, heavy construction)

During the last 12 months, have you had:

1. To move for work reasons? [ ] Yes [ ] No
2. Is housekeeping your main occupation? [ ] Yes [ ] No
3. Have you within the last 12 months received unemployment benefit? [ ] Yes [ ] No
4. Are you at present or receiving rehabilitation allowance? [ ] Yes [ ] No
5. Do you receive a complete or partial disability pension? [ ] Yes [ ] No

---

**F**

**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?** [ ] Yes [ ] No

**Are two or more of your grandparents of Sami origin?** [ ] Yes [ ] No
Appendix B

Questionnaire 1, the 3rd Tromsø Study 1986-87

Norwegian version

English version, preliminary translation
(the final version will be made available at www.tromsostudy.com)
HELESEUNDERSØKELSEN I TROMSØ
(Gjelder bare den person som brevet er adressert til.)

Kvinner

1930-66

1925-66

Født dato Personnr. Kommune Kretsnr.

Møtested Kjønn Første bokstav i etternavn Dag og dato Klokkeslett

Fylkeslegen i Troms
Universitetet i Troms
Statens Helseundersøkelser

Med hilsen

Kommunehelsetjenesten i Tromsø
Helseundersøkelsen kommer nå til Deres distrikt.
Tid og sted for frammeve vil De finne nedenfor.
De finner en orientering om undersøkelsen i
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.

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<th>MAリング 1</th>
<th>MAリング 2</th>
<th>MAリング 3</th>
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<td>MAR 85</td>
<td>S</td>
<td>88</td>
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<tr>
<td>HR 103</td>
<td>D</td>
<td>106</td>
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<td>MAR 91</td>
<td>S</td>
<td>94</td>
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<tr>
<td>HR 109</td>
<td>D</td>
<td>112</td>
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<tr>
<td>MAR 97</td>
<td>S</td>
<td>100</td>
</tr>
<tr>
<td>HR 115</td>
<td>D</td>
<td>119</td>
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</tbody>
</table>
### Familie
- Har en eller flere av foreldre eller søskener hatt hjerteinfarkt eller angina pectoris (hjertekrampe)?

### Egen sykdom
- Har De, eller har De hatt:
  - Hjerteinfarkt?
  - Angina pectoris (hjertekrampe)?
  - Hjerneslag?
  - Sukkervesje?

### Symtomer
- Får De smerten eller ubehag i brystet når De:
  - Går i bakker, trapper eller fort på flat mark?
  - Går i vanlig takt på flat mark?

- Dersom De får smerten eller vomdet i brystet ved vange, pleier De da:
  - Stoppe?
  - Svakne farten?
  - Forsette i samme takt?

### Røyking
- Røyker De daglig for tiden?
- Dersom svaret er "Ja", svar da på dette:
  - Røyker De sigaretter daglig?
    - (håndfulle eller fabrikkframsli)
  - Dersom De ikke røyker sigaretter nå, svar da på dette:
    - Har De røykt sigaretter daglig tidligere?
      - Mindre enn 3 måneder?
      - 3 måneder – 1 år?
      - 1–5 år?
      - Mer enn 5 år?

### Kaffe
- Hvor mange kopper kaffe drikker De vanligvis hver dag?
  - Sett kryss i den ruten som passer best.
    - Drikker ikke kaffe, eller mindre enn en kopp?
    - 1–4 kopper?
    - 5–8 kopper?
    - 9 eller flere kopper?

### Arbeid
- Har De i de siste 12 månedene fått arbeidslagstigning?
- Er De for tiden sykemeldt, eller får De atføringspenger?
- Har De full eller delvis uføretrygd?

### Salt/Fett
- Hvor ofte bruker De salt kjøtt eller salt fisk til middag?
  - Satt kryss i den ruten som passer best.
    - Aldri eller sjelden en gang i måneden?
    - Intil en gang i uken?
    - Intil to ganger i uken?
    - Mer enn to ganger i uken?

### Mosjon
- Bevegelse og kroppslig aktivitet i Døres friluft.
- Satt kryss i den ruten som passer best.
  - Leier, ser på fysisk eller annen stil-
    - Sitter stille med gang eller
      - Arbeidsstedet, søndagsturer m.m.

### Slikriser
- Driver mosjonsrettet, tynge hagearbeid ej?
  - Mer enn to ganger i uken?

### Etterundersøkelse
- Har noen i husstanden Døres (utenom
  - Dom-selv) vært innkalt til nærmere
    - Skriv navnet på legen her
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
A F A M I L Y

Have one or more of your parents or siblings had a heart attack (heart wound) or angina pectoris (heart cramp)?

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<th>Yes</th>
<th>No</th>
<th>Don't know</th>
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</table>

B O W N I L L N E S S E S

Do you have, or have you had:

- A heart attack? ........................................ 13
- Angina pectoris (heart cramp)? ..................... 14
- A cerebral stroke? ................................. 15
- Diabetes? ............................................ 16

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<th>Yes</th>
<th>No</th>
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Are you been treated for:

- High blood pressure? ................................ 17

Do you use:

- Nitroglycerine? .................................... 18

C S Y M P T O M S

Do you get pain or discomfort in the chest when:

- Walking up hills or stairs, or walking fast on level ground? .................... 19
- Walking at normal pace at level ground? ........................................... 20

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<th>Yes</th>
<th>No</th>
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If you get pain or discomfort in the chest when walking, do you usually:

- Stop? ....................................... 21
- Slow down? ................................ 22
- Carry on at the same pace? .................. 23

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If you stop or slow down, does the pain disappear:

- After less than 10 minutes? ................. 22
- After more than 10 minutes? ............... 23

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<tr>
<th>Yes</th>
<th>No</th>
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Do you usually have:

- Cough in the morning? .......................... 23
- Phlegm chest in the morning? .................. 24

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<th>Yes</th>
<th>No</th>
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D E X E R C I S E

Exercise 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 year:

Tick the most appropriate box.

- Reading, watching TV, or other sedentary activity? ....................... 25
- Walking, cycling or other forms of exercise at least 4 hours a week? (include walking or cycling to place of work, Sunday walk/drift, etc.) .... 26
- Participation in recreational sports, heavy gardening, etc.? (note: duration of activity at least 4 hours a week) ....................... 27
- Participation in hard training or sports competitions, regularly several times a week? .............................. 28

<table>
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<th>Yes</th>
<th>No</th>
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E S A L T / F A T

How often do you use salted meat or salted fish for dinner? ............................ 29

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<th>Yes</th>
<th>No</th>
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Tick the most appropriate box.

- Never or less than once a month ............ 26
- Once a week or less ....................... 27
- Twice a week or less .................... 28
- More than twice a week .................. 29

How often do you add extra salt to your dinner?

- Tick the most appropriate box.
  - Rarely or never ......................... 27
  - Sometimes or often .................. 28
  - Always or nearly always .......... 29

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</table>

What type of margarine or butter do you usually use on your bread?

- Do not use margarine or butter on bread ..................... 28
- Butter .................................. 29
- Hard Margarine ................................ 30
- Soft (soya) margarine spread .................. 31
- Butter/ margarine mixtures ................. 32

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<tr>
<th>Yes</th>
<th>No</th>
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What type of cooking fat do you normally use in your household?

