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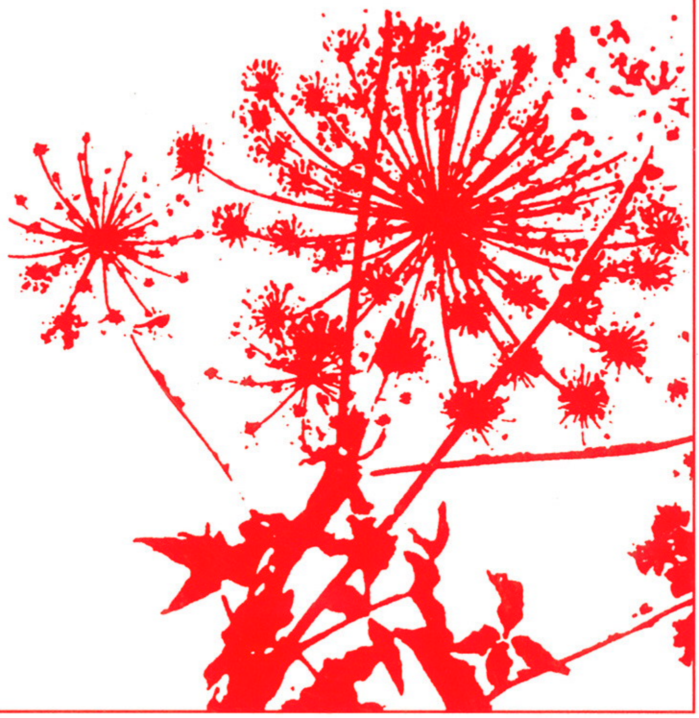

Longitudinal changes in forearm bone mineral density in women and men from 25 to 84 years

The Tromsø Study

by
Nina Emaus

Tromsø 2006

Institute of Community Medicine
University of Tromsø, Norway

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Contents:

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Working with this thesis has been like a four-year long journey with surprises, frustrations, joys and excitements. Most of all, I have learnt a lot and like Askeladden in the Norwegian fairy tales, I have met many good helpers along the road. First of all, I like to thank Merete Albertsen and Henrik Schirmer at the Tromsø Study for welcoming me into The Tromsø V – team, we really had a good time and you were wonderful project leaders. I am also thankful to the population of the Tromsø Study; many of you met even two or three times, providing data for osteoporosis research. Sriharan Sivasingarajah helped me securing data backup and building databases, and together with Jarle Mathiassen gave me necessary IT-support. Mona Ingebrigtsen took care of all reports to the Norwegian Foundation for Health and Rehabilitation, thank you all very much!

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I devote this paper to my two precious children, Eirin and Vegard, as an inspiration for lifelong learning.

Nina Emaus,

Tromsø, October 2005.

1. List of papers

This thesis is based on the following papers:

1. Emaus N, Berntsen GKR, Joakimsen R, Fønnebø V. Bone mineral density measures in longitudinal studies: The choice of phantom is crucial for quality assessment. The Tromsø Study, a Population-based Study. Osteoporosis International, 2005; 16: 1597 – 1603.
2. Emaus N, Berntsen GKR, Joakimsen R, Fønnebø V. Longitudinal Changes in Forearm Bone Mineral Density in Women and Men Aged 25 – 44 years. The Tromsø Study, a Population-based Study. American Journal of Epidemiology, 2005; Vol. 162, No.7: 633 - 643.
3. Emaus N, Berntsen GKR, Joakimsen R, Fønnebø V. Longitudinal Changes in Forearm Bone Mineral Density in Women and Men Aged 45 – 84 years. The Tromsø Study, a Population-based Study. American Journal of Epidemiology, 2006; Vol. 163, No.5: 441 - 449.
4. Lilleeng S, Emaus N, Berntsen GKR, Falch JA, Gjesdal C, Langhammer A, Meyer HE and the Norwegian Epidemiological Osteoporosis Study (NOREPOS) research group. Cross-calibration in densitometry; can in vitro replace in vivo measures? The NOREPOS Study. Manuscript.

2.0. Introduction

2.1. TROST - Tromsø Osteoporosis Study

Osteoporotic fractures constitute a major health problem with substantial morbidity and costs (1, 2). Although the frequency of fractures appears to be increasing in many countries (3), the incidence of fractures varies (4, 5), and together with Northern America, the Scandinavian countries have the highest incidence of hip and forearm fractures in the world (5-11). As a response to the growing awareness of the fragility fracture epidemic, TROST (Tromsø Osteoporosis Study) was established in 1993 as an included part of the Tromsø Study. The main goals of TROST were to identify risk factors for fragility fractures by as cheap and simple methods as possible, and to find ways to implement such knowledge into fracture prevention programmes. TROST works in close collaboration with NOREPOS (Norwegian Epidemiological Osteoporosis Study) which comprise four large population-based multipurpose studies in the cities of Oslo (the Oslo Health Study, HUBRO, 2000-2001), Bergen (the Hordaland Health Study, HUSK, 1998 – 99), Tromsø (The Tromsø Study/Tromsø Osteoporosis Study, TROST, 1994-95 – 2001) and Nord-Trøndelag (the Nord-Trøndelag Health Study, HUNT, 1995-1997) (12).

2.2. Bone fragility

The causation of fracture is complex, but bone fragility is an important contributor to fracture risk (1, 13, 14). Bone fragility, or the opposite: bone strength, is connected to several composites of bone tissue as well as to the turnover rate.

2.2.1. Bone as a tissue

Bone is a dynamic, specialized connective tissue that together with cartilage, makes the skeletal system which in principle has three main functions; mechanical (as support and site of muscle attachment for locomotion), protective (for vital organs and bone marrow) and metabolic (as a reserve of irons, especially calcium and phosphate, for the maintenance of serum homeostasis) (15). There are two main types of bone, cortical (compact) and trabecular (cancellous) bone. They are made of the same cells and the same matrix, but there are structural differences (15) and they can be seen as separate functional entities that do not change with age in the same way (16).

Cortical bone is dense or compact bone. It comprises 85% of the total bone in the body and is most abundant in the long shafts of the appendicular skeleton. As 80-90% of the volume of cortical bone is calcified, the cortical bone fulfils mainly a mechanical and protective function (15). The volume of cortical bone is regulated with bone formation on the periosteal surface, endosteal resorption and resorption within the Haversian canals. With age, these processes might lead to increased porosity of cortical bone. However, periosteal bone formation continues to increase the diameter of cortical bone throughout life, representing a possible compensation for the loss of strength induced by the age related bone mass reduction (17-19). Cortical bone loss is thought to begin after the age of 40, with an acceleration of loss that occurs for 5-15 years after menopause in women. Loss of cortical bone is the major predisposing factor for fractures that occur at the hip and around the wrist (16).

Trabecular bone comprises approximately 15 % of the skeleton, and only 15 – 25% of its volume is calcified, the remainder being occupied by bone marrow, blood vessels and connective tissue (16). In the lumbar spine, the most common site of fracture associated with osteoporosis, trabecular bone comprises more than 65% of the total bone. The inter-trochanteric area of femur comprises 50 % trabecular bone, the neck of femur 25 %. Decline in trabecular bone mass is thought to begin earlier than the decline of cortical bone mass, but there are studies suggesting that decline in trabecular bone begins later, and that its decline is not as prominent as the accelerated loss of cortical bone after menopause (16). The loss of trabecular bone that occurs with aging is not simply due to thinning of the bone plates, but is rather caused by complete perforation and fragmentation of trabeculae (16). The resulting change in architecture leads to a loss of strength not always proportionate of the amount of bone lost (20).

2.2.2. Bone remodelling

The responsiveness of bone to mechanical forces and metabolic regulatory signals are operative throughout life. Bone tissue therefore undergo remodelling, a continual process of resorption and renewal **(21)**. Remodelling is a process both involved in bone development and growth, and in the turnover mechanism by which old bone is replaced by new bone. In the normal adult skeleton, after the period of development and growth, bone is formed mostly where bone resorption has previously occurred, in focal and discrete packets throughout the skeleton (16). The sequence of events at the remodelling unit is the activation-resorption-formation (ARF) sequence that was first described by H. Frost (22). The ARF sequence is regulated through regulatory signals among the cell populations (21), and the complete remodelling cycle at each microscopic site takes about 3-6 months with the same principles in both cortical and trabecular bone (15).

The remodelling that occurs in each basic multicellular unit (BMU), (or bone structural unit), is geographically and chronologically separated from other units. The sequence is always the same, and five different phases can be distinguished over time (16):

1. osteoclastic resorption
2. reversal
3. preosteoblastic migration and differentiation into osteoblasts
4. ostoblastic matrix (osteoid) formation
5. mineralization

In physiological as well as most pathological circumstances, there is a **coupling** between bone formation and previous bone resorption. Packets of bone that are removed during resorption are replaced during formation. The balance in coupling between bone formation and previous bone resorption maintain the material and structural properties of bone, whereas an imbalance of construction and reconstruction during aging lead to bone fragility and loss of strength (16).

2.2.3. Material and structural properties of bone

Bone is formed by collagen fibres (type 1) and non-collagenous proteins. Spindle- or plate-shaped crystals of hydroxyapatite (3Ca3(PO4)2(OH)2) are found on the collagen fibres, within them and in the ground substance, which is primarily composed of glycoproteins and proteglycans. The collagen fibres alternates from layer to layer in adult bone with an orientation giving bones their typical lamellar structure and allowing the highest density of collagen per unit volume of tissue (15). Both the material and structural properties of bone meet the contradictory needs of strength for load bearing, lightness for speed, stiffness for movement against gravity and static loading, as well as flexibility for energy absorption (17). The stiffness of the rope-like triple helical fibres of type 1 collagen with mineral crystals, provide resistance to bending, but excessive stiffness would produce glass-like brittleness (18). The collagen weave confers flexibility that allows storage of energy in reversible (elastic) deformation during impact loading or muscle contraction. When the elastic limit is exceeded, bone can store more energy by plastic (irreversible) deformation, but at the price of micro-damage. If the imparted energy exceeds the elastic and plastic limits of deformation, fractures arise (17).

Strength and lightness are also achieved by the geometrical structure of bones. Long bones are weight bearing and should not bend too much, stiffness favoured over flexibility. The long bones are tubular structures that contain a marrow cavity, so that the cortical mass is placed distant from the central long axis. A unit area of bone placed distant from the long axis confers greater bending strength than the same unit area near the long axis because bending strength is a function of the square of the distance from this long axis (18). Size is therefore an important determinant of bone strength and small changes in size, particularly in external diameter, have a major effect on mechanical properties of bones (23). Thus for load bearing and movement, bones must be stiff, but not too stiff as they become brittle (lose "toughness" or the ability to resist micro-damage). Bones must also be flexible, able to absorb energy in deformation, but not too flexible. As greater bone tissue mineral content or tissue mineral density, confers greater bone stiffness and toleration of greater peak stress, the most important material property of bone is its degree of mineralization (18). For full understanding of the structural and biomechanical components responsible for bone fragility, we would however need more knowledge about the specific material and structural properties such as tissue mineral content, micro-damage burden, porosity, cortical and trabecular architecture, and their interaction (18). The figure below (Fig 1) displays the key components of bone strength, including the interrelationship between bone remodelling, or bone turnover, and bone strength.

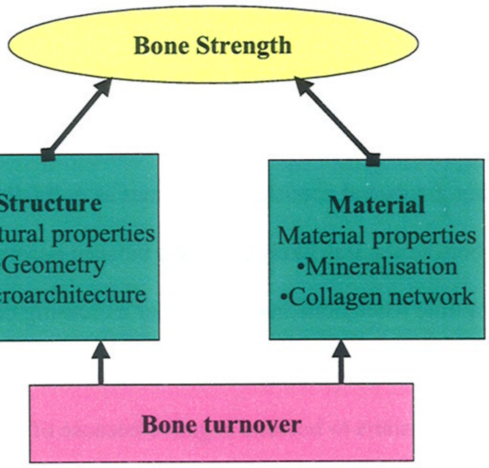


Figure 1. Visualisation of the key components of bone strength, and the interrelationship between bone turnover and bone strength.

2.2.4. Aging and fragility

During advancing age bone remodelling (the focal replacement of old or damaged bone with new bone) becomes impaired. For reasons that are still unclear, less bone is formed by each BMU, which leads to less bone. The amount of trabecular bone lost during aging in women and men is believed to be similar, or only slightly less in men than in women, but bone loss results mainly in thinning of trabeculae in men and in loss of connectivity in women (24). In women, the menopause-related estrogen deficiency increases bone remodelling and makes BMU balance more negative, as oestrogen deficiency increases the life span of osteoclasts and reduces the life span of osteoblasts (25). As the increased remodelling results in an increase in the amount of bone replaced ("turned over"), older, more mineralised bone is replaced by younger less mineralised bone. This less mature bone has reduced stiffness. The same loads are imposed on a structure with diminished cross sectional area. The stress (load per unit area) increase, predisposing to micro-damage and ultimately fracture (18).

During aging, periosteal apposition continues as it did during growth, but more slowly. In both sexes, it is likely that bone balance becomes progressively less positive at a time when bone mass is neither increasing nor beginning to decline. At some time in young adulthood, and well before menopause in women, bone balance probably starts to become negative because of a reduction in the amount of bone formed in the BMU, not because of an increase in the resorption in each BMU. This negative bone balance within each BMU is the structural basis of irreversible bone loss (19).

The larger skeleton achieved during growth produces stronger bones in men than in women, bones that tolerate larger absolute loads. The absolute load imposed on the vertebral body is greater in young men than in women because men are taller and heavier – the larger bone in men is subjected to correspondingly larger loads. Structural failure emerges during aging in men and women because of the changing relationship between the imposed load and the bone's ability to tolerate that load. Periosteal apposition increases the cross sectional area of the bone adding more bone to the outer perimeter of the bone in men. During aging the stress on bone decreases more in men, and strength of the bone decreases less. Structural failure occurs less in men than in women because the relationship between load and bone strength is better maintained in men than in women (18).

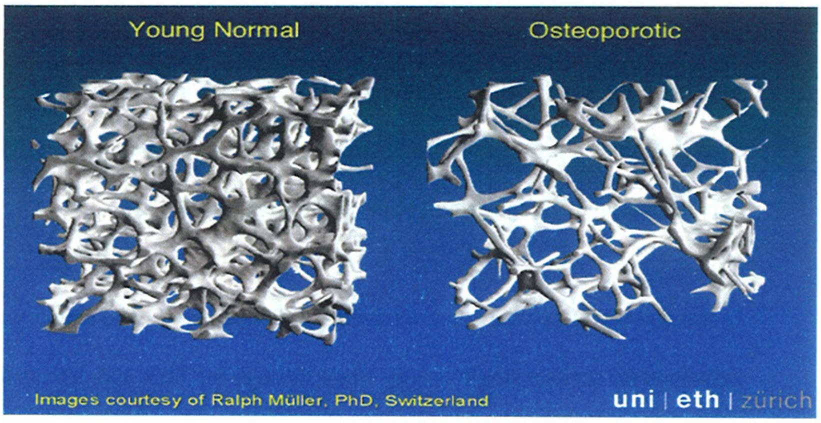


Figure 2. Trabecular bone structure in the lower spine of a young adult compared to an osteoporotic elderly adult with both thinning of trabeculae and loss of connectivity.

2.3. The BMD measurement

The proportional contributions made by differences in bone size, cortical thickness, trabecular number, thickness and connectivity, tissue mineral content, micro damage burden and porosity, to differences between sexes or between races are still not clear (18). Despite its inability to capture all the components of bone strength (26), the densitometry technique development that started out in the 1960-ies (27) set the stage for the first non-invasive measurements of bone strength, represented by bone mineral density. Bone densitometry is a radiographic examination and the BMD results reflect the amount of radiation, which has been absorbed on its way through a defined anatomical site. The first bone densitometers, the Single and Dual Photon Absorptiometric devices (SPA, DPA), used isotopes as their source of radiation. These had relatively low spatial resolution, scans took a long time to complete (20 min) and the radionucleid needed frequent replacement. The development of x-ray based densitometers in the 1980ies, Single and Dual Energy X-ray Absorptiometry (SXA or DEXA/DXA), represented several improvements with shortened scan times, enhanced image resolution and improved precision (28, 29).

In the present study we have used the SXA densitometry. The single x-ray densitometer sends a single energy beam through the limb and detects how much of the radiation is absorbed by the structures that lie between the x-ray source and the detection unit. SXA can only be performed at peripheral sites, as the limb needs to be immersed in a water bath, which behaves like a standardised layer of soft tissue during the scan. With an integrated correction for fat mass, the computer use the x-ray absorption to calculate the amount of bone mineral present in the two-dimensional grey-scale scan image that is generated on basis of the absorption pattern. Each pixel represents the estimated bone mass at that particular anatomical point (30), or bone mineral content per projected area in g/cm ^{2} (29).

2.5. TROST and BMD measurements

The peripheral location and the relatively small amount of surrounding soft tissue made the distal forearm an obvious early choice for the assessment of a subject's bone mineral density. The limited amount of surrounding tissue increased the accuracy and the precision of bone mass measurements, the peripheral scanning site reduced the radiation dose and made the equipment requirements simpler and less expensive (29). In addition, the anatomy of the radius with a thin cortex with mainly trabecular bone at the ultradistal end and pure cortical bone along the radial shaft enabled the examination of both trabecular and cortical bone (29). When it was decided for TROST to have bone density measured in the Tromsø Study 1994-95, the SXA of the forearm was an easy choice. At that time, the DEXA scanning still took 30 minutes, which was too time-consuming for such a large study.

Despite the development and availability of densitometric techniques, BMD and its changes throughout life in both sexes was hardly studied when TROST planned for the Tromsø IV study in 1994. Most of the existing studies were cross-sectional (31-42), the majority of them based on healthy volunteer populations. Some longitudinal studies existed, describing BMD changes in younger (43-51) and older (52-60) women, but studies from general populations were rare (61-67), and to our knowledge only one of them included men (63). Normal BMD changes in both sexes from the younger to the older age groups were therefore not thoroughly described and the pattern of bone loss not well understood (68). As both peak bone mass and subsequent rate of loss both contribute to low bone mass later in life (69), knowledge about normal bone loss rates would be an important part of understanding the mechanisms behind bone fragility and fracture risk later in life. With its connection to the population based Tromsø Study, TROST had a unique possibility to study BMD changes in both sexes, from the younger part of the population to the elderly, both cross-sectionally (Tomsø IV) (70) and longitudinally (Tromsø IV and V), in a Scandinavian high-risk population.