- Tick the most appropriate box.
  - Butter or hard margarine ................. 33
  - Soft (soya) margarine or oil .......... 34
  - Butter/ margarine mixtures ......... 35

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<th>Yes</th>
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F S M O K I N G

Do you smoke daily at present? .......................... 30

If the answer is "YES", then:

- Do you smoke cigarettes daily? (hand-rolled or factory made) .... 31

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<thead>
<tr>
<th>Yes</th>
<th>No</th>
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If you do not smoke cigarettes at present, then:

- Have you previously smoked cigarettes daily? .................. 32

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
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If you answered "Yes", how long is it since you stopped:

- Less than 3 months? ....................... 33
- 3 months to 1 year? ...................... 34
- 1 - 5 years? ................................. 35
- More than 5 years? ...................... 36

To be answered by those who smoke or who have smoked previously:

How many years altogether have you smoked? ................. 37

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<tr>
<th>Yes</th>
<th>No</th>
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How many cigarettes do you smoke or did you smoke daily?

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<th>Yes</th>
<th>No</th>
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Give number of cigarettes per day (hand-rolled + factory made)

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<th>Yes</th>
<th>No</th>
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<tbody>
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<td></td>
<td></td>
</tr>
</tbody>
</table>

Do you smoke anything else other than cigarettes daily?

- Cigars or cigarillos/cheroots? .......... 38
- A pipe? .................................... 39

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If you smoke a pipe, how many packs of tobacco (50 grams) do you smoke per week?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Give the average number of packs per week

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

G C O F F E E

How many cups of coffee do you usually drink daily?

Tick the most appropriate box.

- Do not drink coffee, or less than one cup: .......................... 40
- 1 - 4 cups .......... 41
- 5 - 8 cups ............... 42
- 9 or more cups ................. 43

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

What type of coffee do you usually drink daily?

- Instant coffee ................................ 44
- Caffeine free coffee .......... 45
- Caffeine containing coffee .......... 46

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

H E M P L O Y M E N T

Have you within the last 12 months received unemployment benefits? .................. 50

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Are you at present on sick leave, or receiving rehabilitation allowance? ........ 51

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Do you receive a complete or partial disability pension? .................. 52

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Do you usually work shifts or at night? ................. 53

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

During the last year, have you had:

- Mostly sedentary work? ... (e.g. office work, watchmaker, light manual work) 54
- Work that requires a lot of walking? (e.g. shop assistant, light industrial work, teaching) .................. 55

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Write the doctor's name here: .................. 56

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

I F O L L O W - U P E X A M I N A T I O N

Has any one in your household (other than yourself) been called in to a doctor for further medical examination after the previous cardiovascular disease survey? .......................... 57

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

If this survey suggests that you need a further medical examination, which general practitioner do you wish to be referred to?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Don't write here

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>

No particular doctor

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Appendix C

Questionnaire 1, the 4th Tromsø Study 1994-95

Norwegian version

English version, preliminary translation
(the final version will be made available at www.tromsostudy.com)
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 brosjiyen.

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


Vennlig hilsen
Kommunehelsetjenesten
Fagområdet medisin, Universitetet i Tromsø
Statens helseundersøkelses

"GRIP SJANSEN - MØT FRAM!"
### EGEN HELSE

<table>
<thead>
<tr>
<th>Hvordan er helsen din nå? Sett bare ett kryss.</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
</tr>
</thead>
<tbody>
<tr>
<td>Dårlig ........................................</td>
<td>12</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ikke helt god ..................................</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>God ..............................................</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Svært god ......................................</td>
<td>4</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hvordan har du hatt?</th>
<th>13</th>
<th>14</th>
<th>15</th>
<th>16</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hjerteinfarkt ..........</td>
<td>13</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angina pectoris (øjenblikkelig skmer) ......</td>
<td>16</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hjerneslag/hjerneblødning ......</td>
<td>19</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Astma .......................................</td>
<td>22</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes (sukkessyke) ....</td>
<td>25</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bruker du medisin mot høy blodtrykk?</th>
<th>28</th>
<th>29</th>
<th>30</th>
<th>31</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nå .............................................</td>
<td>28</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Før, men ikke nå ..........................</td>
<td>2</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Aldri brukt ..................................</td>
<td>3</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

| Har du i løpet av de siste åren vært plaget med smerter og/eller stivhet i muskler og ledd som har vært i minst 3 måneder sammenhengende? | 29 |
|--------------------------------------------------------------------------------------------------------------------------|
| JA JEI |

<table>
<thead>
<tr>
<th>Har du de siste to ukene følt deg:</th>
<th>30</th>
<th>31</th>
<th>32</th>
<th>33</th>
<th>34</th>
<th>35</th>
<th>36</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nerves og urolig? .....................</td>
<td>30</td>
<td></td>
<td></td>
<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Plaget av angst? .....................</td>
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<td></td>
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<td></td>
<td></td>
</tr>
<tr>
<td>Trygg og rolig? .....................</td>
<td>32</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Irritabel? ..............................</td>
<td>33</td>
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<td></td>
<td></td>
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<td></td>
</tr>
<tr>
<td>Glød og optimistisk? ..............</td>
<td>34</td>
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<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Nedtørde/diminter? .................</td>
<td>35</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ensom? ....................................</td>
<td>36</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>JA NEI</th>
<th>Litt</th>
<th>En god del</th>
<th>Svært mye</th>
</tr>
</thead>
</table>

### MOSJON

<table>
<thead>
<tr>
<th>Hvordan har din fysiske aktivitet i fritiden vært det siste året? Tenk deg et ukentlig gjennomsnitt for året. Arbeidsvei regnes som fritid.</th>
<th>37</th>
<th>38</th>
<th>39</th>
<th>40</th>
</tr>
</thead>
<tbody>
<tr>
<td>Arbeid ........................................................................................................</td>
<td>37</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ha fritid ....................................................................................................</td>
<td>38</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ha fritid ....................................................................................................</td>
<td>39</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Ha fritid ....................................................................................................</td>
<td>40</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Timer pr. uke</th>
<th>41</th>
<th>42</th>
<th>43</th>
<th>44</th>
</tr>
</thead>
<tbody>
<tr>
<td>Ingen ..........</td>
<td>41</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Under 1 .......</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1-2 ............</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>3 og mer ......</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hard fysisk aktivitet (svett/andpusten)</th>
<th>55</th>
<th>56</th>
<th>57</th>
<th>58</th>
</tr>
</thead>
<tbody>
<tr>
<td>Løpetiser ..................................</td>
<td>55</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Høyt belastende ................................</td>
<td>56</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Høyt belastende ................................</td>
<td>57</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### KAFFE

<table>
<thead>
<tr>
<th>Hvor mange kopper kaffe drikker du daglig?</th>
<th>59</th>
<th>60</th>
<th>61</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sett 0 hvis du ikke drukker kaffe daglig.</td>
<td>59</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Kokkekaffe ....................................</td>
<td>59</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Annen kaffe ...................................</td>
<td>60</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### ALKOHOL

<table>
<thead>
<tr>
<th>Er du total avholdsmann-kvinne?</th>
<th>62</th>
<th>63</th>
<th>64</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hvor mange ganger i måneden drikk drukken · vanligvis alkohol? Regn ikke med lettal.</td>
<td>62</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hvor mange glass øl, vin eller brennevin drukker du vanligvis i løpet av to uker?</td>
<td>63</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hvis du ikke med lettal. Sett 0 hvis du ikke drukker alkohol.</td>
<td>63</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### FETT

<table>
<thead>
<tr>
<th>Hva slags margarin eller smør bruker du vanligvis på breddet? Sett ett kryss.</th>
<th>65</th>
<th>66</th>
<th>67</th>
</tr>
</thead>
<tbody>
<tr>
<td>Bruker ikke smør/margarin. ......................................................................</td>
<td>65</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Meierismør ...............................................................................................</td>
<td>66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hard margarin ............................................................................................</td>
<td>66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bløt (soft) margarin ..................................................................................</td>
<td>66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Smer/margarin blanding .............................................................................</td>
<td>66</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lettmargarin ..............................................................................................</td>
<td>66</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### UTDANNING/ARBEID

<table>
<thead>
<tr>
<th>Hvilken utdanning er den høyeste du har fullført?</th>
<th>68</th>
<th>69</th>
<th>70</th>
<th>71</th>
<th>72</th>
<th>73</th>
<th>74</th>
<th>75</th>
<th>76</th>
<th>77</th>
</tr>
</thead>
<tbody>
<tr>
<td>Grunnskole, 7-10 år ..................................</td>
<td>68</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Realskole, middelskole, yrkesskole, 1-2-årig videregående skole ...........</td>
<td>69</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Artium, øk.gymnas, allmennfaglig retning i videregående skole ..........</td>
<td>70</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Høgskole/universitet, mindre enn 4 år ........</td>
<td>71</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Høgskole/universitet, 4 år eller mer ..........</td>
<td>72</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

### SYKDOM I FAMILIEN

<table>
<thead>
<tr>
<th>Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)?</th>
<th>78</th>
<th>79</th>
<th>80</th>
<th>81</th>
<th>82</th>
<th>83</th>
<th>84</th>
<th>85</th>
</tr>
</thead>
<tbody>
<tr>
<td>JA NEI VET IKKE ................................................................................................................................................</td>
<td>78</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
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
Appendix D

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

Norwegian version

English version, preliminary translation
(the final version will be made available
at www.tromsostudy.com)
10. MOSJON OG FYSISK AKTIVITET

10.1 Hvordan har din fysiske aktivitet i friluven vært det siste året?

- T - Ja
- F - Nei

Hvis du har vært mer aktive i friluven enn i tidligere år:

- Ikkje sportslig aktivitet (ikke øvingsstunden) (jenta i nedre trekk) - Ja
- Ikke sportslig aktivitet (ikke øvingsstunden) (jenta i øvre trekk) - Nei

10.2 Angi bevegete og krassige øvelser i din friluven. Hvis aktiviteten varierer meget fra, mellom sommer og vinter, så ta et gjennomsnitt. Spørsmålet gjelder bare det siste året. (Sett i ruta som passer best)

- Løsner, ser på fysikk eller annen står eller vekkaktivitet
- Sporser, ryker eller beveger deg på annen måte mindre 4 timers aktivitet (jenta i nedre trekk) (Sett i ruta som passer best)

10.3 Driver mosjonstid, tynge hagerarbeid eller driver konkurantemidret regelmessig og flere ganger i uka?

11. FAMILIE OG VENNER

11.1 Bør du sammen med?

- Ektefelle/samband? Ja Nei
- Antall venner

11.2 Hvor mange gode venner har du?

11.3 Hvor ofte besøker interessante store folk men du gjer?

11.4 Hvor mange foreninger, lag, grupper, kirkeverkshus, etc., deltar du i på friluven?

11.5 Føler du at du kan påvirke dem som skjer i lokalsamfunnet der du bor?

12. SYKDOM I FAMILIEN

12.1 Har en eller flere av dine foreldre eller søskenen hatt hjertefaktisk (sår på hjertet) eller arvalga pærvarit (hjertekramp)?

12.2 Kryss av de elektrologene som har eller har hatt innen av sykdommene: (Sett i kryss for hver (nei))

12.3 Hvis noen av elektrologene din har diabetes, i hvilken alder fikk de diagnose? (Hvis for eksempel fleire søskener, før opp den som fikk det tidligst i levetidet);

13. BRUK AV MEDISINER

13.1 Bruker du?

- T - Ja
- F - Nei
- Orde, men ikke nå: Alder

13.2 Hvor ofte har du i løpet av de siste 4 ukene brukt følgende medisiner?

13.3 Før de medisinsene som du har krysset av før i løket, 13.1 og 13.2, og som du har brukt i løpet av de siste 4 ukene?

13.4 Angi nøyaktig og hvilken grunn det er til at du fant at falt disse (syndrom eller symptomer): (Kryss av for hver tjeneste du har brukt medisinenen)

14. RESTEN AV SKJEMAET SKAL BARE BESTVARE AV KVINNER

14.1 Hver gangmer var du da du fikk menstruasjon eller første gang?

14.2 Hva du ikke lenger lår menstruasjon, hvor gammel var du da den slutte?

14.3 Er du gravid nå?

14.4 Hvor mange barn har du falt?

14.5 Bruker du, eller har du brukt?

14.6 Hvis du bruker, hvilken respektive slags medisiner?

14.7 Hvis du bruker, hvilken respektive slags medisiner, hvilket merke bruker du?

Personlig innbjudelse
1. EGEN HELSE

1.1. Hvordan er helsen din nå? (Søtt bare et kryss)
- Dårlig
- Kanskje godt
- Gode
- Så godt som

1.2. Har du eller har du hatt?:
- Astma
- Hengvise
- Kriskn brunkn/køylen
- Diabetes (sukkerhvis)
- Bensjernhet (oestrogen)
- Fibromyalgi/krokn smeteshast

2. MUSKEL OG SKELETTPLAGET

2.1. Har du vært i bevegelse med smerte eller stiftelse i muskulatur og ledd i løpet av de siste 4 uker? (Vennligst angi bare hvis du har hatt plager) - JA NEJ

3. ANDRE PLAGER

3.1. Under innenfor du en liste over ulike problem, har du opplevd noe av dette den siste uken? (Sett et kryss for hver plage)
- Når ikkefrihet
- Fra ade
- Sivellproblemer
- Næringsmidler til tjeneste
- Fantace
- Korps
- Ikke

4. BRUK AV HELSETJENESTER

4.1. Hvor mange ganger har de siste 12 månedene har du selv brukt?
- Næringsmiddelproblemer
- Bedrift
- Psykolog
- Annen
- Leder
- Fysioterapeut
- Kinesisk
- Tannlege
- Alternativ behandler

5. OPPVEKST OLGTLIHKIRGET

5.1. Hvor lenge har du samlet bedd i fylket? (Sett et kryss for hver plage)
- Ar

5.2. Hvor lenge har du satt bedd i kommunen? (Sett et kryss for hver plage)
- Ar

5.3. Hvordan bedde du det mest av tiden før du fylte 16 år? (Kryss av for alt alternativ og specifikk)

6. VEKT

6.1. Anslå din vekst fra du var 25 år gammel: (Sett et kryss for hver plage)
- Hele kg

7. MAT OG DRIKKE

7.1. Hvor ofte spiser du vanligvis disse matvariene? (Sett et kryss for plages)
- Frukt, bær
- Ost (alle typer)
- Pølser
- Kjeks
- Met
- Fisk
- Nøtter
- Sjokolade

8. RØYKING

8.1. Hvor lenge er du vanligvis daglig?
- Antall timer

8.2. Røykte noen av de voksne hjemmene da du vokste opp?
- JA NEJ

9. UTDANNING OG ARBEID

9.1. Hvor mange år har du gått skole?
- Antall år

9.2. Er du i fulltidsopplæring?
- Ja, full tid
- Ja, deltid
- Nei


9.4. Hvis du har vært i dagligskole, har du vært i ferd med å gi deg inn? (Særlig for og mot)

9.5. Arbeider du i en ferdig prosjekt som selve, ansett eller som familiedel meden uten avtalt lønn?
- Selvslett
- Ansatt
- Familieleden

9.6. Mener du at du jobber for å miste ikke adskilte medarbeider eller medlemmer, selv om de er i samme jobb?

9.7. Måler du noen av følgende ytelser?
- Sykepenger (av yrkemål)
- Alterspensjoner
- Fritidsplaner (JAP) eller atterattpensjoner
- Rehabiliterings-/avkulturingspenger
- Utenlandsrett (født eller delt)
- Dagpenger under arbeidslighet
- Sosialhjelp/tilstand
- Overgangssamtal for endelige forsikringer
Personal Invitation
1. YOUR OWN HEALTH