2.4. BMD measurements in longitudinal studies

According to Heaney, few fields of clinical medicine possess tools as precise as bone densitometry (71). However, scanning instabilities and technical malfunctions might influence the quantitative results of bone mineral measurements (29) and bone densitometry can provide misleading information if it is not applied appropriately (26). Rigorous quality control is mandatory in the application of quantitative densitometry, and in longitudinal studies it is important to secure that the documented changes are real and not only due to densitometer drift or fluctuations (72-74) or due to variation between densitometers (72). Quality control of densitometer performance as well as cross-calibration between different machines (75) and different methods can be performed in vivo or in vitro with special-purpose scan phantoms (76). Planning for Tromsø IV and V in 1994, there were studies focusing on the problems of long-term precision within the field of bone mass measurements (62, 72, 77-80), as well as on the problems of comparability of BMD measurements between densitometers, even of the same make and model (81-83). With this awareness, it was important for TROST to develop and evaluate quality control routines for observation of densitometer performance during its studies, as well as comparability of the participating densitometers' measurement level. Our main concern has been how well densitometer phantoms would reflect differences between densitometers and in densitometer performance.

3.0. Aim of thesis

On the given background, the aim of the theses is two-fold:

1. To study BMD changes and its variation in women and men between 25 – 85 years in a population based longitudinal study. (Paper II and III)
2. To study how precision of BMD measurements can be assessed and secured in longitudinal studies. (Paper I and IV)

4.0. Materials and method

4.1. Main study population, TROST (paper I – III)

Through the Tromsø Study, TROST had in Tromsø IV, 1994-95, 10213 subjects invited for bone densitometry measurement and 7948 (78%) persons attended the examination (30, 70). In Tromsø V, 7386 persons still living in Tromsø were invited for a re-examination, and 5771 (78%) attended. This number corresponds to 57% of the originally invited cohort (Figure 2 and table 1). Table 1 displays the attendance rates within three age-groups. All age groups are included in paper I, age groups 25-44 in paper II, and age groups 45-84 in paper III.

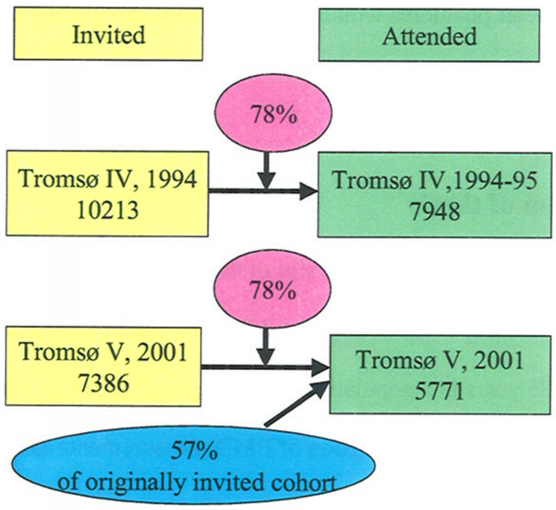


Figure 3. Flow chart presenting numbers of persons invited and attended in the longitudinal study Tromsø IV and Tromsø IV, 1994-95 and 2001.

Table 1. Attendance rates according to three respective age groups in 1994 for both sexes in the longitudinal study, Tromsø IV and Tromsø V, 1994-95 and 2001.

Age	Invited Tromsø IV	Attended Tromsø IV	Response %	Invited Tromsø V	Attended Tromsø V	Response %	Response % of originally invited cohort
Women							
25-44	617	396	64,2	391	258	66,0	41,8
45-64	3358	2738	81,5	2661	2226	83,7	66,3
65-84	1820	1418	77,9	1284	943	73,4	51,8
All	5795	4558	78,7	4341	3427	78,9	59,1
Men							
25-44	427	241	56,4	240	147	61,3	34,4
45-64	2494	1974	79,1	1841	1504	81,7	60,3
65-84	1497	1171	78,2	964	693	71,9	46,3
All	4418	3390	76,7	3045	2344	77,0	53,1

4.2. The course of the longitudinal study (paper I – III)

The course of the longitudinal study is displayed in figure 4. In Tromsø IV, 1994 – 95, we started out with the two densitometers, nicknamed “Adam” and “Eva”. Before starting the second survey in 2001, both densitometers were transported and used in other studies in NOREPOS (12, 84). Starting the second survey, “Eva” had to undergo a major repair and was principally replaced by “Henry”. Three and four months into the second survey, the x-ray tube had to be replaced on both densitometers, which therefore were nicknamed “Adam-01/ 1 and 2” and “Henry – 01/1 and 2” respectively.

Because of the densitometers breakdown, when the Tromsø Study ended phase 1 in December 2001, TROST had only measured BMD on 4681 persons, which corresponded to 63 % of those invited to the survey. As TROST still could use the same localities, we arranged an “extra-invitation” to those who had attended the Tromsø V survey, phase 1, without having the BMD measured. Of the 1527 persons invited, 1090 met (71%), and had their BMD measured in March 2002. With this “extra-invitation”, the total number of persons with repeated BMD measurements reached 5771.

Through both studies, quality control was performed on a daily basis with the aluminium forearm phantom (AFP) provided by the manufacturer. In 1999, the European forearm phantom (EFP) (QRM-Germany) was purchased. This is a semi-anthropomorphic phantom, comprising three hydroxy-apatite bone imitations with different densities within the human range, 0,662 g/cm^2 at the highest density level, 0,415 g/cm^2 at the mid-density level and 0,314 g/cm^2 at the lowest density level. From 1999, and through the second survey, regular measurements with the EFP, was also included into the study protocol. After finishing the survey in March 2002, we had three sources at disposal for retrospective analysis of densitometer performance in our study, and the analysis and comparison of these three sources serve as a background to paper 1.

1. Repeated human measurements at the distal and ultradistal forearm sites in altogether eight densitometer combinations.
2. Repeated measurements of the equipment specific aluminium forearm phantom provided by the manufacturer.
3. Repeated measurements of the European forearm phantom which was purchased in 1999.

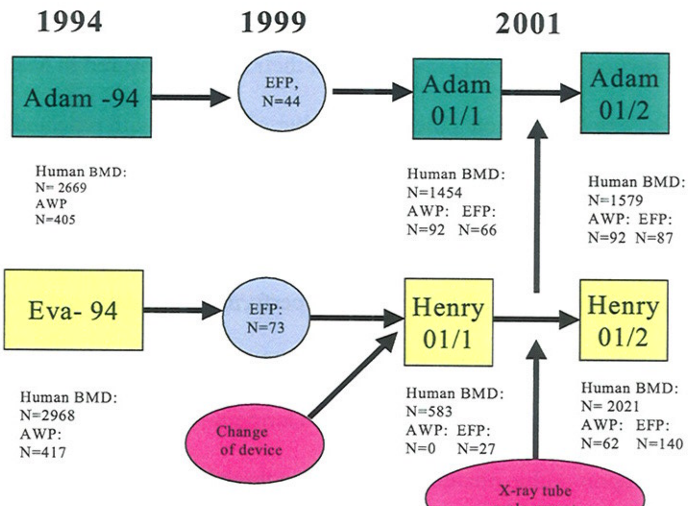


Figure 4. The course of the longitudinal study displayed, Tromsø IV and Tromsø IV, 1994-95 and 2001. Human BMD, n=valid measurements at the distal forearm site.

4.3. Quality control and exclusion of invalid scans (paper I – III)

In both studies, all scans were reviewed and reanalysed from the protocol developed during Tromsø IV (85). Analyses of the scans lead to exclusions of 81 and 113 scans at the distal and ultradistal sites respectively in women, and 53 and 42 scans at the distal and ultradistal sites respectively in men. Reasons for exclusions were, in both studies, mainly excessive movement artefacts at the distal site and region of interest out of scan at the ultradistal site. Table 2 displays the numbers of measured, excluded and valid scans.

Table 2. Valid repeated measurements TROST, Tromsø IV 1994-95 and Tromsø V 2001.

	Repeated measurements Tromsø IV-V	Excluded measurements Tromsø IV	Excluded measurements Tromsø V	Valid repeated measurements Tromsø IV-V
Women				
Distal site	3427	51	32*	3346
Ultradistal	3427	81	37**	3313
Men				
Distal site	2344	32	21	2291
Ultradistal	2344	22	20	2302

* 2 persons had their scans excluded in both studies at the distal site
**4 persons had their scans excluded in both studies at the ultradistal site

4.4. Study population, NOREPOS Study (paper IV)

In this study we wanted a **selected study population** with a wide range of characteristics that possibly could influence BMD measurements. The inclusion criteria are thoroughly described in paper IV. For clarification, volunteers for the study were recruited among employees at the University of Tromsø (UiTØ) and they were asked information about age, height and weight as surrogates for bone mass, bone size and BMI. From this information, persons were selected to the study through the following system, containing at least three persons in each group:

Table 3. Chosen characteristics of study participants for the initial recruitment phase, NOREPOS Study.

Age (years)	Height (cm)	Weight (kg)
25 - 44	<162	57 – 67
45 - 64	163 – 171	67 – 79
65 - 70	>171	80 – 92

20 participants fitting into any of these groups, underwent a preliminary DEXA examination and were included into the study from following criteria; variation in BMD levels (g/cm^2), bone size (cm^2) measured by DEXA (total hip) and variation in BMI (kg/m^2). The chosen range of variation was provided through data from Tromsø V. From these measures we had a total of 9 categories where participants were included until there were a minimum of 3 participants fitting into each category (Table 1, paper IV). Finally a total of 17 participants were included into the study.

4.5. BMD measurements, NOREPOS Study (paper IV)

Bone densitometry was performed as in the main study on the distal forearm, on the five similar SXA-devices formerly used in NOREPOS sub-studies (84), two of these used in the main study. Each of the 17 participants had three measurements done on each densitometer with full repositioning between each measurement, from the same protocol as used in the main study as well as in the former studies in NOREPOS (12). All scans were reviewed and reanalysed according to the same quality control protocol as in the main study (86).

4.6. Data management and statistics.

Data management and statistical analysis are thoroughly described in the respective papers.

5.0. Summary of papers and main results

5.1. The choice of densitometer phantoms in longitudinal studies (paper I)

BMD changes differed significantly on the eight densitometer combinations in the longitudinal study, also when adjusting for sex and age, indicating a difference in densitometer measurement level. The main purpose of this study was to investigate to what degree two different densitometer phantoms reflected densitometer performance which was observed in the human BMD change data. The indicated differences were predicted by the anthropomorphic forearm phantom, EFP, and not by the aluminium forearm phantom, AFP. The EFP measurements indicated that one of the densitometers ("Adam-94" and "Adam-01/1") measured at a higher level (0.005 g/cm²) before x-ray tube replacement compared to the other densitometers. The EFP data also indicated that measurement level within each time of function of the densitometers (CV%) was stable. Based on these results from this, we adjusted the data measured on "Adam-94" and "Adam-01/1" and concluded that daily assessment of densitometer performance in longitudinal studies should be performed by anthropomorphic and not aluminium phantoms.

5.2. BMD changes in women and men 25 – 44 years (paper II)

The main purpose of this study was to describe and compare BMD changes in women and men aged 25 - 44 years. At the distal site, a small annual gain of approximately 0.1 percent turned to a small loss from age 34 and 36 in men and women respectively. In both sexes the change was significantly predicted by age. At the ultradistal site, BMD change was only predicted by age in women, bone loss starting from age 38. A high degree of tracking of BMD measurements were observed in both sexes at both sites. Depending on total BMD change, participants were grouped into "losers", "non-losers" and "gainers", and more than 6 percent lost more than the smallest detectable change, >-3.46 and >-5.14 percent, at the distal and ultradistal sites respectively. In both sexes the bone mineral content (BMC) (g) decreased whereas area (cm^2) increased significantly in "losers" compared to "gainers", representing a possible physiological compensation preserving bone strength. No cohort effects were observed when measures from similar age groups from 1994 and 2001 were compared. We conclude that BMD changes in the age group 25-44 are significantly explained by age, but not by sex.

5.3. BMD changes in women and men 45 – 84 years (paper III)

The main purpose of this study was to describe BMD changes in women and men aged 45 – 84 years. The mean annual bone loss was –0.5 and –0.4 percent in men, –0.9 and –0.8 percent in women not using hormone replacement therapy (HRT), at the distal and ultradistal sites respectively. Age was a negative predictor of BMD change at both sites in men. Women not using HRT had the highest bone loss rates at the ultradistal site 1 – 5 years after menopause. The correlation between the two measurements were high; r=0.93 and r=0.90 in women, and r=0.96 and r=0.93 in men, distal and ultradistal sites respectively. More than 70 percent kept their quartile positions. The degree of tracking of BMD measurements was therefore high. The observed bone loss rates in this study population were not higher compared to other cohorts. We conclude that BMD changes in men are significantly explained by age at the distal and ultradistal forearm sites, whereas women not using HRT experience the highest loss rates 1-5 years after menopause.

5.4. Can in vitro replace in vivo densitometry cross-calibration? (paper IV)

Based on the results from paper I, and on studies reporting conflicting results concerning agreement between in vitro and in vivo measurements, we wanted to study the agreement between AFP, EFP and in vivo densitometry at the distal forearm site in a cross-calibration study. Representing the gold standard for calibration, the human measurements revealed that one of the five densitometers reported a higher BMD level than the other four densitometers. The EFP followed the direction of difference observed in the human measurements better than the AFP, but tended to overestimate the difference between the densitometers. We conclude that densitometers of same make and model might differ significantly in performance. In vivo measurements remain the most valid tool for detection of densitometer differences although differences in densitometer performance are better captured by calcium-hydroxyapatite then aluminium phantoms. In longitudinal studies, regular use of phantoms of calcium-hydroxyapatite is still recommended for daily quality assessment and for comparison of different densitometer's measurement level.

6.0. Discussion

6.1. Internal validity

The internal validity refers to whether results from a study are valid or true for the study population (87). Selection bias, information bias and confounding may threaten the internal validity of a study (87). Bias may be defined as any systematic error in an epidemiologic study that results in an incorrect estimate of the association between exposure and outcome (88). Confounding might be defined as confusion, or mixing, of effects. This definition implies that the effect of the exposure is mixed together with the effect of another variable so that the association between exposure and outcome may be distorted by a third variable, which is related to both the exposure and the outcome (89). Age and sex are very likely to be confounding variables. As those are the most central variables studied in relation to BMD changes in this theses, we have, to avoid confounding, done the analysis both age and sex stratified. We are, therefore, mostly concerned about the possible effect from selection and information bias in our studies on BMD changes (paper II and III), where the aim is to gain knowledge of BMD changes and its variation in both sexes in a normal population.

6.1.1. Selection bias

Selection bias is a systematic error in a study that stems from the procedures used to select subjects and from factors that influence study participation (89). The Tromsø Study is a population based study famous for the high attendance rates in its surveys, and as displayed in table 1, the attendance rates in both Tromsø IV and V were well above 75 % in both sexes. The attendance rates do however vary between the different age groups, being highest in the older age groups, and lowest in the youngest age groups, which comprise the study population of paper II. Data for the first study, Tromsø IV, were compared for non-responders, partial responders and full responders (30, 70), the analysis gave no indication for any differences between these groups (30). After Tromsø V, we could use baseline characteristics from Tromsø IV to compare participants lost for follow-up with those who attended both studies. The results from the analysis are displayed and thoroughly discussed in paper II and III. Here we summarize our main findings.

In the youngest age groups, women and men 25-44 years, participants lost for follow-up were younger than those who participated in both studies. We have presented the data in 5-years age groups, which gives us small numbers in the youngest age groups. It was therefore a great concern to discover possible selection favours. With information gained from questionnaires in Tromsø IV we analysed whether the two groups differed with regard to central lifestyle variables which might influence bone loss rates (90-105). The only observed difference between the two groups was connected to smoking status in both sexes. The percentage of present smokers was equal among participating women compared to participants lost for follow up (p=0.03), but participating women had smoked one year longer than those lost for follow up. Total amount of cigarettes smoked were however not significantly different when the two groups were compared. The percentage of present smokers tended to be higher among the male participants lost for follow-up (p=0.06), but smoking years and total amount of cigarettes smoked were not significantly different in the compared groups. Smoking might influence bone health in a negative direction, with a cumulative effect by age (106), but smoking years did not predict BMD changes in women (p= 0.163 and p=0.222 at the distal and ultradistal site respectively) and smoking status did not predict BMD changes in men (p= 0.238 and p=0.051 at the distal and ultradistal site respectively) in this material. We therefore assume that the results presented in paper II are not seriously influenced by selection bias.

For the older age groups, 45 – 84 years, women lost for follow up were shorter, had a greater BMI, were more often smokers, had a higher percentage perceiving their own health as bad, and had a lower baseline BMD at both the distal and ultradistal site. Men lost for follow up were shorter, weighing less, were more often smokers and more often perceived their own health as bad compared to those who participated in both studies. Baseline BMD at both the distal and ultradistal site was also lower in participants lost for follow-up. As thoroughly discussed in paper III, the differences between the two groups indicate that participants lost for follow-up in general seem to be less healthy or having less healthy life-style than those who participated in both studies. 556 persons with a mean age of 65.8 years, were either dead or had moved out town between the two surveys. When these persons were excluded from the analyses, age, height, weight, BMI and smoking years (women) were no longer significantly different between the two groups, but baseline BMD remained significantly different at both sites. Bone health is a powerful predictor of general health status (107), and despite high attendance rates, we must conclude that there is a possible "healthy" selection bias in the material. Our bone loss rates might therefore be slightly underestimated. As we have discussed in paper III, this tendency towards "healthy" selection bias is also observed in other longitudinal studies within the field of osteoporosis research (108, 109).

As part of the Tromsø study, the Family Intervention Study (FIS) was an open randomised trial aimed at improvement of the cardiovascular risk profile in male subjects who either had a high total cholesterol or a low HDL to total cholesterol ratio (110). In Tromsø IV, 328 male participants, being members of FIS, had their BMD measured. In the presentation of our cross sectional data, these men were excluded from the analysis as they were not viewed as representative of the general population with respect to BMD level (70). In Tromsø V, 251 of the FIS cohort members had the BMD measurements repeated. Since their bone loss rates did not differ significantly in comparison to the other men in the respective age groups, we have not excluded the FIS-cohort members from the BMD change analysis. Table 4 displays the bone loss rates in the respective age groups.

Table 4. Comparison of BMD changes (mg/cm^2) in male participants categorized as "FIS- members" and "non-FIS members".

Age groups	FIS-members, BMD change (mg/cm^2)			Non-FIS members, BMD change (mg/cm^2)			P - value
	n	mg/cm^2	95%CI	n	mg/cm^2	95%CI	
40-44	15	-1.41	(-2.31, -0.51)	30	-0.73	(-1.25, -0.21)	0.15
45-50	113	-1.41	(-1.80, -1.02)	54	-1.62	(-2.36, -0.87)	0.59
50-54	122	-1.60	(-1.98, -1.22)	62	-1.42	(-1.89, -0.96)	0.58
55-59	1	-2.40		604	-1.92	(-2.11, -1.73)	

6.1.2. Information bias

Systematic error in a study can arise because the information collected about or from the study subjects is erroneous (89). The SXA measurement of the distal forearm is thought to be one of the most precise densitometric methods (111-114), and the low coefficient of variation (CV%) on our densitometers during their time of function confirmed that assertion (paper I). From the post hoc analysis (paper I) we found that the AFP and the EFP predicted densitometer performances differently and since the EFP measurements reflected the differences seen in the human material, we decided to use the EFP measurements in the final evaluation of densitometer performance, which lead to an adjustment of minus 0.005 g/cm^2 of the measurement levels of "Adam – 94" and "Adam-01/1" (paper I). In the NOREPOS study (paper IV), we had the opportunity to evaluate densitometer performance through human measurements from a wide range of BMD levels. As the human measurements represent the gold standard, the performance of EFP and AFP is compared directly with the human measurements. From the results we concluded that EFP followed the human measurements, however tending to overestimate the real densitometer differences. These findings indicated that the correction based on the EFP probably represent an "over- adjustment". Table 5 displays the BMD change estimates in mg/cm^2 at the distal forearm sites, unadjusted data and data adjusted on basis of the EFP measurements (paper I). In addition, we display the BMD change estimates which are adjusted on basis of the human measurements: minus 0.003 g/cm^2 of the measurement levels of "Adam – 94" and "Adam-01/1".

Table 5. BMD change estimates in mg/cm² at the distal forearm sites, data adjusted based on EFP (paper I), data adjusted based on human measurements and unadjusted data, Tromsø IV 1994-94 and Tromsø V 2001.

Women	N	Adjusted -0.005 mg/cm² (95%CI)	Adjusted -0.003 mg/cm² (95%CI)	Unadjusted mg/cm² (95%CI)
Age groups				
25-29	36	0.44 (-0.2, 1.09)	0.32 (-0.3, 0.94)	0.14 (-0.47, 0.74)
30-34	75	0.38 (-0.05, 0.82)	0.29 (-0.14, 0.72)	0.16 (-0.28, 0.59)
35-39	72	-0.18 (-0.61, 0.26)	-0.25 (-0.68, 0.18)	-0.35 (-0.79, 0.08)
40-44	70	-0.31 (-0.81, 0.19)	-0.40 (-0.89, 0.09)	-0.54 (-1.01, -0.06)
45-49	82	-2.11 (-2.72, -1.50)	-2.18 (-2.78, -1.58)	-2.27 (-2.87, -1.68)
50-54	862	-3.35 (-3.62, -3.07)	-3.41 (-3.68, -3.14)	-3.51 (-3.78, -3.24)
55-59	686	-3.14 (-3.44, -2.85)	-3.21 (-3.50, -2.94)	-3.32 (-3.61, -3.02)
60-64	548	-2.89 (-3.20, -2.59)	-2.94 (-3.25, -2.64)	-3.02 (-3.33, -2.77)
65-69	545	-3.18 (-3.50, -2.85)	-3.25 (-3.57, -2.93)	-3.37 (-3.69, -3.05)
70-74	355	-2.94 (-3.38, -2.51)	-3.00 (-3.42, -2.57)	-3.07 (-3.50, -2.6)
75+	15	-5.49 (-8.13, -2.85)	-5.67 (-8.34, -3.00)	-5.94 (-8.65, -3.23)
Total	3346	-2.88 (-3.01, -2.75)	-2.95 (-3.08, -2.82)	-3.05 (-3.18, -2.92)
Men				
25-29	24	0.91 (-0.05, 1.87)	0.88 (-0.09, 1.84)	0.83 (-0.16, 1.82)
30-34	29	0.17 (-0.47, 0.80)	0.10 (-0.56, 0.75)	-0.01 (-0.71, 0.68)
35-39	43	-0.78 (-1.38, -0.18)	-0.91 (-1.58, -0.30)	-1.11 (-1.74, -0.48)
40-44	45	-0.96 (-1.40, -0.51)	-1.05 (-1.51, -0.59)	-1.19 (-1.69, -0.69)
45-49	166	-1.49 (-1.84, -1.14)	-1.55 (-1.90, -1.19)	-1.63 (-1.99, -1.26)
50-54	184	-1.54 (-1.83, -1.25)	-1.61 (-1.91, -1.32)	-1.72 (-2.02, -1.42)
55-59	602	-1.92 (-2.12, -1.73)	-1.97 (-2.16, -1.78)	-2.04 (-2.22, -1.84)
60-64	524	-2.70 (-2.96, -2.43)	-2.75 (-3.02, -2.49)	-2.83 (-3.10, -2.57)
65-69	393	-3.24 (-3.59, -2.89)	-3.30 (-3.6, -2.95)	-3.39 (-3.74, -3.04)
70-74	271	-3.77 (-4.21, -3.34)	-3.85 (-4.28, -3.41)	-3.96 (-4.40, -3.52)
75+	10	-3.29 (-5.84, -0.74)	-3.32 (-5.79, -0.85)	-3.37 (-5.72, -1.02)
Total	2291	-2.39 (-2.52, -2.27)	-2.45 (-2.58, -2.33)	-2.54 (-2.67, -2.42)

As reflected in Table 5, the unadjusted BMD change estimates report slightly higher (but not significantly different) bone loss rates (from age group 35-39 and 30 – 34 in women and men respectively), than the adjusted data. The adjusted BMD change estimates are therefore more conservative that the unadjusted. The most conservative BMD change estimates are those based on EFP (paper I, II and III), where the measurements from "Adam-94" and Adam-01/1" where reduced by -0.005 g/cm². These estimates probably represent an underestimation of the real bone loss rates. Adjustments of "Adam-94" and Adam-01/1" with -0.003 g/cm², based on the human material reduced differences observed between densitometer combinations in paper I (from p>0.001 to p=0.865, ANOVA), and most probably represent the "true" BMD changes. With this information bias, our published BMD change estimates are probably slightly underestimated. But, the differences in change estimates are neither statistically nor clinically significant (the mean difference in annual BMD change being less than 0.07 mg/cm², or 0.01 percent points in both sexes), and do not have any significant influence on the reported results.

In paper II and III we have classified women according to menstrual status and use of hormone replacement therapy based on answers to questionnaires. There might be some recall bias influencing the answers which might represent a misclassification with some influence on the reported BMD changes in women, although we believe that the effect is minor.

6.1.3. Summary internal validity

This longitudinal population-based study has an overall high response rate, indicating that the results are generalisable to the majority of the subjects in the source population. The non-response in the younger population (ages 25-44) is probably not related to changes in BMD, but non-response among the older subjects may be due to health related issues which might influence bone loss rates. With the densitometer adjustments we have made in this study, our reported bone loss rates in both sexes, might therefore be slightly underestimated, but with effects we believe are neither statistically nor clinically significant.

6.2. External validity

External validity refers to whether results that are found to be valid for the source population also are generalisable to other populations, the question of generalisability relying heavily on the source population being representative of other populations.

The Tromsø population does not differ substantially from the Norwegian population at large with respect to age and sex distribution (30). The city is situated at 69 degrees north, approximately 400 km north if the Artic Circle. The daylight exposure varies, and the high latitude strongly affects the amount and intensity of UV-exposure available (115). The inhabitants of Tromsø each year experience a "vitamin D winter" of approximately three months, with UV-radiation below the stated threshold need for vitamin D production in the skin (115). The essential role Vitamin D plays in maintaining a healthy mineralized skeleton has long been acknowledged (116, 117). Sunlight causes the photoproduction of vitamin D3 in the skin. Once formed, vitamin D3 is metabolized sequentially in the liver and kidney to 1,25-dihydroxyvitamin D. The major biological function of 1,25-dihydroxyvitamin D is to keep the serum calcium and phosphorus concentrations within the normal range to maintain essential cellular functions and to promote mineralization of the skeleton ans exposure to sunlight provides most humans with their vitamin D requirement (116).

With its location, it could be expected the population of Tromsø having higher bone loss rates, and the results from this longitudinal study therefore not being representative of other populations. There are difficulties in comparing BMD change rates between population, because of the use of different densitometer techniques and different sorting between age groups; but as discussed in papaer III, the loss rates in the age groups 45-84 observed in Tromsø are not higher compared to other cohorts (62-64, 67, 109, 118, 119). Our findings of a small bone loss starting in both sexes in mid-thirthies in the age groups 25-44 are slightly in contrast to some studies reporting no loss in the comparable age groups (120, 121), but in agreement with other researches (17). We therefore believe that the BMD change rates from the distal and ultradistal forearm site in women and men beween 25-84 observed in this study are generalisable to other populations. It would however be interesting to do a direct comparison of BMD-loss rates with other studies internationally.

6.3. Significance of results

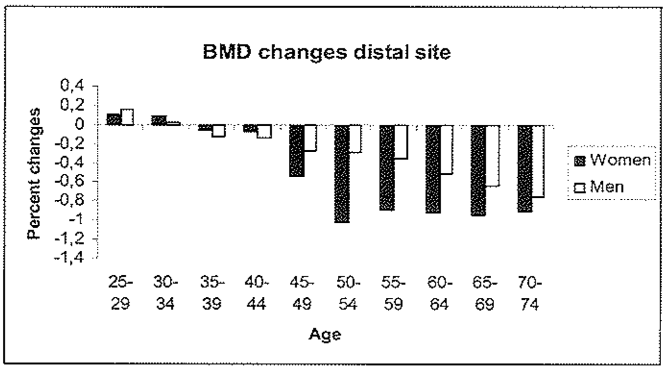
Through this study we have learnt that quality assessment of densitometer measurement levels preferably should be through in vivo cross-calibration. For long-term stability antropomorphic phantoms of hydroxy-apatite represent more valid tools than aluminium phantoms.

At the distal forearm sites, bone density continue to increase before it turns to a small decline from the mid thirthies in both sexes. In men the rates of bone loss increase with increasing age, whereas in women, the rate of loss is highest 1-5 years after menopause. Despite a high degree of tracking of BMD measurements, thare are interindividual variations of bone loss rates within each age group, and in both sexes.

6.3.1. BMD changes and types of bone

With the forearm sites, we had the possibility of studying age related BMD changes in cortical (distal site) as well as trabecular (ultradistal site) bone (Figure 5). In contrast to what is generally believed (16), cortical bone loss started in both sexes in the mid-thirties. In men, BMD loss became significant in the age group 35-39, thereafter it increased linearily with age so that the highest bone loss rates were observed in the oldest age groups. In women, cortical BMD loss became significant in the age group 45-49, doubled in the age group 50-54, whereafter followed a "stable" period with high bone loss rates until old age.

As indicated in the literature (16), the observed changes display a slightly different pattern in trabecular bone. In men, trabecular BMD loss started later than cortical bone loss (became significant from the age group 45-49), therafter it increased linearily by age with the same pattern as observed at the cortical site, but with significantly smaller loss rates in all age groups. In women, the significant increase in trabecular bone in the age group 25-29 turned dramatically to a significant decrease in from age group 45 – 50. The highest bone loss rates were measured in the age group 50-54 (and 1-5 years after menopause), therafter the loss rates actually slowed down. In summary, trabecular bone loss starts at the same time as cortical loss in women, it follows the same change pattern, but it is more pronounced, strongly influenced by the menopause-related estrogen deficency (16-18, 20).



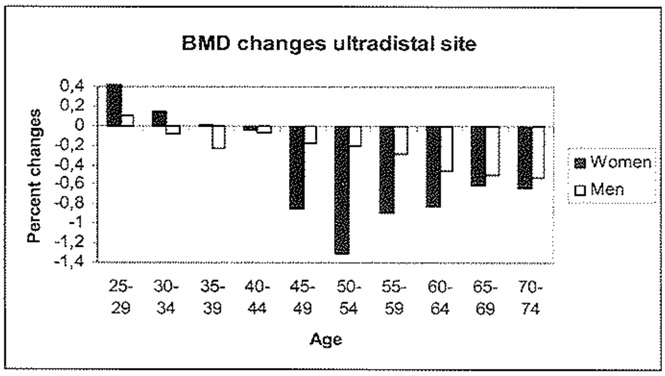


Figure 5. BMD changes in women and men 25-74 years, the Tromsø IV (1994-95) and Tromsø V (2001) longitudinal studies.

6.3.2. BMD changes and bone strength

The results from this longitudinal study confirm findings from other longitudinal studies that BMD continue to decline in both sexes throughout life (66, 108, 109). Comprising age groups from 25 years to old age, the results also demonstrate how women lose bone at a higher rate than men from the age of 45. Women also lose bone from lower baseline density, mean BMD level 0.482 and 0.377 g/cm^2 at the distal and ultradistal sites respectively in women, 0.588 and 0.507 g/cm^2 in men, in the age group 30-34. With the larger skeleton achieved during growth in men, the results from this study displays why bone strength is better maintained throughout life in men compared to women, and why structural failure occurs less in men than in women (18).

6.3.3. Area changes

As geometrical structure contribute significantly to bone strength, we have analysed our data on area changes in both sexes from 25-84 years, the results as annual area changes in mm^2 are displayed in table 6. In men, the area changes are not significantly different from 0 in the age groups 15-44 years. After 45, there is actually a significant area loss in men, with more or less the same picture observed in women too. The changes are in both sexes not significantly explained by age (p=0.73 in women, p=0.49 in men). Our findings of area loss, is in contrast to what is generally believed, that periosteal apposition increases area by age (17) and also confirmed in a longitudinal study of Ahlborg following 108 postmenopausal women over a period of 15 years, concluding that by six years after menopause, BMD had decreased significantly, whereas the periosteal diameter had increased significantly at the distal radius (122). Our findings are however in concordance with Heaney (23) who followed 191 caucasian women, aged 35 – 45 years, more than 20 years. They found that the cortical area of both the metacarpals and radial shaft declined by age with a magnitude similar to our findings, whereas both femur shaft diameter and cortical area increased modestly and significantly with age. According to Heaney, these observed changes at the upper extremity are small enough to be without much structural significance. The greater expansion at femur of 5% over the span of the study, is however considered as increasing the structural stiffness of femoral shaft, more than change in mass would predict (23). In conclusion, at the distal forearm site of the non-dominant hand, we did not observe geometrical changes which possibly could compensate loss of bone strength induced by loss of BMD.

Table 6. Annual area changes (mm^2) in women and men 25.84 in the longitudinal study, Tromsø IV and Tromsø V, 1994-95 – 2001, with 95 percent confidence intervals (95% CI)

	Women		**Men**	
Age groups	Mean change	95% CI	Mean change	95% CI
25-29	-0.036	(-0.101, 0.028)	-0.052	(-0.144, 0.04)
30-34	-0.038	(-0.08, 0.005)	-0.024	(-0.094, 0.046)
35-39	-0.053	(-0.101, -0.006)	-0.042	(-0.111, 0.027)
40-44	-0.053	(-0.091, -0.015)	-0.047	(-0.110, 0.016)
45-49	0.018	(-0.038, 0.073)	-0.047	(-0.081, -0.014)
50-54	-0.031	(-0.049, -0.012)	-0.049	(-0.079, -0.019)
55-59	-0.030	(-0.05, -0.01)	-0.050	(-0.069, -0.031)
60-64	-0.045	(-0.067, -0.023)	-0.052	(-0.073, -0.030)
65-69	-0.053	(-0.077, -0.029)	-0.054	(-0.08, -0.029)
70-74	-0.068	(-0.101, -0.035)	-0.061	(-0.088, -0.035)
75+	-0.019	(-0.206, 0.168)	-0.110	(-0.278, 0.057)
Total	-0.040	(-0.05, -0.031)	-0.052	(-0.062, -0.042)

6.3.4. BMD measures and fracture risk

The limitation of BMD in assessing bone strength and fracture risk, is recently emphasized by Kanis (123) stating that BMD forms only one component of bone strength and one component of fracture risk. The ability of bone mineral density to predict fracture is comparable to the use of blood pressure to predict stroke, and better than serum cholesterol to predict myocardial infarction (124-126). Accuracy is improved by site-specific measurements, so that for forearm fractures, the risk should ideally be measured at the forearm, and for hip fracture, at the hip (123, 125). Measurements at any sites, predict any osteoporotic fracture equally well, with a gradient of risk approximately 1.5 per standard deviation decrease in bone mineral density (125). It should also be recognised that, just because BMD is normal, there is no guarantee that fracture will not occur (123) and most fractures indeed occur in persons without osteoporosis (127). Conversely, if BMD is in the osteoporotic range, fractures are more likely, but might not necessarily occur. The low sensitivity is one of the reasons why widespread population base screening is not widely recommended (127). Kanis (123) suggests the following use of BMD measurements in the assessment of fracture risk:

Assessment of fracture probability based solely on clinical risk factors. This is supposed to identify three groups of individuals:

1. Individuals at very high risk of fracture, a BMD test would not alter their classification. These patients can be offered treatment irrespective of BMD. In practice, BMD might be measured so that response to treatment can be monitored (Although there is a poor correlation between increases in BMD seen with anti-resorptive treatment and the degree to which these drugs reduce the risk of fractures (128)).
2. Individuals at very low probability of osteoporotic fractures, a BMD test would not alter their classification.
3. An intermediate group are those in whom fracture probability is close to an intervention threshold where the probability is high that a BMD test might re-categorise individuals at high to low risk, or vice versa.

One of the main findings of our longitudinal study is that the degree of tracking of BMD measurements is high (paper II and III). There is thus a high correlation between baseline and follow-up BMD measure even after more than six years, and most persons keep their quartile position according to the population distribution of BMD levels. One BMD measure therefore expresses a person's BMD level well. Repeated BMD measurements should rarely be regarded necessary. Based on these considerations, we are very supportive of the restrictive use of BMD measures, as suggested by Kanis (123).

7.0. Concluding remarks and further perspectives

Despite its limitations both in explaining bone strength and in prediction of future fracture, the diagnosis of osteoporosis still depends on the measurements of bone mineral density. TROST has, through the Tromsø study, Tromsø IV and V, gained repeated BMD forearm measurements from a population based sample comprising both sexes. We have therefore been able to describe changes in BMD and its variation from young adulthood into old age. We have also been able to evaluate densitometer performance and we have made a contribution into the research on quality assessment in studies using bone densitometry.