1.1 What is your current state of health? (Tick one only)

- Poor ........................................... 1
- Not so good .................................. 2
- Good .......................................... 3
- Very good .................................... 4

1.2 Do you have, or have you had?:

- Asthma ........................................  □
- Hay fever .....................................  □
- Chronic bronchitis/emphysema ............  □
- Diabetes .......................................  □
- Osteoporosis ..................................  □
- Fibromyalgia/chronic pain syndrome ......  □
- Psychological problems for which you have sought help  □
- A heart attack ................................  □
- Angina pectoris (heart cramp) ...............  □
- Cerebral stroke/brain haemorrhage ........  □

1.3 Have you noticed attacks of sudden changes in your pulse or heart rhythm in the last year? .......  □

1.4 Do you get pain or discomfort in the chest when: Walking up hills, stairs or walking fast on level ground?

- No ................................................  □
- Yes ..............................................  □

1.5 If you get such pain, do you usually:

- Stop? ..........................................  □
- Slow down? ...................................  □
- Carry on at the same pace? .................  □

1.6 If you stop, does the pain disappear within 10 minutes? ........................................  □

1.7 Can such pain occur even if you are at rest? .......  □

2. MUSCULAR AND SKELETAL COMPLAINTS

2.1 Have you suffered from pain and/or stiffness in muscles and joints during the last 4 weeks? (Give duration only if you have had problems)

- Neck/shoulders .........................  □
- Arms, hands .................................  □
- Upper part of your back...................  □
- Lumbar region ..............................  □
- Hips, legs, feet .............................  □
- Other places ...............................  □

2.2 Have you ever had:

- Fracture in the wrist/forearm ..........  □
- Hip fracture? ...............................  □

3. OTHER COMPLAINTS

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)

- Sudden fear without reason .............  □
- Feel afraid or anxious .....................  □
- Faintness or dizziness .....................  □
- Feel tense or upset ........................  □
- Tend to blame yourself ..................  □
- Sleeping problems .......................  □
- Depressed, sad .............................  □
- Feeling of being useless, worthless ....  □
- Feeling that everything is a struggle .....  □
- Feeling of hopelessness with regard to the future  □

4. USE OF HEALTH SERVICES

4.1 How many times in the last 12 months have you been to/used: (Tick once for each line)

- A general medical practitioner (GP) ....  □
- Medical officer at work ..................... □
- Psychologist or psychiatrist ..............  □
- Other specialist ............................  □
- Emergency GP ..............................  □
- Hospital admission .........................  □
- Home nursing care .......................... □
- Physiotherapist .............................  □
- Chiropractor ...............................  □
- Dentist ......................................  □
- Alternative practitioner .................  □

5. CHILDHOOD/YOUTH AND AFFILIATION

5.1 How long altogether have you lived in the county? (Put 0 if less than half a year)

5.2 How long altogether have you lived in the municipality? (Put 0 if less than half a year)

5.3 Where did you live most of the time before the age of 16? (Tick one option and specify)

- Same municipality .........  □
- Another municipality in the county .......... □
- Another county in Norway ...... □
- Outside Norway ..........  □

5.4 Have you moved within the last five years? □

6. BODY WEIGHT

6.1 Estimate your body weight when you were 25 years old: □
# 7. FOOD AND BEVERAGES

## 7.1 How often do you usually eat these foods? (Tick once per line)

<table>
<thead>
<tr>
<th>Food Item</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Fruit, berries</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cheese (all types)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Potatoes</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Boiled vegetables</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fresh vegetables/salad</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fatty fish (e.g. salmon, trout, mackerel, herring)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## 7.2 What type of fat do you usually use? (Tick once per line)

<table>
<thead>
<tr>
<th>Type of Fat</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Don't use</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Butter</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Hard margarine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Soft/light margarine</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Oils</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## 7.3 Do you use the following dietary supplements:

<table>
<thead>
<tr>
<th>Diet Supplement</th>
<th>Yes, daily</th>
<th>Sometimes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cod liver oil, fish oil capsules</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## 7.4 How much do of the following do you usually drink? (Tick once per line)

<table>
<thead>
<tr>
<th>Drink Type</th>
<th>rarely/never</th>
<th>1-3 times /week</th>
<th>1-6 glasses /week</th>
<th>1-2 glasses /day</th>
<th>2-3 glasses /day</th>
<th>3 times or more /day</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full milk, full-fat curdled milk, yoghurt</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Semi-skinned milk, semi-skinned curdled milk, low-fat yoghurt</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Skimmed milk, skimmed curdled milk</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Extra semi-skinned milk</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Juice</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Water</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mineral water (e.g. Farris, Ramlesia etc.)</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cola-containing soft drink</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other soda/soft drink</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## 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? (Put 0 for the types you don't drink daily)

<table>
<thead>
<tr>
<th>Drink Type</th>
<th>Number of cups</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filtered coffee</td>
<td></td>
</tr>
<tr>
<td>Boiled coffee/coarsely ground coffee for brewing</td>
<td></td>
</tr>
<tr>
<td>Other type of coffee</td>
<td></td>
</tr>
<tr>
<td>Tea</td>
<td></td>
</tr>
</tbody>
</table>

## 7.7 Approximately how often have you during the last year consumed alcohol? (Do not count low-alcohol and alcohol-free beer)

<table>
<thead>
<tr>
<th>Alcohol Consumption</th>
<th>1</th>
<th>2</th>
<th>3</th>
<th>4</th>
<th>5</th>
<th>6</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never consumed</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-3 times per month</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>About 1 time a week</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>A few times last year</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>About 1 time a month</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## 7.8 When you drink alcohol, how many glasses or drinks do you normally drink?

<table>
<thead>
<tr>
<th>Number of glasses or drinks</th>
</tr>
</thead>
</table>

## 7.9 Approximately how many times during the last year have you consumed alcohol equivalent to 5 glasses or drinks within 24 hours?

<table>
<thead>
<tr>
<th>Number of times</th>
</tr>
</thead>
</table>

## 7.10 When you drink, do you normally drink:

<table>
<thead>
<tr>
<th>Alcohol Type</th>
<th>Beer</th>
<th>Wine</th>
<th>Spirits</th>
</tr>
</thead>
</table>

# 8. SMOKING

## 8.1 How many hours a day do you normally spend in smoke-filled rooms?

<table>
<thead>
<tr>
<th>Number of total hours</th>
</tr>
</thead>
</table>

## 8.2 Did any of the adults smoke at home while you were growing up?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
</table>

## 8.3 Do you currently, or did you previously live together with a daily smoker after your 20th birthday?

<table>
<thead>
<tr>
<th>Yes, now</th>
<th>Yes, previously</th>
<th>Never</th>
</tr>
</thead>
</table>

## 8.4 Did you/do you smoke daily?

<table>
<thead>
<tr>
<th>If NEVER: Go to question 9 : (EDUCATION AND WORK)</th>
</tr>
</thead>
</table>

## 8.5 If you smoke daily now, do you smoke:

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
</table>

## 8.6 If you previously smoked daily, how long is it since you stopped?

<table>
<thead>
<tr>
<th>Number of years</th>
</tr>
</thead>
</table>

## 8.7 If you currently smoke, or have smoked before:

<table>
<thead>
<tr>
<th>How many cigarettes do you or did you normally smoke per day?</th>
</tr>
</thead>
</table>

## 8.8 How old were you when you began smoking daily?

<table>
<thead>
<tr>
<th>Age in years</th>
</tr>
</thead>
</table>

## 8.9 How many years in all have you smoked daily?

<table>
<thead>
<tr>
<th>Number of years</th>
</tr>
</thead>
</table>

# 9. EDUCATION AND WORK

## 9.1 How many years of education have you completed?

<table>
<thead>
<tr>
<th>Number of years</th>
</tr>
</thead>
</table>

## 9.2 Do you currently have paid work?

<table>
<thead>
<tr>
<th>Yes, full-time</th>
<th>Yes, part-time</th>
<th>No</th>
</tr>
</thead>
</table>

## 9.3 Describe the activity at the workplace where you had paid work for the longest period in the last 12 months. (e.g. Accountancy firm, school, paediatric department, carpentry workshop, garage, bank, grocery store, etc.)