Further research based on these data from TROST, are warranted. In Tromsø V, TROST had BMD measured at the total hip in 4938 persons. In the forthcoming Tromsø VI repeated measurements are planned for. This will provide opportunity to describe BMD changes at the hip, where the most serious osteoporotic fractures occur. In addition to BMD change data, fractures in the respective population are registered from 2001 to July 2005. We have the opportunity to assess the association between fracture risk and rate of bone loss, independent of BMD level. The rate of lifetime bone loss has not yet been estimated based on "hard data". On the longitudinal TROST data the lifetime bone loss and it variation can be studied. Furthermore, with information on lifestyle variables from Tromsø IV and V, we also have the opportunity to assess the association between different lifestyles, and changes in life style and the life time bone loss. Firm knowledge of possible associations can help to develop well documented bone loss and thereby fracture preventive strategies.

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ERRATA

Paper I: Human measurements, 7 948 persons (4558 women and 3390 men) had bone mineral density measured in Tromsø IV, 1994-95.

AUTHORSHIP PAPER IV

The first author had main responsibility for the statistical analysis, the second author for data collection and text writing.

Paper 1

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ORIGINAL ARTICLE

Bone mineral density measures in longitudinal studies: The choice of phantom is crucial for quality assessment. The Tromsø study, a population-based study

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Abstract Determination of change in bone mineral density (BMD) requires high-precision densitometry techniques. The purpose of the study is to investigate to what degree different densitometer phantoms reflect observed changes in human BMD and to investigate to what degree fluctuations in densitometers' measurement level influence bone loss estimates. Densitometer influence was assessed using the aluminum forearm phantom (AFP) provided by the manufacturer, the European forearm phantom (EFP) of semi-anthropomorphic calcium-hydroxyapatite, and repeated population measurements on different densitometer combinations. The mean follow-up time was 6.4 years (SD 0.6). Measured population bone loss varied from 4.6%/year to 3.2%/year, depending on densitometer combinations. These variations could not be explained by differences in sex, age, height, weight and baseline BMD. They were predicted by EFP measurements, but not AFP measurements. The EFP measurements indicate that X-ray tube replacement changed the densitometers' measurement level in one of three instances, whereas "wear and tear" did not. We used the EFP data for adjustment of the densitometers' measurement levels. After adjustment, the overall crude bone loss was reduced from 4.14% to 3.92%. Mean annual loss was reduced from 0.64% or 0.61%. We conclude that densitometer performance might influence the accuracy of bone loss estimates. Changes in performance are not detected by aluminum phantoms. Quality control of BMD measurements in longitudinal studies should be performed with anthropomorphic calcium-hydroxyapatite phantoms in order to detect possible differences between the participating densitometers' measurement levels.

Keywords Bone mineral density · Quality assessment · Population-based · Tromso study

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Introduction

Peak bone mass and postmenopausal and age-related bone loss determine the likelihood of developing clinical osteoporosis [1]. To accurately delineate differences and determinants of bone loss, a large sample must be followed over time [2]. Determination of bone mass change requires densitometry techniques with high precision [3–6]. The ultimate goal is to verify that observed change in measured bone density is real and not due to densitometer drift or fluctuation [7, 8].

Peripheral bone mineral density (BMD) measurement is associated with fracture risk at peripheral and central sites [9–12], and single X-ray absorptiometry (SXA) is a relevant tool for monitoring BMD changes due to high precision, ease of use, low radiation doses and moderate cost [13–18]. Baseline and follow-up examinations should be acquired on the same make and model [19]. Clinically relevant differences may occur even among devices from the same manufacturer [20], or after maintenance or upgrade [7, 21]. Quality control and calibration are performed using phantoms, which more or less resemble normal anatomy [20]. Phantoms of calcium hydroxyapatite in tissue-equivalent plastic most closely mimic human bone and soft tissue [7].

By the use of an anthropomorphic spine phantom, Orwoll et al. found a minor, but significant, drift in several DXA densitometers used in a longitudinal study [22]. They concluded that densitometer performance was most frequently affected by discrete "step" alterations that often could be explained in light of events described in the research protocol [22]. In our 6-year longitudinal study, using two SXA devices, breakdowns have occurred that required both X-ray tube and total densitometer replacement. This could influence the densitometers' measurement level and estimated individual changes in BMD. We have investigated how two different types of phantoms, the aluminum forearm phantom (AFP) provided by the manufacturer and the semi-anthropomorphic European forearm phantom (EFP), predict densitometer performance.

The purpose of the present study is therefore:

- To investigate to what degree two different densitometer phantoms reflect observed changes in human BMD
- To investigate to what degree fluctuations in densitometer measurement level influence estimates of bone loss

Materials and methods

Human measurements

The Tromsø Osteoporosis Study (TROST) is part of the Tromsø study, a longitudinal population-based multipurpose study focusing on lifestyle- related diseases. The first Tromsø study (Tromsø I) took place in 1974 and the fifth survey in 2001 (Tromsø V). In 1994 (Tromsø IV) 10,213 persons were invited for an extended examination including a bone mineral density measurement on 7,938 subjects (4,552 women and 3,386 men) from 25–84 years (attendance rate 78%) [23]. In 2001, 7,386 of these still living in Tromsø were invited for a reexamination. Of the invited, 5,771 subjects (3,427 women and 2,344 men), 78%, attended (57% of the originally invited population in 1994).

Bone densitometry was performed on the distal forearm (radius and ulna from the 8-mm point and 24 mm proximally) using two SXA devices (DTX-100; Osteometer MediTech, Hawthorne, CA, USA). Participants were allocated to the two densitometers dependant on accessibility. The same protocol was used in both studies. Only measurements from the distal site are presented in this study, as the ultradistal measurements followed the same pattern. All scans were reviewed and reanalyzed according to a rigorous quality-control protocol [24]. This led 136 distal scans to be excluded from the baseline and three distal scans from the follow-up study. Reasons for exclusion of invalid scans were mainly serious movement artifacts [24]. After exclusion of invalid scans 5,637 people (3,346 women and 2,291 men) remained with valid repeated measurements at the distal forearm site. Mean follow-up time was 6.4 years (SD 0.6). Informed consent was obtained prior to both examinations. The regional committee of research ethics recommended, and the Norwegian Data Inspectorate approved the study.

The timeline of the study is shown in Table 1. In Tromsø IV two densitometers, nicknamed "Adam-94" and "Eva-94", were used (Table 1). The densitometers were used in other studies before the start of Tromsø V. When Tromsø V was about to start in March 2001, Eva-94 had a breakdown and was replaced by a new DTX-100 device from the supplier, "Henry-01/1." Three months into the Tromsø V survey, in June 2001, the X-ray tube had to be replaced, and it was renamed "Henry-01/2". In September 2001, 6 months into the Tromsø V survey, the Adam-94 X-ray tube also had to be replaced. Consequently, when used in the 2001 survey, Adam-94 was named "Adam-01/1" and "Adam-01/2" (Table 1). Because of these events, the densitometers participating in both studies are classified as six separate units, with two units from Tromsø IV and four units from Tromsø V.

Starting Tromsø IV, Eva-94 and Adam-94 were cross-calibrated in vivo to the same measurement level with support from the manufacturer, and the devices had an equal measurement level as evaluated by the AFP at the time. During Tromsø IV, we also performed an in vitro precision study [16]. This study indicated a systematic difference between the two densitometers' measurement levels, and this data led to adjustment of

Table 1 General view of the course of the longitudinal study from 1994 to 2002. *TROST* (Tromsø Osteoporosis Study, *AFP* aluminum forearm phantom, *EFP* European forearm phantom, *BMD* bone mineral density)

	1994–1995[1]		1999[2]	2001–2002[3]		
	Human			Human		
Densitometers[4]	BMD	AFP	EFP	BMD	AFP	EFP
Adam-94	n =2,669	n =405	n =44			
Eva-94	n =2,968	n =417	n =73			
Adam-01/1[5]				n =1,454	n =92	n =66
Adam-01/2[6]				n =1,579	n =92	n =87
Henry-01/1[5]				n =583	n =0	n =27
Henry-01/2[6]				n =2,021	n =62	n =140

[1]Tromsø IV 1994–1995
[2]European forearm phantom (*EFP*) became available
[3]Tromsø V 2001 – 2002
[4]Age and sex distribution is not significantly different on the different machines
[5]Before X-ray tube replacement
[6]After X-ray tube replacement

our reported baseline cross-sectional data [23], since Adam-94 measured at a higher level than Eva-94.

Aluminium forearm phantom (AFP)

In Tromsø IV, measurements were performed on both densitometers once or twice daily with the aluminum forearm phantom provided by the manufacturer (Table 1). In Tromsø V, measurements were performed once daily with the same aluminum forearm phantom. Stability was regarded as adequate if phantom measurements were within ±1.5% limits of the calibration value on both densitometers. No correction of stability was required during the time of function of any of the six units. The measurements from Henry-01/1 and Henry-01/2 were from the last 3 months of the study only, unfortunately, due to loss of backup data.

European forearm phantom (EFP) (QRM-Germany)

In 1999 the recently developed European forearm phantom (EFP) (QRM-Germany) was purchased [25–27], a semi-anthropomorphic phantom, comprising three hydroxyapatite bone imitations with different densities within the human range, 0.662 g/cm^2 at the highest density level, 0.415 g/cm^2 at the mid-density level and 0.314 g/cm^2 at the lowest density level. Several EFP measurements were performed on the two machines before they were used in other studies (Table 1). Throughout Tromsø V, we continued the EFP measurements regularly. All EFP scans were analyzed by the same two people according to protocol using the special calculation option in the densitometer's software.

Statistical analysis

Bone loss was estimated by calculating the BMD differences between Tromsø V and Tromsø IV. This estimate was divided by each participant's follow-up time to calculate bone loss rates. Bone loss rates in different densitometer combinations were compared by one-way analysis of variance (ANOVA) with post hoc pairwise comparisons, applying the Bonferroni correction. Chi-square testing and one-way ANOVA were used to compare the sex and age distribution, height, weight, body mass index (BMI), baseline BMD and the mean phantom measurement level between densitometers. Internal variation within each densitometer was expressed as coefficient of variance. In addition, internal variation was studied by dividing the EFP measurements of each of the six densitometers arbitrarily into subgroups corresponding to periods of 2–3 months, comparing these by one-way ANOVA. In the final presentation of BMD change in humans (Table 2), the Adam-94 and Adam-01/1 measurements are adjusted on the basis of the mean difference between these two densitometers and the other four measured by EFP. A p value less than 0.05 is regarded as statistically significant. All statistical analyses were performed using SPSS software, version 11.

Results

Human measurements

Bone loss in humans according to eight possible densitometer combinations are displayed in Table 2. Individuals measured on the different densitometer combinations do not differ significantly with regard to sex (p =0.469), age (p =0.276), height (p =0.069), weight (p =0.069) and baseline BMD (p =0.848), but do with regard to BMI (p =0.039). Overall mean crude bone loss is 0.0185 g/cm^2 or 4.14%. Mean annual loss, which "adjusts" for difference in mean time between studies, is 0.003 g/cm^2 or 0.64%. Bone loss is equal to or higher than the mean in all combinations comprising Adam-94, and smaller than the mean in all combinations comprising Eva-94 (Table 2). Mean bone loss is significantly different when comparing densitometer combinations ($p < 0.001$), also when adjusting for BMI.

Table 2 Bone loss estimates in the longitudinal study, not adjusted and adjusted data. (*TROST* Tromsø Osteoporosis Study), 1994–95 and 2001

Densitometercombinations	n	Not adjusted data, mean loss				Adjusted data, mean loss			
		g/cm^2	SD	%	SD	g/cm^2	SD	%	SD
Adam-94/Adam-01/1	685	−0.0187	(0.02)	−4.17	(5.4)	−0.0187	(0.02)	−4.22	(5.5)
Adam-94/Adam-01/2	771	−0.0213	(0.02)	−4.80	(5.3)	−0.0163	(0.02)	−3.73	(5.4)
Adam-94/Henry-01/1	283	−0.0190	(0.02)	−4.20	(5.3)	−0.0140	(0.02)	−3.14	(5.4)
Adam-94/Henry-01/2	930	−0.0208	(0.02)	−4.58	(6.2)	−0.0158	(0.03)	−3.50	(6.3)
Eva-94/Adam-01/1	769	−0.0145	(0.02)	−3.25	(5.3)	−0.0195	(0.02)	−4.35	(5.3)
Eva-94/Adam-01/2	808	−0.0178	(0.02)	−4.00	(5.3)	−0.0178	(0.02)	−4.00	(5.4)
Eva-94/Henry-01/1	300	−0.0177	(0.02)	−4.06	(5.4)	−0.0177	(0.02)	−4.06	(5.4)
Eva-94/Henry-01/2	1.091	−0.0177	(0.02)	−4.04	(5.8)	−0.0177	(0.02)	−4.04	(5.8)
Total mean	5.637	−0.0185	(0.02)	−4.14	(5.6)	−0.0174	(0.02)	−3.92	(5.6)

Aluminium forearm phantom (AFP)

AFP measurements (Table 3 and Fig. 1) indicate that the mean bone density level varies between the different densitometers, with a range from 0.392 g/cm^2 in Eva-94 to 0.396 g/cm^2 in Henry-01/2 ($p < 0.001$), the only densitometers that are not significantly different are Adam-01/1 and Adam-01/2. Therefore, according to AFP, X-ray-tube replacement does not change the densitometers' measurement levels, while long-term drift does (Adam-94 compared with Adam-01/1). The CV% is below 0.8% on the densitometers used in Tromsø IV, and below 0.3% on the ones used in Tromsø V. From the AFP measurements, we would expect the estimates of bone loss in humans to be smallest in combinations comprising Henry-01/2. We would also expect the combinations Eva-94/Adam-01/1 and Eva-94/Adam-01/2 to be equal (Table 2). This pattern is not seen in the human material (Table 2 and Fig. 2). Differences in bone loss observed in humans are thus not reflected in the AFP measurements.

European forearm phantom (EFP) (QRM-Germany)

The EFP measurements (Table 4 and Fig. 1) indicate that the mean bone density level varies on the different densitometers. At the highest density level, the range of variation between the densitometers is 0.011 g/cm^2, at the mid-density level 0.007 g/cm^2, and at the lowest density level 0.006 g/cm^2. The CV% varies from 0.2% to 1.7% (mean 0.9%) depending on density level. At all density levels, Adam-94 and Adam-01/1 measure significantly higher than the other densitometers. Henry-01/2 measures the lowest values, but only statistically significantly different from Adam-94 and Adam-01/1. The mean difference between Adam-94 and Adam-01/1 and the other densitometers is 0.005 g/cm^2.

There are thus differences between the densitometers' measurement levels. Adam-94 measures higher than Eva-94. From this, we would expect the highest bone loss estimates in the human material to be seen in Adam-94 combined either with Adam-01/2, Henry-01/1 or Henry-01/2 and the smallest estimate to be seen in the combination Eva-94 and Adam-01/1. This is actually the pattern seen in the human material (Table 2 and Fig. 2). From this we conclude that the EFP measurements reflect the differences in bone loss observed in the human material.

For further study of internal variation, the EFP measurements are also used to compare different time periods within each densitometer. There are no significant differences in level of measurement when the three periods of Adam-01/1 are compared or when the three periods of Adam-01/2 are compared with each other. Adam-94 is also not significantly different in level of measurement compared with any of the time periods of Adam-01/1. There are no significant differences in level of measurement between the five time periods of Henry-01/2, except at the low BMD level between two of the time periods. Eva-94 and Henry-01/1 are also not significantly different in level of measurement from any of the time periods of Henry-01/2, except at the low BMD level between two of the time periods. From these EFP measurements, we conclude that each densitometer is stable and does not vary according to measurement level during its specific time of function. This is illustrated in Fig. 3 with EFP measurements from the high density level.

Human measurements after adjustments

Since EFP measurements predicted the differences observed in the human material, we adjusted the measurement level of Adam-94 and Adam-01/1 by the mean 0.005 g/cm^2 difference (Table 2). Mean bone loss throughout the study period is reduced from −0.0185 g/cm^2 to −0.0174 g/cm^2 or from −4.14% to −3.92%. Mean annual loss is reduced from −0.00285 g/cm^2 to −0.00269 g/cm^2, or from −0.64% to −0.61%. The variation between the densitometer combinations is still

Table 3 Aluminum forearm phantom measurements from the different densitometers in the longitudinal study. *TROST* (Tromsø Osteoporosis Study), 1994–95 and 2001

Densitometers	n	Mean g/cm^2	SD	CV%
Adam-94	405	0.393	0.003	0.76
Eva-94	417	0.392	0.003	0.77
Adam-01/1	92	0.394	0.006	1.5
Adam-01/2	92	0.394	0.001	0.25
Henry-01/2	62	0.396	0.001	0.25
Pairwise differences[1]	Eva-94 p value	Adam-01/1 p value	Adam-01/2 p value	Henry-01/2 p value
Adam-94	0.001	0.002	0.001	0.001
Eva-94		0.001	0.001	0.001
Adam-01/1			1.000	0.001
Adam-01/2				0.001

[1]The densitometers compared, p value

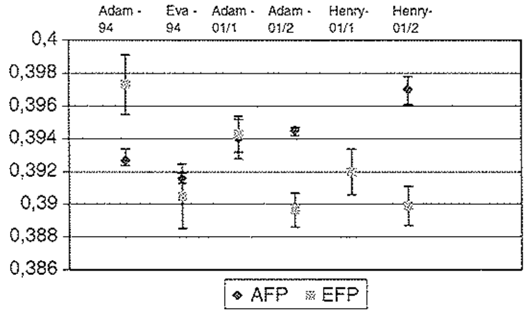

Fig. 1 Measurements based on aluminium forearm phantom (*AFP*) and European forearm phantom (*EFP*)

significant ($p < 0.001$) for annual bone loss (g/cm^2 and %), also when adjusting for BMI (p = 0,005). But the range of variation is reduced, from 0.007 to 0.005 g/cm^2 for total bone loss and from 1.6 to 1.2 for total bone loss %.

Discussion

In this longitudinal study we found that estimates of bone loss were influenced by differences in the densitometers' measurement level. Differences seen in the population material were predicted by the measurements of the EFP, and not by the AFP.

One of the strengths of this study is that phantom measurements can be compared with measured BMD change in a large population sample. The participants were allocated to the densitometers dependant on machine availability, not through randomizing procedures. However, as the participants' age, sex, height, weight and baseline BMD distribution were not significantly different when the different densitometer combinations were compared, we assumed that estimates of bone loss should be approximately the same in the different densitometer combinations.

One of the limitations of the study is that we do not have aluminum phantom measurements on Henry-01/1. However, since these measurements were stable (CV 0.25%) throughout the last part of the study (Henry-01/2), we think that this would not change our estimates. Another limitation is that the EFP became available only in 1999, 4 years after the completion of Tromsø IV. The densitometers from Tromsø IV had hardly been used in the period between 1995 and 1999. After 1999, the densitometers were used in other studies; several measurements were performed, and the densitometers were transported. Because of this, the time span between 1999 and 2001 was the most vulnerable period for the densitometers. The difference seen between Adam-94 and Eva-94 in 1999 also corresponds to the differences seen in the in vitro precision study that was performed during Tromsø IV [16]. Adam-94 and Adam-01/1 are also comparable—whereas Adam-01/2 is not—indicating that it is not wear and tear, but the change of X-ray tube that introduces the change in performance. We

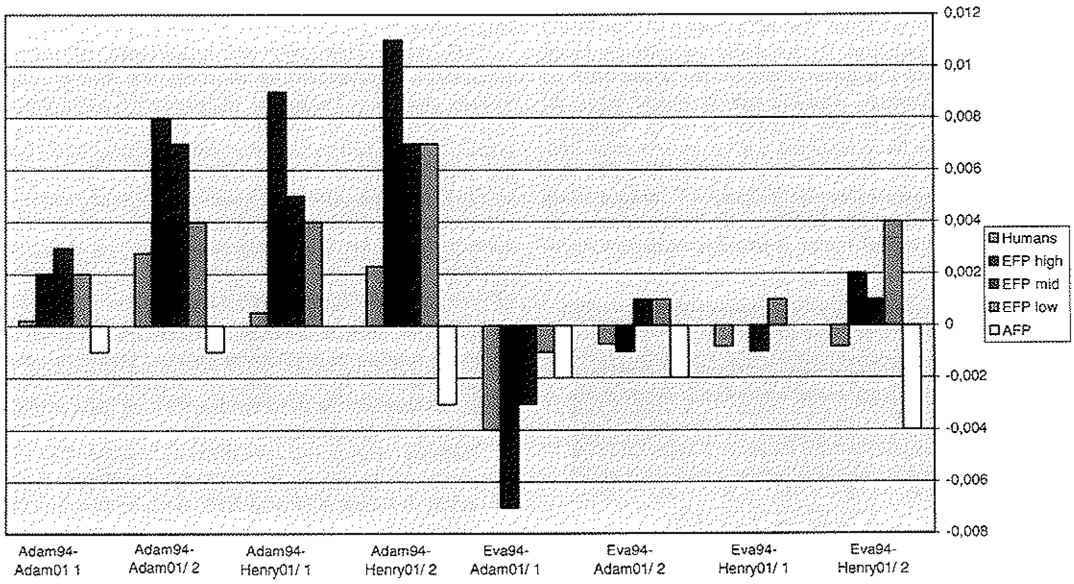

Fig. 2 Measurements in human material compared with aluminium forearm phantom (*AFP*) and European forearm phantom (*EFP*). EFP measurements reflect the differences in bone loss observed in the human material

Table 4 European forearm phantom (*EFP*) measurements from the different densitometers in the longitudinal study. *TROST* (Tromsø Osteoporosis Study, *BMD* bone mineral density), 1994–95 and 2001

Densitometers		High BMD				Mid BMD				Low BMD		
		mean				mean				mean		
	n	g/cm^2	SD	CV%	n	g/cm^2	SD	CV%	*n*	g/cm^2	SD	CV%
Adam-94	15	0.634	0.004	0.6	15	0.397	0.003	0.8	14	0.289	0.005	1.7
Eva-94	25	0.625	0.007	1.1	24	0.391	0.005	1.3	24	0.286	0.003	1.0
Adam-01/1	22	0.632	0.003	0.5	22	0.394	0.003	0.8	22	0.287	0.003	1.0
Adam-01/2	29	0.626	0.001	0.2	29	0.390	0.003	0.8	29	0.285	0.003	1.1
Henry-01–1	9	0.625	0.003	0.5	9	0.392	0.002	0.5	9	0.285	0.003	1.1
Henry-01–2	46	0.623	0.006	1.0	47	0.390	0.004	1.0	7	0.282	0.004	1.4

[1]Densitometers compared, *p* value

therefore think that the measurements from 1999 are representative of the measurement level in Tromsø IV, but we might have missed some long-term densitometer drift.

After 6 years' use, central elements of both the original densitometers had to be replaced. We do not believe our densitometers to be of lesser quality than other densitometry devices, regardless of model or manufacturer. What we have observed in our study might apply to any other device used in longitudinal studies, and as such, be of relevance for devices of any make and model.

We have assumed that the phantoms themselves do not change over time. This might be a possible information bias. Phantoms are, however, regarded to be stable at any point in time [28].

When comparing the various densitometer combinations, we found that differences in bone loss estimates were predicted by the EFP measurements, making them the appropriate reference for adjustment of the BMD levels in the population. In this study we used the mean difference for all the three BMD-levels of the EFP as basis for adjustments. Another option would be to do the adjustments according to BMD level by regression estimates, as we have reported earlier on our cross-sectional data [16, 23]. However, the BMD differences seen between the machines in the Tromsø IV human study were not dependant on BMD level. Furthermore, we found that the use of linear regression estimates introduced a greater variation in adjusted values of the population material than the mean difference.

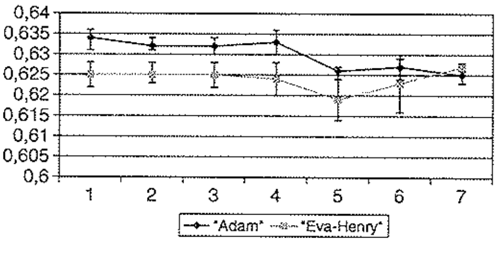

Fig. 3 Based on European forearm phantom (*EFP*) measurements from the high density level, we conclude that each densitometer is stable and does not vary according to measurement level during its specific time of function

After adjustment, the mean total bone loss was reduced from 4.15% to 3.93% in 6 years. As the 1-year bone loss rate can be estimated to be approximately 1% after menopause in women [4, 5], our initial apparently small overestimation could be argued to be of little clinical relevance, and by epidemiological standards the error of our BMD change measurements is small. However, the adjustment can affect results, especially in subgroups where we would not expect bone loss, such as young women and men. The uncorrected densitometer differences could report a false bone loss in these groups. An overestimation of bone loss might also introduce bias when defining the age of peak bone mass and the commencement of bone loss. When measurement of BMD is used to monitor treatment progress, the accuracy of the measured bone change is also of ultimate importance.

This study highlights the importance of careful assessment of densitometer performance during longitudinal studies. Changes in densitometer performance might influence the accuracy of bone loss estimates. Important differences between densitometers and changes in densitometer performance might not be detected by aluminum phantoms. Further studies are needed to evaluate how different phantoms mimic human bone density. Based on the experiences from this study, we propose the following recommendations for quality control of BMD measurements in longitudinal studies:

- Different devices of the same manufacturer (even the same model) give different results. Therefore, even when follow-up of patients in longitudinal studies is performed on the same device, its long term stability should be documented
- Different phantoms give different results. The estimates of densitometer BMD level differed significantly between AFP and EFP, both in direction and magnitude
- In vivo and in vitro results are different. Semi-anthropomorphic phantoms reflect in vivo results in a better way than aluminum phantoms. Therefore, during study periods, daily measurements should be

performed with an anthropomorphic phantom of calcium hydroxyapatite in tissue-equivalent plastic

– Repeated phantom measurements should be used to evaluate possible differences between the participating densitometers' measurement levels. Events that may interfere with densitometer function (transportation, X-ray tube replacement or any maintenance) should be carefully monitored.

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Paper II

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Longitudinal Changes in Forearm Bone Mineral Density in Women and Men Aged 25–44 Years

The Tromsø Study: A Population-based Study

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The aim of this study was to describe and compare bone mineral density (BMD) development in Norwegian women and men aged 25–44 years in a population-based, longitudinal study. BMD was measured twice at distal and ultradistal forearm sites by single x-ray absorptiometry in 258 women and 147 men (mean follow-up time, 6.4 (standard deviation, 0.6) years). At the distal site, a small annual gain of approximately 0.1% became a small loss beginning at age 34 years in men and age 36 years in women. At the ultradistal site, BMD change was predicted by age in women only, and bone loss started at age 38 years. A high degree of tracking of BMD measurements was observed for both sexes and both sites, $r > 0.93$. Depending on total BMD change, participants were grouped into "losers," "nonlosers," and "gainers," and more than 6% lost more than the smallest detectable amount of BMD: ≥3.46% at the distal site and ≥5.14% at the ultradistal site. In both sexes, bone mineral content (grams) decreased, whereas area (centimeters squared) increased significantly in "losers" compared with "gainers." This finding might represent physiologic compensation preserving bone strength. No cohort effects were observed when 1994 and 2001 measures from similar age groups were compared.

bone density; bone development; densitometry; follow-up studies; forearm; longitudinal studies; men; women

Abbreviations: BMAD, bone mineral apparent density; BMC, bone mineral content; BMD, bone mineral density.

Osteoporotic fractures are a major health problem, with substantial morbidity and costs (1, 2). The cause of fracture is complex, but bone fragility is an important contributor to fracture risk (3). Bone mineral density (BMD) is a good surrogate measure of bone strength, predicting 60–70 percent of its variation (4). A strong relation between BMD level and the probability of fracture has been documented (5). Although fracture risk is best predicted by BMD measurements from the same anatomic site, no site is superior with respect to predicting all types of fragility fracture (5). Single x-ray absorptiometry of the distal forearm is thought to be one of the most precise densitometric methods (6–9), and peripheral BMD measurements can be used to assess fracture risk at both peripheral and central sites (5, 10, 11).

BMD in the elderly is a function of the amount of bone gained during growth and the amount of bone lost during aging (12, 13). As such, both peak BMD and subsequent bone loss, as a result of decreasing bone mass and development of microarchitectural abnormalities and microdamage, are important determinants of the risk of osteoporotic fracture later in life (14–17). Although a period of stability after completion of growth is generally assumed, bone loss probably begins when growth ceases (18) and might therefore start during the early adult years in both women and men. The ages at which peak bone values are reached, premenopausal bone loss occurs in women, and bone loss occurs in young men have not yet been determined with certainty (19–22). The associations among change in BMD (in grams per centimeter squared), area (in centimeters squared), and

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bone mineral content (BMC) (in grams) in young women and men are not clear either (23).

Longitudinal studies on BMD changes during the third to fifth decades of life in women (24–37) exist, but only those of Sowers et al. (27, 29), Guthrie et al. (30), Chapurlat et al. (31), Melton et al. (32), and Bainbridge et al. (36) are population based. Some longitudinal studies on BMD changes in young males have been published (28, 34, 38–40); only the study of Khosla et al. (39) is population based. Longitudinal studies including both sexes are scarce and are based on healthy volunteers (28, 34). Because studies based on selected populations may be subject to selection bias (41), their accuracy might be questioned (20). Development of bone mass in the age group 25–44 years therefore has not been investigated sufficiently. In this age group, tracking and cohort effects have, to our knowledge, not been studied. The aim of the present study was to describe, compare, and explore aspects of BMD development in men and women aged 25–44 years in a population-based longitudinal study through the following research questions:

- How does BMD develop in a general population between ages 25 and 44 years?
- Is BMD development similar in the two sexes?
- How well does initial BMD predict BMD at follow-up after 6 years?
- Can any cohort effects be seen before middle age?

MATERIALS AND METHODS

Study design and subjects

The Tromsø Osteoporosis Study (TROST) is part of the Tromsø study, a longitudinal, population-based, multipurpose study focusing on lifestyle-related diseases (42). The Tromsø study was initiated in 1974, with surveys repeated in 1979–1980, 1986–1987, 1994–1995, and 2001. In 1994 (Tromsø IV), the Tromsø Osteoporosis Study measured bone density in 637 subjects (396 women and 241 men) aged 25–44 years. These numbers corresponded to 64 percent of the women and 56 percent of the men invited to participate (43). In 2001 (Tromsø V), 631 of the subjects still living in Tromsø were invited for a reexamination. Bone densitometry was performed on 405 subjects (258 women and 147 men)—65 percent of the invited women and 60 percent of the invited men. The follow-up examination included 42 percent of the women and 34 percent of the men originally invited in 1994. After we excluded invalid scans, 253 repeated measurements at both sites in women and 141 and 142 repeated measurements at the distal and ultradistal sites, respectively, in men remained. Mean age at baseline was 36 (standard deviation, 5.3) years for participating women and 36.5 (standard deviation, 5.8) years for participating men. Mean follow-up time was 6.4 (standard deviation, 0.6) years.

Informed consent was obtained prior to both examinations. The regional Committee of Research Ethics and the Norwegian Data Inspectorate approved the study.

Measurements

Bone densitometry was performed at both surveys at the distal and ultradistal forearm sites with two single x-ray absorptiometry devices (DTX-100; Osteometer MediTech, Inc., Hawthorne, California). The distal site includes both the radius and ulna from the 8-mm point (the point at which the ulna and radius are separated by 8 mm) and 24 mm proximally. The ultradistal site includes only the radius and stretches from the 8-mm point up to the radial endplate. The nondominant arm was measured except when it was considered ineligible because of wounds, plaster casts, and so on.

Starting at the second survey, one of the two densitometers underwent a major repair. Later, the x-ray tube had to be replaced in both densitometers. Quality control routines, in which the European Forearm Phantom (QRM GmbH, Meohrendorf, Germany) was used, revealed that one of the machines measured at a higher BMD level before the x-ray tube was replaced, the mean difference being 0.005 g/cm^2. The European Forearm Phantom data were used to adjust the differences in densitometer measurement level. The internal variation in each machine studied by using the coefficient of variation (coefficient of variation percent = standard deviation/mean × 100) and by comparing the European Forearm Phantom measurement level during different time periods was satisfactory, with a mean coefficient of variation of 0.9 percent (44).

The same protocol was used in both studies. Quality control with respect to precision and correction of artifacts in Tromsø IV has been reported previously (9, 45). Four trained technicians, one of whom also conducted the Tromsø IV analysis, reanalyzed the scans from Tromsø V. To test for reliability, we obtained three intra-tests (each technician compared with himself or herself) and three inter-tests (each technician compared with the other technicians). Each pair of technicians reviewed a minimum of 27 and a maximum of 127 similar scans. We missed one intra- and inter-test possibility for one technician reviewing 19 of the scans included in this study. At the distal site, there were no significant differences with respect to BMD between the technicians in either intra- or inter-testing. At the ultradistal site, however, there were significant differences in BMD between the technicians in two of the three intra- and two of the three inter-tests. From these tests, we could determine that the measurements of one technician, who reviewed 245 scans, were approximately 0.001 g/cm^2 lower than those of the others. This difference would entail an effect of less than 1 percent on the annual bone loss estimates (in grams per centimeter squared) and reduce the percentage change estimates by 0.02 percentage points. We compared annual change estimates (in grams per centimeter squared), and they were not technician influenced, $p > 0.29$, at any sites (analysis of variance). We therefore decided not to correct the data.

Other measurements

Height and weight were measured, using a Jenix DS-102 stadiometer (Dong Sahn Jenix Co., Ltd., Seoul, Korea), to the nearest centimeter and half kilogram, respectively; study participants wore light clothing without shoes. Conditions

TABLE 1. Comparison of participants lost to follow-up (participating in Tromsø IV only) with those who participated in both the Tromsø IV (1994–1995) and Tromsø V (2001) longitudinal studies, Norway

Baseline characteristic	Tromsø IV only			Tromsø IV and Tromsø V			*p* value
	No.	Mean	SD*	No.	Mean	SD	
Women							
Age (years)	138	32	4.9	256	36	5.3	0.001
Height (cm)	138	166	6.2	256	165	6.6	0.15
Weight (kg)	138	65	11.2	255	65	10.9	0.79
Body mass index (kg/m^2)	138	24	3.7	255	24	3.7	0.65
Current smoker (%)	138	41		256	45		0.44
Smoking pack-years (no.)	81	14	6.3	166	15	6.5	0.03
Self-perceived health "good" (%)	138	80		256	86		0.10
Physical activity: sedate (%)	137	12		253	18		0.28
Physical activity: moderate (%)		24			26		
Physical activity: active (%)		64			56		
Calcium intake (mg)	119	808	353	226	749	277	0.09
Baseline distal BMD* (g/cm^2)	136	0.473	0.036	253	0.472	0.047	0.84
Baseline ultradistal BMD (g/cm^2)	134	0.379	0.045	253	0.372	0.050	0.21
Men							
Age (years)	94	34	5.8	145	36.5	5.8	0.002
Height (cm)	93	179	6.8	145	178	6.7	0.10
Weight (kg)	93	80	10.8	145	80	9.9	0.87
Body mass index (kg/m^2)	93	25	3.1	145	25	2.7	0.38
Current smoker (%)	93	46		145	34		0.06
Smoking pack-years (no.)	60	14	6.5	90	15	7.6	0.63
Self-perceived health "good" (%)	94	89		145	88		0.82
Physical activity: sedate (%)	94	12		145	21		0.11
Physical activity: moderate (%)		14			16		
Physical activity: active (%)		74			63		
Calcium intake (mg)	83	894	314	137	891	321	0.95
Baseline distal BMD (g/cm^2)	94	0.577	0.045	141	0.578	0.048	0.88
Baseline ultradistal BMD (g/cm^2)	94	0.487	0.059	142	0.482	0.058	0.54

* SD, standard deviation; BMD, bone mineral density.

that unduly influenced the measurements were recorded. Body mass index was calculated as weight in kilograms divided by the square of height in meters.

Questionnaires

The Tromsø IV participants filled in two self-administered questionnaires on different lifestyle variables, one before entering the study and one during the study. We used data on self-perceived health, level of physical activity, smoking status, and calcium intake to assess possible selection bias in the material. Women's menstrual status at baseline was also derived from answers on the questionnaires or from measured follicle-stimulating hormone levels in 152 of the participants. Women who were not using hormone replacement therapy, who were not pregnant, whose time since last menstruation was less than 180 days, or whose follicle-stimulating hormone level was less than 23 were classified as premenopausal ($n = 234$). Women who were not using hormone replacement therapy, who were not pregnant, and whose time since last menstruation was 180–365 days were classified as perimenopausal ($n = 1$). Women not using hormone replacement therapy and whose time since last menstruation was more than 365 days were classified as postmenopausal ($n = 5$). Finally, women using hormone replacement therapy were classified as hormone replacement therapy users ($n = 5$). When information about menstruation or follicle-stimulating hormone levels was lacking, menopausal status was defined as missing ($n = 13$). Results of analyses conducted with and without data on nonpremenopausal women were similar, which is why we chose to present the analysis for the entire population only.