<table>
<thead>
<tr>
<th>Business:</th>
</tr>
</thead>
</table>

## 9.4 Which occupation/title have or had you at this workplace?

<table>
<thead>
<tr>
<th>Occupation:</th>
</tr>
</thead>
</table>

## 9.5 In your main occupation, do you work as self-employed, as an employee or family member without regular salary?

<table>
<thead>
<tr>
<th>Self-employed</th>
<th>Employee</th>
<th>Family member</th>
</tr>
</thead>
</table>

## 9.6 Do you believe that you are in danger of losing your current work or income within the next two years?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
</table>

## 9.7 Do you receive any of the following benefits?

<table>
<thead>
<tr>
<th>Benefit Type</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sickness benefit (are on sick leave)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Old age pension, early retirement (AFP) or survivor pension</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Rehabilitation/reintegration benefit</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Disability pension (full or partial)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Unemployment benefits during unemployment</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Social welfare benefits</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Transition benefit for single parents</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
10. EXERCISE AND PHYSICAL ACTIVITY

10.1 How has your physical activity in leisure time been during this last year? (Think of a weekly average for the year. Time spent going to work is count as leisure time. Answer both questions.)

- Light activity (not sweating/out of breath)...
  - None
  - Hours per week
    - Less than 1
    - 1-2
    - 3 or more

- Hard physical activity (sweating/out of breath)...
  - 1
  - 2
  - 3
  - 4

10.2 Indicate exercise and physical exertion in your leisure time. If activity varies much e.g. between summer and winter, then give an average. The question refers only to the last year. (Tick the most appropriate box)

- Reading, watching television or other sedentary activity...
- Walking, cycling or other forms of exercise at least 4 hours a week...
  (Include walking or cycling to work, Sunday walk/stroll, etc.)
- Participation in recreational sports, heavy gardening, etc.?
- Participation in hard training or sports competitions, regularly several times a week...

11. FAMILY AND FRIENDS

11.1 Do you live with: Spouse/partner?

11.2 How many good friends do you have?

11.3 How much interest do people show for what you do? (Tick only once)

11.4 How many associations, sport clubs, groups, religious communities or similar do you take part in? (Write 0 if none)

11.5 Do you feel that you can influence what happening in your local community where you live? (Tick only once)

12. ILLNESS IN THE FAMILY

12.1 Have one or more of your parents or siblings had a heart attack (heart wound) or angina pectoris (heart cramp)?

12.2 Tick for the relatives who have or have had any of the illnesses: (Tick for each line)

- Cerebral stroke or brain haemorrhage
- Myocardial infarction before age of 60 years
- Asthma
- Cancer
- Diabetes

12.3 If any relatives have diabetes, at what age did they get diabetes (if for e.g. many siblings, consider the one who got it earliest in life): Mother’s age

13. USE OF MEDICINES

13.1 Do you use:

- Medications for high blood pressure
- Cholesterol-lowering medications

13.2 How often have you during the last 4 weeks used the following medicines? (Tick once for each line)

- Painkillers without prescription
- Painkillers with prescription
- Sleeping pills
- Tranquilizers
- Antidepressants
- Other prescription medicines...

13.3 For those medicines you have checked in points 13.1 and 13.2, and that you’ve used during the last 4 weeks:

Enter the name and the reason that you are taking/have taken these (disease or symptom): (Tick for each duration you have used the medicine)

14. THE REST OF THE FORM IS TO BE ANSWERED BY WOMEN ONLY

14.1 How old were you when you started menstruating?

14.2 If you no longer menstruating, how old were you when you stopped menstruating?

14.3 Are you pregnant at the moment?

14.4 Do you use, or have you ever used? (Tick once for each line)

14.5 Do you use, or have you ever used? (Tick once for each line)

14.6 If you use/have used prescription estrogen: How long have you used it?

14.7 If you use contraceptive pills, mini pill, contraceptive injection, hormonal IUD or estrogen, what brand do you use?
Appendix E

Questionnaire 1, the 6th Tromsø Study 2007-08

Norwegian version

English version, preliminary translation
(the final version will be made available
at www.tromsostudy.com)
**HELSE OG SYKDOMMER**

1. Hvordan vurderer du din egen helse sånn i alminnelighet?
   - Meget god
   - God
   - Verken god eller dårlig
   - Dårlig
   - Meget dårlig

2. Hvordan synes du at helsen din er sammenlignet med andre på din alder?
   - Mye bedre
   - Litt bedre
   - Omtrent lik
   - Litt dårligere
   - Mye dårligere

3. Har du eller har du hatt?
   - Ja
   - Nei
   - Alder første gang
   - Hjerteinfarkt
   - Angina pectoris (hjertekrampe)
   - Hjerneslag/hjerneblødning
   - Hjerteflimmer (atrieflimmer)
   - Høyt blodtrykk
   - Beinskjørhet (osteoporose)
   - Astma
   - Kronisk bronkitt/emfysem/KOLS
   - Diabetes
   - Psykiske plager (som du har søkt hjelp for)
   - Lavt stoffskifte
   - Nyresykdom, unntatt urinveisinfeksjon
   - Migrene

4. Har du langvarige eller stadig tilbakevendende smerter som har vart i 3 måneder eller mer?
   - Ja
   - Nei

5. Hvor ofte har du vært plaget av søvnløshet de siste 12 måneder?
   - Aldri, eller noen få ganger
   - 1-3 ganger i måneden
   - Omtrent 1 gang i uken
   - Mer enn 1 gang i uken

6. Under finner du en liste over ulike problemer. Har du opplevd noe av dette den siste uken (til og med i dag)? (Sett ett kryss for hver plage)
   - Ikke plaget
   - Litt plaget
   - Ganske Veldig mye
   - Mye
   - Veldig
   - Plutselig frykt uten grunn
   - Føler deg redd eller engstelig
   - Matthet eller svimmelhet
   - Føler deg anspent eller oppjaget
   - Lett for å klandre deg selv
   - Søvnproblemer
   - Nedtrykt, tungstindig
   - Følelse av å være unyttig, lite verd
   - Følelse av at alt er et slit
   - Følelse av håpløshet mht. framtida

7. BRUK AV HELSETJENESTER
   - Hvis JA; Hvor mange ganger?
   - Fastlege/allmennlege
   - Psykiater/psykolog
   - Legespesialist utenfor sykehus (utenom fastlege/allmennlege/psykiater)
   - Fysioterapeut
   - Kiropraktor
   - Annen behandler (homøopat, akupunktør, fotsoneterapeut, naturmedisiner, håndspålegger, healer, synsk, el.)
   - Tannlege/tannpleier

8. Har du i løpet av de siste 12 måneder vært hos:
   - Innlagt på sykehus
   - Konsultasjon ved sykehus uten innleggel;
     - Ved psykiatrisk poliklinikk
     - Ved annen sykehospoliklinikk

9. Har du gjennomgått noen form for operasjon i løpet av de siste 3 årene?
   - Ja
   - Nei
**BRUK AV MEDISINER**

10 Bruker du, eller har du brukt, noen av følgende medisiner? (Sett ett kryss for hver linje)

<table>
<thead>
<tr>
<th>Medisin</th>
<th>Aldri</th>
<th>brukt</th>
<th>Nå</th>
<th>Før</th>
<th>Alder første gang</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medisin mot høyt blodtrykk...</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Kolesterolenkende medisin...</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Medisin mot hjertesykdom...</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Vanndrivende medisin...</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Medisin mot beinskjørhet (osteoartritis)</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Insulin</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Diabetesmedisin (tabletter)</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Stoffskiftemedisinene</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Thyroxin/levaxin</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

11 Hvor ofte har du i løpet av de siste 4 ukene brukt følgende medisiner? (Sett ett kryss pr linje)

<table>
<thead>
<tr>
<th>Medisin</th>
<th>Ikke brukt</th>
<th>siste 4 ukere</th>
<th>Sjeldnere enn hver uke</th>
<th>Hver uke, men ikke daglig</th>
<th>Daglig</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smertestillende på resept</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Smertestillende reseptfri</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Sovemidler</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Beroligende medisiner</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Medisin mot depresjon</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

12 Skriv ned alle medisiner – både de med og uten resept – som du har brukt regelmessig i siste 4 ukers periode. (Ikke regn med vitaminer, mineraler, urter, naturmedisin, andre kosttilskudd etc.)

**FAMILIE OG VENNER**

13 Hvem bor du sammen med? (Sett kryss for hvert spørsmål og angi antall)

<table>
<thead>
<tr>
<th>Foreldre</th>
<th>Barn</th>
<th>Søsken</th>
</tr>
</thead>
<tbody>
<tr>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

14 Kryss av for de slektninger som har eller har hatt

<table>
<thead>
<tr>
<th>Slektning</th>
<th>□</th>
<th>□</th>
<th>□</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hjerteinfarkt</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Hjerteinfarkt før fylte 60 år</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Angina pectoris (hjertekrampe)</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Hjerneslag/hjerneblødning</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Beinskjørhet (osteoartritis)</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Magesår/tolvfingertarmsår</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Astma</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Diabetes</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Demens</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Psykiske plager</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
<tr>
<td>Rusproblemer</td>
<td>□</td>
<td>□</td>
<td>□</td>
</tr>
</tbody>
</table>

15 Har du nok venner som kan gi deg hjelp når du trenger det?

| □ Ja | □ Nei |

16 Har du nok venner som du kan snakke fortrolig med?

| □ Ja | □ Nei |

17 Hvor ofte tar du vanligvis del i foreningsvirksomhet som for eksempel syklubb, idrettslag, politiske lag, religiøse eller andre foreninger?

| □ Aldri, eller noen få ganger i året | □ 1-2 ganger i måneden |
| □ 3-4 ganger i måneden | □ 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 |

19 Hva er din hovedaktivitet? (Sett ett kryss)

| □ Yrkesaktiv heltid | □ Hjemmeværerende |
| □ Yrkesaktiv deltids | □ Pensjonist/trygdet |
| □ Arbeidsledig | □ Student/militærtjeneste |

**VED FRAMMØTE** vil du bli spurtt om du har brukt antibiotika eller smertestillende medisiner de siste 24 timene. Om du har det, vil vi be om at du oppgir preparat, styrke, dose og tidspunkt.
20 Mottar du noen av følgende ytelser?
- Alderstrygd, fortløpspenso (AFP) eller etterlattepensjon
- Sykepenger (er sykemeldt)
- Rehabiliterings-/attføringspenger
- Uføretryelse/pensjon, hel
- Uføretryelse/pensjon, delvis
- Dagganger under arbeidsledighet
- Overgangstønad
- Sosialhjelp/-stønad

21 Hvor høy var husholdningens samlede bruttoinntekt siste år? Ta med alle inntekter fra arbeid, trygder, sosialhjelp og lignende.
- Under 125 000 kr
- 125 000-200 000 kr
- 201 000-300 000 kr
- 301 000-400 000 kr
- Over 800 000 kr

22 Arbeider du utendørs minst 25 % av tiden, eller i lokaler med lav temperatur, som for eksempel lager-/industrihaller?
- Ja
- Nei

FYSISK AKTIVITET

23 Hvis du er i lønnet eller ulønnet arbeid, hvordan vil du beskrive arbeidet ditt?
- For det meste stilslittende arbeid (f.eks. skrivebordsarbeid, montering)
- Arbeid som krever at du går mye (f.eks ekspeditararbeid, lett industriarbeid, undervisning)
- Arbeid der du går og løfter mye (f.eks postbud, pleier, bygningsarbeidere)
- Tungt kroppsarbeid

24 Angi bevegelse og kroppslig anstrengelse i din fritid. Hvis aktiviteten varierer meget f.eks mellom sommer og vinter, så ta et gjennomsnitt. spørsmålet gjelder bare det siste året. (Sett kryss i den ruta som passer best)
- Leser, ser på fjernsyn eller annen stilslittende beskjedfertighet
- Spaserer, sykle eller beveger deg på annen måte minst 4 timer i året (her skal du også regne med gang eller sykling til arbeidsplassen, sandagsturer med mer)
- Driver mosjonsidrett, tyngre hagearbeid, snømåking e.l. (merk at aktiviteten skal vare minst 4 timer i uka)
- Trener hardt eller driver konkurranseidrett regelmessig og flere ganger i uka

25 Hvor ofte driver du mosjon? (Med mosjon mener vi at du f.eks går en tur, går på ski, svømmer eller driver trening/idrett)
- Aldri
- Sjeldnere enn en gang i uken
- En gang i uken
- 2-3 ganger i uken
- Omtrent hver dag

26 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

27 Hvor lenge holder du på hver gang i gjennomsnitt?
- Mindre enn 15 minutter
- 15-29 minutter
- Mer enn 1 time

ALKOHOL OG TOBAKK

28 Hvor ofte drikker du alkohol?
- Aldri
- Månedlig eller sjeldnere
- 2-4 ganger hver måned
- 2-3 ganger pr. uke
- 4 eller flere ganger pruke

29 Hvor mange enheter alkohol (en øl, et glass vin, eller en drink) tar du vanligvis når du drikker?
- 1-2
- 3-4
- 5-6
- 7-9
- 10 eller flere

30 Hvor ofte drikker du 6 eller flere enheter alkohol ved en anledning?
- Aldri
- Sjeldnere enn månedlig
- Månedlig
- Ukentlig
- Daglig eller nesten daglig

31 Røyker du av og til, men ikke daglig?
- Ja
- Nei

32 Har du røukt/røyker du daglig?
- Ja, nå
- Ja, tidligere
- Aldri

33 Hvis du har røukt daglig tidligere, hvor lenge er det siden du sluttet?
- Antall år

34 Hvis du røyker daglig nå eller har røkt tidligere: Hvor mange sigaretter røyker eller røykte du vanligvis daglig?
- Antall sigaretter

35 Hvor gammel var du da du begynte å røyke daglig?
- Antall år

36 Hvor mange år til sammen har du røkt daglig?
- Antall år

37 Bruker du, eller har du brukt, snus eller skrå?
- Nei, aldri
- Ja, av og til
- Ja, men jeg har sluttet

38 Hvor ofte drikker du snus eller skrå?
- Aldri
- Månedlig eller sjeldnere
- 2-4 ganger hver måned
- 2-3 ganger pr. uke
- 4 eller flere ganger pruke

39 Hvor mange enheter snus eller skrå tar du vanligvis når du drikker?
- Antall enheter

40 Hvor ofte drikker du snus eller skrå ved en anledning?
- Aldri
- Månedlig eller sjeldnere
- 2-4 ganger hver måned
- 2-3 ganger pr. uke
- 4 eller flere ganger pruke