Statistical analysis

BMD measurements from intra- and inter-testing were compared by using a one-sample paired t test. To investigate

TABLE 2. Baseline characteristics of the participants in the Tromsø IV (1994–1995) and Tromsø V (2001) longitudinal studies, Norway, according to 5-year age groups

Baseline characteristic	Age group (years) 25–29			30–34			35–39			40–44			Trend *p* value
	No.	Mean	SD*	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD	
Women													
Height (cm)	37	167	6.0	76	165	6.7	73	165	7.0	72	165	6.4	0.43
Weight (kg)	36	65	10.3	76	65	11.2	73	64	10.9	72	66	11.0	0.53
Body mass index (kg/m^2)	36	23	3.2	76	24	4.1	73	24	3.5	72	24	3.7	0.30
Calcium intake (mg)	33	795	251	67	778	301	64	762	272	60	679	257	0.06
Premenopausal (%)	33	89		67	88		70	96		64	89		
Perimenopausal (%)	0	0		1	1		0	0		0	0		
Postmenopausal (%)	0	0		3	4		0	0		2	3		
HRT* user (%)	1	3		0	0		1	1.5		3	4		
Menopause status missing (%)	3	8		5	7		2	2.5		3	4		
Distal BMD* (g/cm^2)	36	0.462	0.04	75	0.482	0.04	72	0.467	0.05	70	0.473	0.05	0.85
Ultradistal BMD (g/cm^2)	36	0.365	0.05	75	0.377	0.05	73	0.373	0.05	69	0.372	0.05	0.86
Men													
Height (cm)	25	179	7.1	31	178	7.1	45	179	6.2	46	177	6.8	0.15
Weight (kg)	25	78	11.1	31	77	9.7	45	80	7.9	46	83	10.6	0.01
Body mass index (kg/m^2)	25	25	2.7	31	24	2.8	45	25	2.1	46	27	2.9	0.001
Calcium intake (mg)	24	810	310	29	953	229	41	921	313	41	871	387	0.90
Distal BMD (g/cm^2)	24	0.562	0.04	29	0.588	0.05	43	0.579	0.04	45	0.584	0.05	0.37
Ultradistal BMD (g/cm^2)	24	0.479	0.04	29	0.507	0.06	44	0.479	0.06	45	0.477	0.06	0.15

* SD, standard deviation; HRT, hormone replacement therapy; BMD, bone mineral density.

possible selection bias, we compared basic characteristics of those participating in both surveys with those participating in only Tromsø IV by using independent two-sample *t*-test and chi-square testing for continuous and categorical variables, respectively. BMD change was estimated by determining the difference between Tromsø V and Tromsø IV measurements. Annual BMD change was calculated as the difference between the two measurements divided by the length of each participant's follow-up time. Dividing the difference by the baseline measure and multiplying by 100 enabled us to estimate the annual percentage changes. In this paper, these changes are presented, by 5-year age groups at baseline, as milligrams per centimeter squared with 95 percent confidence intervals. Annual change in area (centimeters squared), BMC (grams), and bone mineral apparent density (BMAD) was calculated in the same way. BMAD at the distal site was estimated according to Katzman et al.: BMAD = BMD/area (46). Since all areas of the distal site have a constant length of 24 mm, the area is a direct measure of average bone width and is therefore presented as milligrams per centimeter squared. Since both length and width vary for the ultradistal area, BMAD was not calculated for this site.

Regression analysis was used to investigate how age and sex influenced BMD, area, and BMAD changes. Interaction between age and sex was analyzed, and a p value of >0.10 was interpreted as no significant interaction between the variables. To estimate peak bone mass, we plotted annual change against baseline age by using scatter plots with a regression line. The point at which the line of regression crossed zero on the *y*-axis was interpreted as "end-of-gain and start-of-loss age."

The amount of total BMD change was used to categorize the groups into "losers," "nonlosers," and "gainers." The minimal difference, which represents true biologic change with 95 percent certainty (95 percent detection limit), can theoretically be calculated by using the following formula: Delta = $1.96 \times \sqrt{2} \times$ coefficient of variation percent (47). For an intermediate term between two measurements, median coefficients of variation estimated on our data were 1.25 at the distal site and 1.86 percent at the ultradistal site (9). Participants gaining or losing more than ± 3.46 percent were categorized as true "gainers/losers" at the distal site. At the ultradistal site, the equivalent detection limit was ± 5.14 percent. Area and BMC development in the different loss groups was compared by analysis of variance.

Tracking between the first and second measurements was assessed by using Pearson's correlation coefficient. We further divided BMD values measured at baseline and at follow-up into four quartiles, the highest categorized as position 1 and the lowest as position 4 in both studies. The values from both studies were categorized respectively, and each subject's position in both studies was compared. The distribution of quartile BMD positions at baseline according

TABLE 3. Annual bone mineral density changes in participants in the Tromsø IV (1994–1995) and Tromsø V (2001) longitudinal studies, Norway, comparing age groups by sex

Age group	Distal site					Ultradistal site				
	No.	Change (mg/cm²)	95% CI*	Annual change (%)	ANOVA* p value	No.	Change (mg/cm²)	95% CI	Annual change (%)	ANOVA p value
Women										
25–29	36	0.44	−0.2 to 1.1	0.11	0.047	36	1.39	0.4 to 2.4	0.43	0.003
30–34	75	0.38	−0.1 to 0.8	0.08		75	0.44	−0.1 to 1.0	0.13	
35–39	72	−0.18	−0.6 to 0.3	−0.05		73	−0.04	−0.8 to 0.79	−0.01	
40–44	70	−0.31	−0.8 to 0.2	−0.07		69	−0.55	−1.3 to 0.2	−0.13	
Men										
25–29	24	0.91	−0.1 to 1.9	0.16	0.000	24	0.44	−1.1 to 2.0	0.10	0.250
30–34	29	0.17	−0.5 to 0.8	0.03		29	−0.40	−1.4 to 0.6	−0.06	
35–39	43	−0.78	−1.4 to −0.2	−0.13		44	−1.05	−2.0 to −0.1	−0.21	
40–44	45	−0.96	−1.4 to −0.5	−0.16		45	−0.50	−1.3 to 0.3	−0.09	

* CI, confidence interval; ANOVA, analysis of variance.

to the different loss groups was assessed with chi-square testing, Fisher's exact test.

To assess the cohort effect, we extracted four comparable cohort groups comprising persons aged 33–35 and 43–45 years in 1994 and those aged 33–35 and 43–45 years in 2001. BMD level for the relevant cohort groups was compared by independent two-sample t test. The statistical analysis was performed with SPSS software, version 11 (SPSS, Inc., Chicago, Illinois). A p value of <0.05 was regarded as statistically significant.

RESULTS

Comparison of responders and nonresponders

Data for the first study in Tromsø IV were compared for nonresponders, partial responders, and full responders. The analysis gave no indication of any differences between the groups (43). After Tromsø V, we could use baseline characteristics from Tromsø IV to compare participants lost to follow-up with those who attended both studies. The results from the analysis are displayed in table 1.

Changes in BMD

The general characteristics at baseline of those who participated in both studies are displayed in table 2 according to 5-year age groups. Changes in BMD in both sexes according to 5-year age groups are shown in table 3 and figure 1.

At the distal site, BMD change was predicted by baseline age ($p < 0.001$) but not by sex ($p = 0.089$). There was no significant interaction between baseline age and sex ($p = 0.127$). For every 5-year increase in age, the BMD-change estimate declined by 0.1 percentage points. Before peak bone density was attained, growth was reduced by 0.1 percentage points for every 5 years. After peak bone density was achieved, bone loss increased by 0.1 percent every 5 years. Peak bone density was attained by age 36 years in women and by age 34 years in men (figure 2).

At the ultradistal site, BMD change was predicted by sex ($p = 0.038$), and a linear association was found between baseline age and BMD change in women ($p = 0.005$). In men, the linear BMD change estimate was not significantly

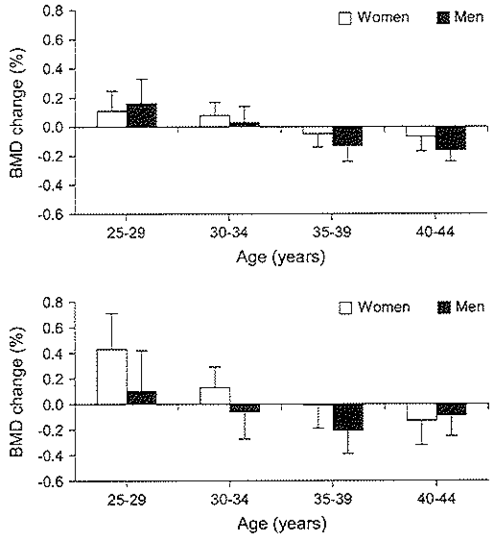

FIGURE 1. Annual percentage changes in bone mineral density (BMD), with 95% confidence intervals, at the distal site (top) and the ultradistal site (bottom), by age in women and men in the longitudinal Tromsø IV (1994–1995) and Tromsø V (2001) studies, Norway. Trend: $p = 0.005$ for women and $p < 0.001$ for men at the distal site, and $p = 0.001$ for women and $p = 0.248$ for men at the ultradistal site.

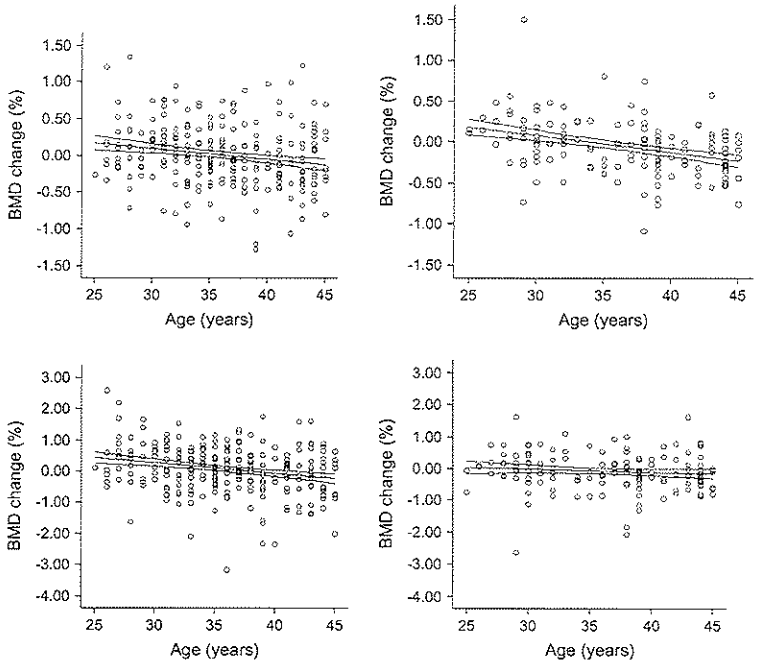

FIGURE 2. Annual percentage changes in bone mineral density (BMD), with the line of regression and its 95% confidence interval, at the distal site (top two parts) and the ultradistal site (bottom two parts) in women (left) and men (right) in the longitudinal Tromsø IV (1994–1995) and Tromsø V (2001) studies, Norway. Peak BMD occurs where the line of regression crosses 0 on the *y*-axis: age 36 years at the distal site in women, age 34 years at the distal site in men, and age 38 years at the ultradistal site in women; no linear association was found between age and BMD change at the ultradistal site in men.

different from zero ($p = 0.239$). A smaller BMD change in the age group 40–44 years compared with the previous age groups indicated a possible nonlinear association at the ultradistal site for men; therefore, test of linear interaction between age and sex was not assessed.

In women, the BMD change estimate at the ultradistal site declined by −0.15 percentage points for every 5-year increase in age. Before peak bone density was attained by age 38 years, growth was reduced by 0.15 percentage points for every 5 years. After peak bone density was achieved, bone loss increased by 0.15 percentage points for every 5 years (figure 2).

One man in the age group 25–29 years and one in the age group 40–44 years had an annual loss of -0.013 g/cm^2 and an annual increase of 0.008 g/cm^2, respectively. Excluding these outliers did not alter the lack of association between age and BMD change at the ultradistal site ($p = 0.061$) for men (figure 2).

Changes in area and BMAD

BMD is size dependent, and BMD changes may reflect changes in size rather than in mineral content. We therefore calculated area and BMC changes, and the results are given in table 4. The area declined slightly and similarly at the distal site, and it increased slightly and similarly in the two sexes at the ultradistal site. Changes in BMAD followed the same pattern as BMD changes in both sexes at the distal forearm site and was negatively predicted by age ($p = 0.001$) but not by sex ($p = 0.16$).

"Losers," "nonlosers," and "gainers"

Table 5 displays the distribution of "losers," "nonlosers," and "gainers" for both sexes. The distribution of quartile BMD positions at baseline was not significantly different between loss groups. At both sites and in both sexes, BMC followed the same pattern as BMD, declining in "losers" and increasing in "gainers," whereas the area increased significantly in "losers" and declined in "gainers" (figure 3).

Tracking and cohort effects

The correlations between the BMD measurements in the two studies were high and were similar for the two sexes:

TABLE 4. Annual changes in area, BMC,* and BMAD* in participants in the Tromsø IV (1994–1995) and Tromsø V (2001) longitudinal studies, Norway, comparing age groups (years) by sex

	Distal site					Ultradistal site				
	No.	Mean	95% CI*	Annual change (%)	ANOVA* p value	No.	Mean	95% CI	Annual change (%)	ANOVA p value
				Women						
Area (mm^2)										
25–29	36	−0.036	−0.10 to 0.03	−0.05	0.93	36	0.014	−0.15 to 0.18	0.06	0.11
30–34	75	−0.038	−0.08 to 0.04	−0.05		75	0.144	0.05 to 0.24	0.34	
35–39	72	−0.053	−0.10 to 0.01	−0.07		73	0.267	0.10 to 0.44	0.84	
40–44	70	−0.053	−0.09 to −0.02	−0.07		69	0.275	0.11 to 0.44	0.63	
BMC (mg)										
25–29	36	−0.73	−3.95 to 2.50	−0.02	0.004	36	4.90	−2.55 to 12.34	0.40	0.79
30–34	75	−0.69	−3.27 to 1.89	−0.02		75	6.04	1.88 to 10.2	0.40	
35–39	72	−4.99	−7.35 to −2.62	−0.16		73	9.39	2.89 to 15.88	0.76	
40–44	70	−6.66	−9.83 to −3.49	−0.19		69	6.77	−0.2 to 13.74	0.43	
BMAD (mg/cm^3)										
25–29	33	0.11	−0.05 to 0.26	0.17	0.54					
30–34	66	0.09	−0.01 to 0.19	0.14						
35–39	69	0.02	−0.08 to 0.13	0.03						
40–44	63	0.01	−0.08 to 0.11	0.01						
				Men						
Area (mm^2)										
25–29	24	−0.052	−0.14 to 0.04	0.16	0.96	24	0.330	0.7 to 0.59	0.64	0.42
30–34	29	−0.024	−0.09 to 0.05	0.03		29	0.102	−0.14 to 0.34	0.23	
35–39	43	−0.042	−0.11 to 0.03	−0.13		44	0.063	−0.15 to 0.28	0.21	
40–44	45	−0.047	−0.11 to 0.02	−0.16		45	0.233	−0.01 to 0.48	0.52	
BMC (mg)										
25–29	24	3.52	−5.97 to 13.01	0.09	0.001	24	17.16	2.6 to 32.17	0.72	0.16
30–34	29	−1.29	−7.22 to 4.63	−0.03		29	1.21	−12.42 to 14.84	0.13	
35–39	43	−11.40	−16.32 to −6.48	−0.24		44	−3.75	−14.75 to 7.24	−0.07	
40–44	45	−12.56	−17.49 to −7.62	−0.26		45	6.20	−6.06 to 18.46	0.38	
BMAD (mg/cm^3)										
25–29	24	0.15	0.02 to 0.29	0.22	0.03					
30–34	29	0.04	−0.07 to 0.15	0.07						
35–39	43	−0.06	−0.19 to 0.07	−0.08						
40–44	45	−0.08	−0.16 to 0.01	−0.10						

* BMC, bone mineral content; BMAD, bone mineral apparent density; CI, confidence interval; ANOVA, analysis of variance.

distal and ultradistal sites for women: $r = 0.97$ and $r = 0.93$; distal and ultradistal sites for men: $r = 0.97$ and $r = 0.94$, respectively ($p < 0.001$). The correlations in area and BMC were also high at the distal site: $r > 0.97$ for both sexes. At the ultradistal site, the correlations between area measurements were $r = 0.88$ for women and $r = 0.86$ for men, and the correlations between BMC measurements were $r = 0.74$ for women and $r = 0.60$ for men.

For both sexes, 75–80 percent kept their quartile BMD position from the first to the second survey, whereas 10–13 percent either lost or gained one position at the distal site. This loss or gain was evenly distributed from all original quartile positions. A similar pattern was seen at the ultradistal site: 72–73 percent kept their quartile position, 11–12 percent lost one quartile, and 12–14 percent gained one quartile, also from all quartile positions. Two percent—four women—lost two quartiles, all from the highest quartile. From the analysis, we concluded that only those who were close to the quartile "borders" changed positions, and the changes occurred in any direction. As such, the degree of tracking was extremely high for both sexes before middle age.

The BMD levels of the different cohort groups are shown in table 6. No significant differences in BMD levels between the compared cohort groups ($p > 0.5$) were observed.