41 Hvor mange år til sammen har du drikket snus eller skrå?
- Antall år
### KOSTHOLD

<table>
<thead>
<tr>
<th>Spis du vanligvis frokost hver dag?</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Ja  □ Nei</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hvor mange enheter frukt og grønsaker spiser du i gjennomsnitt per dag? (Med enhet menes f.eks. en frukt, glass juice, potet, posrjon grønsaker)</th>
</tr>
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<tbody>
<tr>
<td>□ □ □ □ □ □</td>
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<table>
<thead>
<tr>
<th>Hvor mange ganger i uken spiser du varm middag?</th>
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<tbody>
<tr>
<td>□ □ □ □ □ □ □ □</td>
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</tbody>
</table>

<table>
<thead>
<tr>
<th>Hvor ofte spiser du vanligvis disse matvarene? (Sett ett kryss pr. linje)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poteter                     □  □  □  □  □</td>
</tr>
<tr>
<td>Pasta/ris                   □  □  □  □  □</td>
</tr>
<tr>
<td>Kjøtt (ikke kvernet)        □  □  □  □  □</td>
</tr>
<tr>
<td>Kvernet kjøtt (pølser, hamburger o.l) □  □  □  □  □</td>
</tr>
<tr>
<td>Grønsaker, frukt, bær.      □  □  □  □  □</td>
</tr>
<tr>
<td>Mager fisk                   □  □  □  □  □</td>
</tr>
<tr>
<td>Feit fisk                    □  □  □  □  □  (f.eks. laks, ørret, makrell, sild, kveite, uer)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hvor mye drikker du vanligvis av følgende? (Sett ett kryss pr. linje)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Melk, kefir, yoghurt                                                   □  □  □  □  □</td>
</tr>
<tr>
<td>Fruktjuice                                                             □  □  □  □  □</td>
</tr>
<tr>
<td>Brus/leskedrikker med sukker                                           □  □  □  □  □</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hvor mange kopper kaffe og te drikker du daglig? (sett 0 for de typene du ikke drikker daglig)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Filterkaffe                                                                   □  □  □  □  □</td>
</tr>
<tr>
<td>Kokekaffe/presskanne                                                         □  □  □  □  □</td>
</tr>
<tr>
<td>Annen kaffe                                                                     □  □  □  □  □</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hvor ofte spiser du vanligvis fiskelever? (For eksempel i målge)</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Sjelden/aldri  □ 1-3 g i året</td>
</tr>
<tr>
<td>□ 7-12 g i året                                      □ Oftere</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Bruker du følgende kosttilskudd?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Daglig Iblant Nei</td>
</tr>
</tbody>
</table>

| Tran, trankapsler          □  □  □  □  □ |
| Omega 3 kapsler (fiskeole, selolje) □  □  □  □  □ |
| Kalktabletter              □  □  □  □  □ |

### SPØRSMÅL TIL KVINNER

<table>
<thead>
<tr>
<th>Er du gravid nå?</th>
</tr>
</thead>
<tbody>
<tr>
<td>□ Ja  □ Nei  □ Usikker</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hvor mange barn har du født?</th>
</tr>
</thead>
<tbody>
<tr>
<td>Antall</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hvis du har født, fyll ut for hvert barn: fødselsår og vekt samt hvor mange måneder du ammet. (Angi så godt som du kan)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Barn</td>
</tr>
<tr>
<td>1</td>
</tr>
<tr>
<td>2</td>
</tr>
<tr>
<td>3</td>
</tr>
<tr>
<td>4</td>
</tr>
<tr>
<td>5</td>
</tr>
<tr>
<td>6</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Hvor mange enheter frukt og grønsaker spiser du i gjennomsnitt per dag? (Med enhet menes f.eks. en frukt, glass juice, potet, posrjon grønsaker)</th>
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| Omega 3 kapsler (fiskeole, selolje) □  □  □  □  □ |
| Kalktabletter              □  □  □  □  □ |

#### Ved Frammøte

VED FRAMMØTE vil du få utfyllende spørsmål om menstruasjon og eventuell bruk av hormoner. Skriv gjerne ned på et papir navn på hormonpreparater du har brukt, og ta det med deg. Du vil også bli spurt om din menstruasjon har opphørt og eventuelt når og hvorfor.
HEALTH AND DISEASES

1. How do you in general consider your own health to be?
   - Very good
   - Good
   - Neither good nor bad
   - Bad
   - Very bad

2. How is your health compared to others in your age?
   - Much better
   - A little better
   - About the same
   - A little worse
   - Much worse

3. Do you have, or have you had?
   - Yes  No
   - A heart attack
   - Angina pectoris (heart cramp)
   - Cerebral stroke/brain hemorrhage.
   - Atrial fibrillation
   - High blood pressure
   - Osteoporosis
   - Asthma
   - Chronic bronchitis/Emphysyma/COPD...
   - Diabetes mellitus
   - Psychological problems (for which you have sought help)
   - Low metabolism
   - Kidney disease, not including urinary tract infection (UTI)
   - Migraine

4. Do you have persistent or constantly recurring pain that has lasted for 3 months or more?
   - Yes  No

5. How often have you suffered from sleeplessness during the last 12 months?
   - Never, or just a few times
   - 1-3 times a month
   - Approximately once a week
   - More than once a week

6. Below you find a list of different situations. Have you experienced some of them in the last week (including today)? (Tick once for each complaint)
   - Sudden fear without reason
   - You felt afraid or worried
   - Faintness or dizziness
   - You felt tense or upset
   - Easily blamed yourself
   - Sleeping problems
   - Depressed, sad
   - You felt useless, worthless
   - Feeling that life is a struggle
   - Feeling of hopelessness with regard to the future

USE OF HEALTH SERVICES

7. Have you during the last 12 months visited:
   - Yes  No  No. of times
   - General practitioner (GP)
   - Psychiatrist/psychologist
   - Medical specialist outside hospital (other than general practitioner/psychiatrist)
   - Physiotherapist
   - Chiropractor
   - Alternative practitioner (homeopath, acupuncturist, foot zone therapist, herbal medical practitioner, laying on hands practitioner, healer, clairvoyant, etc.)
   - Dentist/dental service

8. Have you during the last 12 months been to a hospital?
   - Yes  No  No. of times
   - Admitted to a hospital
   - Had consultation in a hospital without admission:
     - At psychiatric out-patient clinic
     - At another out-patient clinic

9. Have you undergone any surgery during the last 3 years?
   - Yes  No
USE OF MEDICINE

10 Do you take, or have you taken some of the following medications? (Tick once for each line)

<table>
<thead>
<tr>
<th>Medications</th>
<th>Never used</th>
<th>Now</th>
<th>Earlier</th>
<th>Age first time</th>
</tr>
</thead>
<tbody>
<tr>
<td>Medications for high blood pressure</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lipid lowering drugs</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medications for heart disease</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diuretics</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Medications for osteoporosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tablets for diabetes</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Metabolic disorder medications</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Thyroxine/levaxin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

11 How often have you during the last 4 weeks used the following medications? (Tick once for each line)

<table>
<thead>
<tr>
<th>Medications</th>
<th>Not used the last 4 weeks</th>
<th>Less than every week</th>
<th>Every week, but not daily</th>
<th>Daily</th>
</tr>
</thead>
<tbody>
<tr>
<td>Painkillers with prescription</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Insulin</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Tranquilizers</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Antidepressants</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

12 State the names of all medications -both those with or without prescription- which you have used regularly during the last 4 weeks. Do not include vitamins, minerals, herbs, natural remedies, other nutritional supplements, etc.

__________________________________________________________________________________________________________________________________________________________________________________________________________________________

FAMILY AND FRIENDS

13 Who do you live with? (Tick for each question and give the number)

<table>
<thead>
<tr>
<th>Family member</th>
<th>Yes</th>
<th>No</th>
<th>Number</th>
</tr>
</thead>
<tbody>
<tr>
<td>Spouse/partner</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Other people older than 18 years</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>People younger than 18 years</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

14 Tick for the relatives who have or have had

<table>
<thead>
<tr>
<th>Condition</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>A heart attack</td>
<td></td>
<td></td>
</tr>
<tr>
<td>A heart attack before age 60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Angina pectoris (heart cramp)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Cerebral stroke/brain haemorrhage</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Osteoporosis</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Stomach/duodenal ulcer</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Asthma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dementia</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Psychological problems</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Problem with substance abuse</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

15 Do you have enough friends who can give you help when you need it?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

16 Do you have enough friends whom you can talk confidentially with?

<table>
<thead>
<tr>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

17 How often do you normally take part in organised gatherings, e.g. sports clubs, political meetings, religious or other associations?

<table>
<thead>
<tr>
<th>Frequency</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Never, or just a few times a year</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>1-2 times a month</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Approximately once a week</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>More than once a week</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

WORK, SOCIAL SECURITY AND INCOME

18 What is the highest level of education you have completed? (Tick once)

<table>
<thead>
<tr>
<th>Level of Education</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary or secondary school</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Technical or vocational school</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>High secondary school (A-level)</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>College/university less than 4 years</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>College/university 4 years or more</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>

19 What is your main activity? (Tick once)

<table>
<thead>
<tr>
<th>Activity</th>
<th>Yes</th>
<th>No</th>
</tr>
</thead>
<tbody>
<tr>
<td>Full time work</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Part time work</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Retired/benefit recipient</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Unemployed</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td>Student/military service</td>
<td>Yes</td>
<td>No</td>
</tr>
</tbody>
</table>
How often do you exercise?

- Never
- Less than once a week
- Once a week
- 2-3 times a week
- Approximately every day

How many years in all have you smoked daily?

Number of years: 35

How old were you when you began smoking daily?

Number of years: 22

Do you work outdoor at least 25% of the time, or in cold buildings (e.g. storehouse/industry buildings)?

- Yes
- No

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

Describe your exercise and physical exertion in leisure time. If your 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.

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

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
- 15-29 minutes
- More than 1 hour

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
3-4
7-9

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

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
- 15-29 minutes
- More than 1 hour

How often do you drink 6 units of alcohol or more in one occasion?

- Never
- Less frequently than monthly
- Monthly
- Weekly
- Daily or almost daily

Do you smoke sometimes, but not daily?

- Yes
- No

Do you/did you smoke daily?

- Yes, now
- Yes, previously
- Never

If you previously smoked daily, how long is it since you stopped?

Number of years:

If you currently smoke, or have smoked before:

How many cigarettes do you or did you usually smoke per day?

Number of cigarettes:

How old were you when you began smoking daily?

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
### QUESTIONS FOR WOMEN

<table>
<thead>
<tr>
<th>Question</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Are you pregnant at the moment?</td>
<td>☐ Yes ☐ No ☐ Uncertain</td>
</tr>
<tr>
<td>How many children have you given birth to?</td>
<td>☐ ☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>If you have given birth, fill in for each child: birth year, birth weight and months of breastfeeding (Fill in the best you can)</td>
<td>Child</td>
</tr>
<tr>
<td></td>
<td>1</td>
</tr>
<tr>
<td></td>
<td>2</td>
</tr>
<tr>
<td></td>
<td>3</td>
</tr>
<tr>
<td></td>
<td>4</td>
</tr>
<tr>
<td></td>
<td>5</td>
</tr>
<tr>
<td></td>
<td>6</td>
</tr>
<tr>
<td>Have you during pregnancy had high blood pressure?</td>
<td>☐ Yes ☐ No</td>
</tr>
<tr>
<td>If yes, during which pregnancy?</td>
<td>☐ The first ☐ Second or later</td>
</tr>
<tr>
<td>Have you during pregnancy had proteinuria?</td>
<td>☐ Yes ☐ No</td>
</tr>
<tr>
<td>If yes, during which pregnancy?</td>
<td>☐ The first ☐ Second or later</td>
</tr>
<tr>
<td>Were any of your children delivered prematurely (a month or more before the due date) because of preeclampsia?</td>
<td>☐ Yes ☐ No</td>
</tr>
<tr>
<td>If yes, which child?</td>
<td>1st child</td>
</tr>
<tr>
<td>How old were you when you started menstruating?</td>
<td>☐ ☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>Do you currently use any prescribed drug influencing the menstruation?</td>
<td>☐ Yes ☐ No</td>
</tr>
<tr>
<td>Oral contraceptives, hormonal intrauterine or similar</td>
<td>☐ Yes ☐ No</td>
</tr>
<tr>
<td>Hormone treatment for menopausal problems</td>
<td>☐ Yes ☐ No</td>
</tr>
</tbody>
</table>

### DIET

<table>
<thead>
<tr>
<th>Question</th>
<th>Options</th>
</tr>
</thead>
<tbody>
<tr>
<td>Do you usually eat breakfast every day?</td>
<td>☐ Yes ☐ No</td>
</tr>
<tr>
<td>How many units of fruit or vegetables do you eat on average per day?</td>
<td>(units means for example a fruit, a cup of juice, potatoes, vegetables)</td>
</tr>
<tr>
<td></td>
<td>Number</td>
</tr>
<tr>
<td>How many times a week do you eat warm dinner?</td>
<td>Number</td>
</tr>
<tr>
<td>How often do you usually eat these food products?</td>
<td>(Tick once for each line)</td>
</tr>
<tr>
<td></td>
<td>0-1 times/mth</td>
</tr>
<tr>
<td>Potatoes</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>Pasta/rice</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>Meat (not processed)</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>Processed meat</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>Fruits, vegetables, berries</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>Lean fish</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>Fatty fish (e.g. salmon, trout, mackerel, herring, halibut, redfish)</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>How much do you usually drink the following?</td>
<td>(Tick once for each line)</td>
</tr>
<tr>
<td>Milk, curdled milk, yoghurt</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>Juice</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>Soft drinks with sugar</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>How many cups of coffee and tea do you drink daily?</td>
<td>(Put 0 for the types you do not drink daily)</td>
</tr>
<tr>
<td></td>
<td>Number of cups</td>
</tr>
<tr>
<td>Filtered coffee</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>Boiled coffee (coarsely ground coffee for brewing)</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>Other types of coffee</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>Tea</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>How often do you usually eat cod liver and roe?</td>
<td>(i.e. “mølje”)</td>
</tr>
<tr>
<td></td>
<td>☐ Rarely/never ☐ 1-3 times/year ☐ 4-6 times/year ☐ 7-12 times/year ☐ More than 12 times/year</td>
</tr>
<tr>
<td>Do you use the following supplements?</td>
<td>Daily Sometimes No</td>
</tr>
<tr>
<td>Cod liver oil or fish oil capsules</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>Omega 3 capsules (fish oil, seal oil)</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
<tr>
<td>Vitamins and/or mineral supplements</td>
<td>☐ ☐ ☐ ☐ ☐</td>
</tr>
</tbody>
</table>

When attending the survey centre you will get a questionnaire about menstruation and possible use of hormones. Write down on a paper the names of all the hormones you have used and bring the paper with you. You will also be asked whether your menstruation have ceased and possibly when and 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
- härdot
- hofte
- kne
- lårskaf
- 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.

_Annett*: 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.