TABLE 5. Distribution of participants in the Tromsø IV (1994–1995) and Tromsø V (2001) longitudinal studies, Norway, into different loss groups based on the total percentage of loss compared with baseline bone mineral density

	Losing (>−3.46%)			Not losing (±3.46%)			Gaining (>3.46%)		
	No. or mean	%	95% CI*	No. or mean	%	95% CI	No. or mean	%	95% CI
Distal site: women (n = 253)	17	7	4 to 10	210	83	78 to 88	26	10	6 to 14
Area change (cm²)†	0.093		0.022 to 0.164	−0.025		−0.038 to −0.011	−0.143		−0.189 to −0.096
BMC* change (g)†	−0.130		−0.171 to −0.089	−0.025		−0.033 to −0.018	0.071		0.047 to 0.096
Distal site: men (n = 141)	8	6	2 to 10	129	91.5	88 to 96	4	2.5	0.2 to 5.8
Area change (cm²)‡	0.083		−0.086 to 0.251	−0.032		−0.053 to −0.01	−0.12		−0.584 to 0.344
BMC change (g)†	−0.195		−0.311 to −0.079	−0.046		−0.063 to −0.027	0.017		−0.232 to 0.576
	Losing (>−5.14%)			Not losing (±5.14%)			Gaining (>5.14%)		
	No. or mean	%	95% CI	No. or mean	%	95% CI	No. or mean	%	95% CI
Ultradistal site: women (n = 253)	28	11	7 to 15	185	73	67 to 79	40	16	11 to 21
Area change (m²)§	0.179		−0.013 to 0.37	0.147		0.098 to 0.195	0.000		−0.158 to 0.158
BMC change (g)†	−0.082		−0.166 to −0.001	0.05		0.032 to 0.071	0.105		0.047 to 0.164
Ultradistal site: men (n = 142)	13	9	4 to 14	129	91.5	88 to 96	6	4	1 to 7
Area change (m²)§	0.202		−0.01 to 0.405	0.123		0.042 to 0.205	−0.225		−0.897 to 0.447
BMC change (g)†	−0.148		−0.244 to −0.051	−0.045		0.002 to 0.0879	0.035		−0.346 to 0.416

* CI, confidence interval; BMC, bone mineral content.
† Difference between groups, $p < 0.001$, analysis of variance (ANOVA).
‡ Difference between groups, $p < 0.03$, ANOVA.
§ Difference between groups not significant, ANOVA.

DISCUSSION

The main finding from this population-based, longitudinal study was that BMD change at the distal forearm site was similar in the two sexes. An annual increase of approximately 0.1 percent in the age group 25–34 years became a small loss at the distal site beginning at age 34 years in men and at age 36 years in women. There was a high degree of tracking, and no cohort effects were observed when measures from similar age groups were compared in 1994 and 2001. A small group of women and men lost a substantial amount of BMD before middle age; however, this loss seemed to be compensated for by an area increase (in centimeters squared).

One of the strengths of this study is its long follow-up period. With the precision of current methods for measuring bone mass, accurate estimates of rates of bone loss require long periods of follow-up (48), with the small magnitude of the decrease occurring before middle age (49). More than 6 years of follow-up, including strict quality control of densitometer performance in both studies, provided the opportunity for accurate documentation of changes in bone mass.

Nonresponse may generate selection bias. For both sexes, participants lost to follow-up were younger than those participating in both studies. Since we analyzed the data in 5-year age groups, this bias should not have influenced the estimates, giving smaller numbers for the youngest age groups only. For women, the percentage of present smokers was equal in the two groups, but participating women had smoked 1 year longer than participants lost to follow-up ($p = 0.03$). However, the total number of cigarettes smoked was not significantly different when the two groups were compared. The percentage of present smokers tended to be higher among the male participants lost to follow-up ($p = 0.06$), but smoking pack-years and total number of cigarettes smoked were not significantly different in the compared groups. Smoking might influence bone health in a negative direction, with a cumulative effect by age (50). In our study, smoking pack-years did not predict BMD changes in women ($p = 0.163$ and $p = 0.222$ at the distal and ultradistal sites, respectively), and smoking status did not predict BMD changes in men ($p = 0.238$ and $p = 0.051$ at the distal and ultradistal sites, respectively). We therefore assume that our results were not influenced by selection bias. To test for its possible effect at the ultradistal site in men, we calculated how BMD changes would be influenced by an increase in the proportion of current smokers in the data, and the effect was negligible.

The findings from our study support the indication that bone loss starts during the third decade of life (18). Comparable studies with different results have been published. Chapurlat et al. (31) used dual energy x-ray absorptiometry to follow 196 premenopausal women over 3 years in a population-based study. They found that women aged 30–50 years had an annual BMD increase of 0.24, 0.4, and 0.02 percent at the midshaft, distal, and ultradistal radius sites, respectively. The rate of change was not significantly different when women aged 30–40 and 40–50 years were compared. Khosla et al. (39) followed a population-based sample of 315 men aged 22–90 years over 4 years by using dual

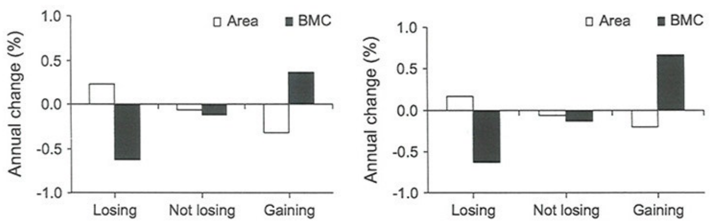

FIGURE 3. Annual percentage changes in area and bone mineral content (BMC) at the distal site in women (left) and men (right) according to three change groups in the longitudinal Tromsø IV (1994–1995) and Tromsø V (2001) studies, Norway. Trend: $p < 0.001$ for area and BMC in women, and $p < 0.001$ for area and $p = 0.004$ for BMC in men.

energy x-ray absorptiometry. Men aged 22–39 and 40–59 years had an annual BMD increase of 0.4 and 0.24 percent, respectively, at the mid-distal radius (39). Age-stratified analysis was not presented. No longitudinal results from the ultradistal radius are reported for young men.

Our findings of bone loss starting at the distal forearm site in the third decade of life are in contrast to Chapurlat et al. (31) and Khosla et al. (39) reporting no loss in the comparable age groups. This discrepancy might be influenced by differences in machine performance, length of follow-up, or variations in the population. Our study has its strengths, with the longest follow-up, high response rates, and strict quality control routines. The coefficient of variation reported in the study by Khosla et al. is 2.1 percent compared with our 0.9 percent (43). However, our study was based on a Scandinavian population that, together with North-American Whites, is known to have the highest incidence of forearm, proximal humerus, and hip fractures (51–55). The discrepancy in findings might therefore represent true population differences, which should be studied further.

Eighty-five percent of the total bone in the body is cortical, and it is relatively most abundant in the long bone shafts of the appendicular skeleton (56). With the distal site containing mainly cortical and the ultradistal site mainly trabecular bone (57), both types can be studied as at the distal forearm. Because of the different environments of the bone cells, decline in trabecular bone mass is thought to begin earlier than cortical bone mass (56). An earlier and greater bone loss would therefore be expected at the ultradistal site. However, opinions differ regarding this issue (56), and our findings are in concordance with recent studies from other comparable sites. Bainbridge et al. (36), who followed a cohort of 614 women aged 24–44 years over 6 years, reported an annual bone loss of −0.3 percent beginning by the mid-twenties at the femoral neck (75 percent cortical bone), with no evidence of early bone loss at the lumbar spine (>60 percent cancellous bone) (36).

BMD changes did not differ significantly at the distal site when the two sexes were compared. At the ultradistal site, the trend regarding change was significant in women but not in men, with women gaining significantly in the age group 25–29 years. The main impact of estrogen deficiency is on trabecular bone (58). Because this study comprised mostly premenopausal women whose sex hormone levels are expected to be high, it was actually not surprising to find that the youngest women, those aged 25–29 years, gained a significant amount of BMD at the ultradistal forearm site (table 3, figures 1 and 2).

An annual loss of −0.1 percent over 10 years indicates a loss of approximately 1 percent from peak value, before the more extensive loss starts at middle age in women. As stated by Riis (59), this loss might not be of any clinical relevance, and the degree of tracking in BMD measurements is high. Tracking of a characteristic is defined as the ability to maintain the same position within a distribution over time (60, 61) or the ability to predict future values from earlier

TABLE 6. Cohort-effect analysis of the bone mineral density (g/cm^2) of participants in the Tromsø IV (1994–1995) and Tromsø V (2001) longitudinal studies, Norway

	Aged 33–35 years in 1994			Aged 33–35 years in 2001			Aged 43–45 years in 1994			Aged 43–45 years in 2001		
	No.	Mean	SD*	No.	Mean	SD	No.	Mean	SD	No.	Mean	SD
Women												
Distal site	52	0.488	0.042	27	0.471	0.038	33	0.476	0.051	45	0.462	0.051
Ultradistal site	52	0.382	0.050	27	0.383	0.045	33	0.369	0.051	45	0.375	0.051
Men												
Distal site	12	0.575	0.045	16	0.572	0.049	31	0.582	0.051	25	0.573	0.051
Ultradistal site	12	0.493	0.066	16	0.481	0.049	31	0.474	0.059	25	0.471	0.059

* SD, standard deviation.

measurements (62, 63). Despite the high degree of tracking, there was some interindividual variation in both sexes, with 6–7 percent losing more than 3.46 percent of their BMD in 6 years (more than 0.5 percent annually). This represents a substantial amount of early bone loss, which might lead to an early increased fracture risk (64). It is interesting to note that the area (in centimeters squared) increased significantly in "losers" compared with "gainers," which might represent a physiologic compensation of periosteal apposition resulting in an increased area that seeks to preserve bone strength (18, 23, 65, 66).

We observed no cohort effect when measurements from similar age groups in the studies were compared, indicating that BMD changes can be derived from cross-sectional studies in this age group. This observation is in contrast to that of Melton (67), who argued that cross-sectional data tend to overestimate bone loss rates observed longitudinally at many sites, and to our own cross-sectional data that indicated higher bone loss rates in both sexes at both forearm sites (43).

In conclusion, changes in BMD in the age group 25–44 years are significantly explained by age, but not by sex. The degree of tracking between measurements is high, but a clinically significant group of both women and men experience bone loss before middle age. However, the observed loss might be compensated for by an increase in area, which preserves bone strength. This effect needs to be explored further in other populations.

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Paper III

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Original Contribution

Longitudinal Changes in Forearm Bone Mineral Density in Women and Men Aged 45–84 Years: The Tromsø Study, a Population-based Study

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The aim of this study was to describe changes in bone mineral density in Norwegian women and men aged 45–84 years in a population-based, longitudinal study. Bone mineral density (g/cm^2) was measured at distal and ultradistal forearm sites with single x-ray absorptiometric devices in 3,169 women and 2,197 men at baseline in 1994–1995 and at follow-up in 2001 (standard deviation, 0.4 years). The mean annual bone loss was −0.5% and −0.4% in men and −0.9% and −0.8% in women not using hormone replacement therapy at the distal and ultradistal sites, respectively. In men, age was a negative predictor of bone mineral density change at both sites. Women not using hormone replacement therapy had the highest bone loss at the ultradistal site 1–5 years after menopause. The correlation between the two measurements was high: $r = 0.93$ and $r = 0.90$ in women and $r = 0.96$ and $r = 0.93$ in men for the distal and ultradistal sites, respectively. More than 70% kept their quartile positions, indicating a high degree of tracking of bone mineral density measurements. Although the study population live above the polar circle, the rate of bone loss was not higher at the distal and ultradistal forearm sites compared with that of other cohorts.

bone density; densitometry; follow-up studies; forearm; longitudinal studies; men; women

Abbreviations: HRT, hormone replacement therapy; SD, standard deviation; TROST, Tromsø Osteoporosis Study.

Osteoporotic fractures in both sexes constitute a major health problem with substantial morbidity and cost (1, 2). The causation of fracture is complex, but bone fragility is an important contributor to fracture risk (3). Bone mineral density is a good surrogate measure of bone strength, predicting 60–70 percent of its variation (4). A strong relation between bone mineral density level and the probability of fracture has been documented (5). Bone mineral density in the elderly is a function of the amount of bone gained during growth and the amount of bone lost during aging (6, 7). Bone loss estimates derived from cross-sectional studies may be subject to cohort effects, and longitudinal studies provide the best foundation for precise estimations of bone loss (8, 9).

Bone mineral density changes in women through menopause (10–14) and in old age (15–22) have been described through longitudinal, population-based surveys. These changes in men are, however, not extensively explored longitudinally in population-based samples (23–25). Studies, based on representative samples, comprising both sexes from the same population are even more rare, and those existing are from elderly populations (26–30). Longitudinal, population-based studies describing bone mineral density changes in both sexes from middle age into old age are therefore still lacking.

The Tromsø Osteoporosis Study (TROST) is part of the Tromsø Study in northern Norway. With a follow-up of more than 6 years, TROST has obtained repeated bone mineral density measurements from the distal and ultradistal forearm sites of 3,169 women and 2,197 men aged 45–84 years. The aim of this study was to describe and compare

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variations in bone mineral density changes in women and men from middle into old age. With the long follow-up, we also wanted to study the degree of tracking of bone mineral density measurements by assessing how well the second measurement was predicted by the first.

MATERIALS AND METHODS

Study participants

The Tromsø Study is a longitudinal, population-based, multipurpose study that focuses on lifestyle-related diseases (31). It was initiated in 1974 (Tromsø I), with the surveys repeated in 1979–1980, 1986–1987, and 1994–1995; the fifth survey was performed in 2001 (Tromsø V). In 1994–1995 (Tromsø IV), TROST had bone density measured on a total of 7,311 subjects (4,162 women and 3,149 men) aged from 45 to 84 years. These numbers corresponded to 80 and 79 percent of the invited women and men, respectively. In 2001, the 6,755 persons still alive and still living in Tromsø were invited for another examination. Bone densitometry was performed on a total of 5,366 subjects (3,169 women and 2,197 men), which corresponds to 80 and 78 percent of the invited women and men, respectively. The follow-up examination therefore included 61 and 55 percent of the women and men originally invited in 1994. The mean age at baseline in 1994 was 60 (standard deviation (SD), 7.4) years and 61 (SD, 7.2) years for the participating women and men, respectively. The mean follow-up time was 6.5 (SD, 0.4) years. The participants signed a declaration of consent prior to both examinations. The Regional Committee of Research Ethics recommended the study, with approval by the Norwegian Data Inspectorate.

Comparison of responders with nonresponders

Data for the first study, Tromsø IV, were compared for nonresponders, partial responders, and full responders. For nonresponders, we had only age and sex data; for partial responders, we had data from the first part of the examination in addition to one or two questionnaires; and for full responders, we had a complete data set. The analysis gave no indication for any differences among the groups (32). After Tromsø V, we could use baseline characteristics from Tromsø IV to compare participants who attended both studies with those lost to follow-up, because either they missed participating for unknown reasons or they were ineligible (deceased or moved out of town). Comparisons of the three groups are displayed in table 1. Participants attending both studies were younger and taller, had a lower body mass index (women), and had better self-perceived health. They also smoked less and had a higher bone mineral density at both forearm sites.

Measurements

Bone densitometry was performed in both surveys at the distal and ultradistal sites of the forearm with two single x-ray absorptiometric devices (DTX-100; Osteometer MediTech, Inc., Hawthorne, California). The distal site includes both the radius and the ulna from the 8-mm point (point where the ulna and radius are separated by 8 mm) and 24 mm proximally. The ultradistal site includes only the radius and stretches from the 8-mm point up to the radial endplate. The nondominant arm was measured except when it was ineligible because of wounds, plaster casts, and so on.

In both studies, by use of the same protocol, participants were allocated to the two densitometers depending on accessibility. Quality control with respect to precision and correction of artifacts in Tromsø IV was reported previously (33, 34). In the second survey, Tromsø V, one of the two densitometers had a major repair, and the x-ray tube had to be replaced on both densitometers during the survey. Quality control routines, using the European forearm phantom (QRM GmbH, Möhrendorf, Germany), revealed that one of the machines measured at a higher bone mineral density level before the x-ray tube replacement than the other one did, the mean difference being 0.005 g/cm^2 (35). The European forearm phantom data were used to adjust the differences in densitometer measurement level. The internal variation of each machine was studied by both coefficient of variation, which is equal to the standard deviation/mean $\times$ 100, and comparison of the European forearm phantom measurement levels at different time periods and was found to be satisfactory, with a mean coefficient of variation of 0.9 percent measured with the European forearm phantom (35).

All scans were reviewed and reanalyzed, and the results from Tromsø IV have been described previously (34). The scans from Tromsø V were analyzed by four technicians, one of whom also did the analysis in Tromsø IV. To test for reliability, we obtained three intraobserver tests (each technician compared with him/herself) and three interobserver tests (each technician compared with the other technicians). Each pair corrected a minimum of 27 and a maximum of 127 similar scans. We missed one intraobserver test and one interobserver test possibility, with one technician reviewing 273 (5 percent) of the scans. At the distal site, there were no significant differences among the technicians with respect to bone mineral density, either in intraobserver or in interobserver testing. At the ultradistal site, there were significant differences among the technicians with respect to bone mineral density in two of the three intraobserver tests and in two of the three interobserver tests. From these tests, we could derive that one of the technician's measurements was approximately 0.001 g/cm^2 lower than the others. This would entail an effect of less than 1 percent on the annual bone loss estimates (g/cm^2) and reduce the estimates of percentage of change by 0.02 percentage points. We also compared annual change estimates (g/cm^2), and they were not technician influenced ($p >$ 0.29) at any sites (analysis of variance). We therefore decided not to do any correction of the data. After exclusion of invalid scans, which were due mostly to excessive movement artifacts, there remained 3,093 and 3,060 repeated measurements for women and 2,150 and 2,160 repeated measurements for men at the distal and ultradistal sites, respectively.

TABLE 1. Comparison of participants lost to follow-up (participating in Tromsø IV only) with those who participated in both the Tromsø IV (1994–1995) and Tromsø V (2001) longitudinal studies, Norway*

Baseline characteristics	Participating in the Tromsø IV and Tromsø V studies (mean (SD†) or %)	Participating only in the Tromsø IV Study but eligible for the Tromsø V Study (mean (SD) or %)	Participating only in the Tromsø IV Study and ineligible for the Tromsø V Study‡ (mean (SD) or %)	p value (ANOVA†)
Women				
Age, years	60 (7.4)	62.6 (8.2)	65.7 (7.9)	0.001
Height, cm	162 (6.2)	161 (6.5)	160 (6.6)	0.001
Weight, kg	68.0 (11.5)	68.8 (13.4)	67.2 (13.3)	0.105
Body mass index, kg/m^2	25.9 (4.2)	26.5 (5.0)	26.2 (5.1)	0.009
Present smokers, %	29.3	34.2	43.1	0.001§
Smoking, years	25.4 (12.5)	27.5 (13.8)	33.0 (14.0)	0.001
Self-perceived health "good," %	52.8	45.1	31.6	0.001§
Baseline distal BMD†, g/cm^2¶	0.408 (0.07)	0.395 (0.07)	0.376 (0.08)	0.001
Baseline ultradistal BMD, g/cm^2¶	0.309 (0.07)	0.298 (0.07)	0.283 (0.07)	0.001
Men				
Age, years	61 (7.2)	62.7 (8.1)	65.9 (7.0)	0.001
Height, cm	175 (6.6)	174 (6.8)	174 (7.5)	0.001
Weight, kg	80.5 (11.7)	79.4 (12.5)	78.6 (14.7)	0.005
Body mass index, kg/m^2	26.2 (3.2)	26.1 (3.6)	25.9 (4.2)	0.369
Present smokers, %	31.4	40.7	41.2	0.001§
Smoking, years	29.9 (13.4)	34.1 (13.9)	36.7 (13.8)	0.001
Self-perceived health "good," %	61.6	54.2	39.7	0.001§
Baseline distal BMD, g/cm^2¶	0.541 (0.06)	0.527 (0.07)	0.514 (0.08)	0.001
Baseline ultradistal BMD, g/cm^2¶	0.442 (0.07)	0.432 (0.07)	0.418 (0.08)	0.001

* Participating in the Tromsø IV and Tromsø V studies: 3,169 women and 2,197 men; participating only in the Tromsø IV Study but eligible for the Tromsø V Study: 781 women and 608 men; participating only in the Tromsø IV Study and ineligible for the Tromsø V Study: 212 women and 344 men.

† SD, standard deviation; ANOVA, analysis of variance; BMD, bone mineral density.

‡ Deceased or moved out of town.

§ Chi-square testing.

¶ Invalid scans excluded.

Other measurements

Height and weight were measured to the nearest centimeter and half kilogram. The participants wore light clothing without shoes. Body mass index was calculated as weight in kilograms divided by the square of the height in meters.

Questionnaires

Two self-administered questionnaires were filled in by the participants in Tromsø IV, one before entering the study and the other during the study, in which the participants provided data on different lifestyle variables at baseline. We used data on smoking status and self-perceived health to assess possible selection bias. Women's menstrual status at baseline was also derived from answers to the questionnaires. Women using hormone replacement therapy (HRT) were classified as "HRT users." Women who were aged more than 44 years, were not using HRT, and were either pregnant or had a time from the last menstrual period of less than 180 days were classified as "premenopausal." Women who were aged more than 44 years, were not using HRT, were not pregnant, and had a time from the last menstrual period of between 180 and 364 days were classified as "perimenopausal." Women who were aged more than 44 years, were not using HRT, and had a time from the last menstrual period of 1 year or more were classified as "postmenopausal." When information about menstruation was lacking completely and menstrual status could not be determined, menstruation status was defined as "missing." For further classification of HRT use in the period of follow-up, we have used information provided from questionnaires in Tromsø IV.

Statistical analysis

Bone mineral density measurements from intra- and interobserver testing were compared by use of a one-sample paired t test. Change in bone density was estimated by calculating the difference between measurements from

TABLE 2. Annual bone mineral density changes in mg/cm² and percentage (%) with 95% confidence intervals in men and women (not using hormone replacement therapy), according to 5-year age group, the Tromsø IV (1994–1995) and Tromsø V (2001) longitudinal studies, Norway

Age group (years)	No.	Annual bone mineral density changes				No.	Annual bone mineral density changes			
		mg/cm²	95% confidence interval	%	95% confidence interval		mg/cm²	95% confidence inteval	%	95% confidence interval
		Men, distal site					*Men, ultradistal site*			
45–49	166	−1.49	−1.84, −1.14	−0.27	−0.34, −0.21	167	−0.89	−1.40, −0.37	−0.18	−0.30, −0.06
50–54	184	−1.54	−1.83, −1.25	−0.28	−0.33, −0.22	184	−1.01	−1.39, −0.62	−0.21	−0.29, −0.13
55–59	602	−1.92	−2.12, −1.73	−0.35	−0.39, −0.32	605	−1.36	−1.62, −1.10	−0.29	−0.35, −0.23
60–64	524	−2.70	−2.96, −2.43	−0.52	−0.57, −0.46	525	−1.98	−2.28, −1.68	−0.46	−0.53, −0.39
65–69	393	−3.24	−3.59, −2.89	−0.63	−0.70, −0.56	394	−2.13	−2.51, −1.76	−0.50	−0.60, −0.41
70–74	271	−3.77	−4.21, −3.34	−0.75	−0.85, −0.66	275	−2.23	−2.70, −1.77	−0.53	−0.66, −0.40
75–≥80	10	−3.29	−5.84, −0.74	−0.60	−1.12, −0.08	10	−2.16	−4.41, 0.08	−0.47	−1.03, 0.09
Total	2,150	−2.53	−2.65, −2.40	−0.48	−0.51, −0.46	2,160	−1.70	−1.85, −1.55	−0.39	−0.42, −0.35
		Women, distal site					*Women, ultradistal site*			
45–49	33	−2.47	−3.39, −1.56	−0.54	−0.75, −0.34	33	−3.11	−4.68, −1.54	−0.85	−1.28, −0.42
50–54	358	−4.57	−4.98, −4.16	−1.03	−1.12, −0.94	355	−4.54	−4.98, −4.10	−1.30	−1.42, −1.18
55–59	360	−3.67	−4.05, −3.30	−0.89	−0.98, −0.79	355	−2.59	−2.96, −2.22	−0.89	−0.98, −0.79
60–64	325	−3.58	−3.95, −3.22	−0.92	−1.02, −0.82	323	−2.27	−2.63, −1.90	−0.82	−0.90, −0.64
65–69	363	−3.49	−3.89, −3.10	−0.94	−1.05, −0.83	356	−1.74	−2.19, −1.28	−0.61	−0.80, −0.42
70–74	234	−3.21	−3.68, −2.74	−0.90	−1.03, −0.76	232	−1.83	−2.40, −1.26	−0.63	−0.88, −0.37
75–≥80	10	−6.04	−9.46, −2.62	−1.74	−2.53, −0.95	10	−3.53	−6.66, −0.40	−1.40	−2.53, −0.27
Total	1,683	−3.12	−3.26, −2.98	−0.77	−0.80, −0.73	1,664	−2.06	−2.22, −1.90	−0.61	−0.67, −0.56

Tromsø V and Tromsø IV. This total estimate was divided by the length of each participant's follow-up time to calculate the annual changes that are presented by 5-year age groups as mg/cm² and percent, with 95 percent confidence intervals. Regression analysis was used to investigate how age and sex predicted changes in bone mineral density. The difference in annual bone loss rates in women according to reported HRT use in the follow-up period and years since menopause was analyzed by use of analysis of variance, applying the Bonferroni correction.

To investigate the variation of changes in bone mineral density and to identify possible "fast losers," we used the annual loss estimates to categorize the participants into groups of "losers," "nonlosers," and "gainers" through calculation of the minimal difference, which represents the true biologic change with 95 percent certainty (95 percent detection limit). It is theoretically given by the following formula: Δ percent = $z \times$ coefficient of variation $\times \sqrt{2}$ (36). The median coefficient of variation estimated on our material was for an intermediate term between two measurements of 1.25 and 1.86 percent at the distal and ultradistal sites, respectively (33). Persons with an annual loss or gain of more than ±3.46 percent were categorized as true "gainers/losers" at the distal site. At the ultradistal site, the equivalent 95 percent detection limit was ±5.14 percent.

Tracking was assessed by use of Pearson's correlation coefficient and correlation with ranking of the variables. We divided values for bone mineral density measured at baseline and at follow-up into four quartiles, the highest quartile being categorized as position 1 and the lowest quartile being categorized as position 4. The values from both studies were categorized, respectively, and each participant's positions in both studies were compared.

The statistical analysis was performed by use of SPSS, version 11, software (SPSS, Inc., Chicago, Illinois). A p value of less than 0.05 was regarded as statistically significant.

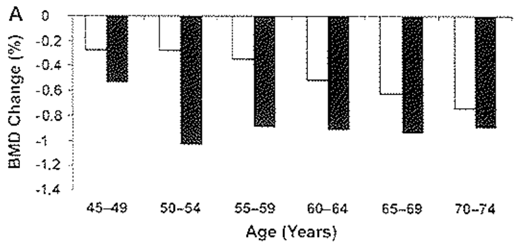
RESULTS

Changes in bone mineral density by age

Annual changes in bone mineral density according to 5-year age groups in men and in women reporting no HRT use in the follow-up period are displayed in table 2 and in figure 1. In men, the rate of bone mineral density loss was associated with age at both sites ($p < 0.001$), with an increase in the rate of loss of approximately 0.2 percent per 10-year increase in age (beta, −0.02). In women, a smaller bone mineral density loss rate in the age group 45–49 years compared with the other age groups indicated a possible nonlinear association at both sites. The test of linear interaction between age and sex was therefore not assessed.

Bone mineral density changes in women

The highest rate of bone loss was seen in women who were not using HRT and in women who had stopped using



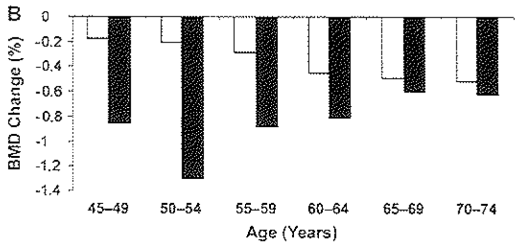


FIGURE 1. Distal (A) and ultradistal (B) sites: annual percentage of change in bone mineral density (BMD) by age in men and women (not using hormone replacement therapy) in the longitudinal Tromsø IV (1994–1995) and Tromsø V (2001) studies, Norway. Black bars, women; white bars, men.

HRT during the follow-up period (table 3). The differences between the groups also remained significant ($p < 0.001$) at both sites after adjustment for age. Among postmenopausal women not using HRT, the highest bone loss rates were seen in the period 1–3 years after menopause at the ultradistal site (table 4) ($p > 0.001$) and also, when adjusting for age, with the same trend at the distal site ($p = 0.065$). Women reporting to be premenopausal at baseline and not using HRT in the period of follow-up had bone mineral density loss rates at the ultadistal site that were not significantly different from those of women 1–3 and 4–5 years after menopause. At the distal site, their bone mineral density loss rates were not significantly different from those of any other group (table 4).

"Fast losers"

Among women not using HRT, 1 percent ($n = 16$) were losing more than −3.6 percent annually at the distal site. Their mean age was 62.0 (SD, 8.6) years. Nine of these women were in the lowest bone mineral density quartile at baseline, and in the second survey they were all in the lowest bone mineral density quartile. Only three men lost more than −3.6 percent annually at the distal site. At the ultradistal site, only three women lost more than −5.14 percent annually.

Tracking of bone mineral density measurements

The correlations in the measurements between the two studies are significant ($p < 0.001$) and high at the distal and ultradistal sites, respectively, in men ($r = 0.96$ and $r = 0.95$) and in all women ($r = 0.93$ and $r = 0.90$). Including only women reporting no HRT use, the correlation coefficient is $r = 0.94$ and 0.91 at the distal and ultradistal sites, respectively. The ranked correlation is slightly less but also high.

Among men, 79 and 75 percent keep their quartile position from the first to the second survey, and 10 and 12 percent either lose or gain one position, from all quartiles, at the distal and ultradistal sites, respectively. Among all the women, 74 and 70 percent keep their quartile position, whereas 12 and 14 percent either lose or gain one or two quartile positions at the distal and ultradistal sites, respectively. A similar pattern is seen also when only the women not using HRT are included in the analyses; 75 and 69 percent of the women keep their quartile position, 14 and 16 percent lose, and 10 and 11 percent gain one position at the

TABLE 3. Annual bone mineral density changes in mg/cm² and percentage (%) with 95% confidence intervals in women, according to reported hormone replacement therapy use in the follow-up period, the Tromsø IV (1994–1995) and Tromsø V (2001) longitudinal studies, Norway

Hormone replacement therapy status	No.	Mean age (years)	Mean bone mineral density changes			
			mg/cm²	95% confidence interval	%	95% confidence interval
Distal site						
Not using	1,683	61.23	−3.73	−3.91, −3.56	−0.93	−0.98, −0.89
Stopped using	174	56.28	−3.96	−4.58, −3.34	−0.91	−1.05, −0.77
Started using	251	55.98	−1.00	−1.43, −0.57	−0.22	−0.34, −0.11
Using	273	55.97	−0.46	−0.80, −0.12	−0.10	−0.18, −0.02
Ultradistal site						
Not using	1,664	61.22	−2.67	−2.87, −2.47	−0.84	−0.91, −0.77
Stopped using	174	56.28	−3.54	−4.18, −2.91	−1.03	−1.22, −0.85
Started using	250	56.05	0.39	−0.21, 0.99	0.27	0.01, −0.54
Using	265	55.84	0.05	−0.41, 0.51	0.08	−0.08, 0.24

TABLE 4. Bone mineral density changes in mg/cm^2 and percentage (%) with 95% confidence intervals in women not using hormone replacement therapy who were classified according to menopausal status and years since menopause, the Tromsø IV (1994–1995) and Tromsø V (2001) longitudinal studies, Norway

	No.	Mean age (years)	Mean bone mineral density changes			
			mg/cm^2	95% confidence interval	%	95% confidence interval
Distal site						
Premenopausal	106	50.10	−3.87	−4.57, −3.17	−0.85	−1.01, −0.69
1–3 years since menopause	142	53.56	−4.84	−5.55, −4.13	−1.10	−1.26, −0.94
4–5 years since menopause	101	55.09	−4.47	−5.17, −3.76	−1.07	−1.24, −0.90
6–10 years since menopause	270	57.72	−3.73	−4.12, −3.34	−0.91	−1.01, −0.82
>10 years since menopause	846	65.94	−3.38	−3.64, −3.13	−0.90	−0.97, −0.83
Ultradistal site						
Premenopausal	106	50.10	−4.59	−5.41, −3.77	−1.25	−1.47, −1.03
1–3 years since menopause	139	53.59	−4.66	−5.39, −3.93	−1.32	−1.53, −1.11
4–5 years since menopause	100	55.12	−3.18	−3.90, −2.46	−1.03	−1.26, −0.80
6–10 years since menopause	268	57.69	−2.49	−2.93, −2.05	−0.79	−0.93, −0.65
>10 years since menopause	832	65.94	−1.99	−2.26, −1.72	−0.68	−0.79, −0.58

distal and ultradistal sites, respectively. In both sexes, at both sites, the changes are all from original quartile positions.

DISCUSSION

The main findings from this population-based survey are that the mean annual bone mineral density loss in men aged 45–84 years is less than −0.5 and 0.4 percent, negatively predicted by age, at the distal and ultradistal sites, respectively. In women not using HRT, the equivalent bone mineral density changes are −0.9 and −0.8 percent. There is a high degree of tracking in bone mineral density measurements.

Two of the strengths of this study are its long follow-up and a high attendance rate of more than 78 percent in both studies. The single x-ray absorptiometric measurement of the distal forearm is thought to be one of the most precise densitometric methods (33, 37–39), and we had densitometer performance strictly controlled in both studies. Although fracture risk is best predicted by bone mineral density measurements from the same anatomic site, no site is superior with respect to prediction of all types of fragility fractures (5). When central dual x-ray absorptiometry is not available, peripheral bone mineral density measurement can be used to assess fracture risk at both peripheral and central sites (5, 40, 41), and they still constitute a valuable tool for the diagnosis of osteoporosis (42).

Irrespective of high response rates, nonresponse may generate selection bias. As displayed in table 1, participants lost for follow-up in general seem to be less healthy or having a less healthy lifestyle than those who participated in both studies. As smoking status is associated with greater bone loss rates (43) and low self-perceived health might indicate a greater degree of comorbidity (44), we possibly have some "healthy selection bias" in the material. Similar findings are observed in other longitudinal studies within the field. In a prospective osteoporosis study in Rochester, Minnesota, nonrespondents were less healthy than were full respondents (45). In the Framingham Osteoporosis Study, cohort members without longitudinal data were more likely to be older, to have a lower mean baseline bone mineral density, and to have lower physical activity scores, and they were less likely as participants to have reported good health (30). The Rotterdam Study also reported selection in favor of the more mobile and healthy population with probably lower rates of bone loss, and loss to follow-up was most likely related to illness, so that true progression was probably underestimated (28). Despite some possible selection bias, with the high attendance rates, we do feel confident that the results from our study are comparable to other population-based studies in the field.

At the forearm site, we have the possibility of comparing age-related changes of both trabecular and cortical bone, as the distal site contains mainly cortical and the ultradistal site contains mainly trabecular bone (46). We have compared our results with findings from other longitudinal, population-based studies on bone mineral density changes, limited to studies with data from the distal and ultradistal radius.

Annual percentages of decline of approximately 1.0 percent were seen at the distal and proximal radius in previous studies of 1,000 Japanese-American postmenopausal women aged 55–74 years (15, 16, 18) and of 271 White women aged 55–80 years (17). The loss rates in both of these studies are slightly higher at the distal site than that in our cohort for the concurrent age groups. In men, we observed an increasing rate of bone loss at the distal site with increasing age, from about −0.30 percent per year at ages 45–59 years to 0.75 percent per year at ages 70–74 years. Similar trends were seen in a large study of Japanese-American men aged 51–82 years (23, 24) and in the Mayo Clinic study of the Rochester, Minnesota, population (23, 24). The Framingham longitudinal study reported annual loss rates of −1.2 and −0.9

percent at the distal radius and of −1.0 and −0.8 percent at the ultradistal site in elderly women and men (aged 67–95 years) (30). These rates are slightly higher than those in our cohort at similar age groups. In summary, despite difficulties in comparing studies, the population of Tromsø living above the Arctic Circle does not seem to have higher bone loss rates than do other comparable populations.

Because of the different environments of the bone cells, decline in trabecular bone mass is thought to begin earlier than that in cortical bone mass, which is thought to occur increasingly after the age of 40 years and to be mainly age related (47). Our findings of bone mineral density development in the age group 45–84 years are supportive of this concept. In men, with age being a negative predictor of bone mineral density changes at both sites, the loss rates are higher at the distal than at the ultradistal site. In women not using HRT, the ultradistal site bone loss rates decrease from −1.3 percent in the age group 50–54 years to −0.6 percent in the age group 65–69 years, indicating that the most dramatic trabecular bone loss in women had occurred before that age. This is also supported by the findings of highest bone loss rates in women 1–5 years after menopause, findings which are comparable to those of Guthrie et al. (12) and Ahlborg et al. (48), who studied bone loss in relation to menopause in a longitudinal study of more than 16 years (healthy volunteers).

Tracking of a characteristic is defined as the ability to maintain the same position within a distribution over time (49, 50) or as the ability to predict future values from earlier measurements (51). As such, the term "tracking" is used to describe the extent of predictability or relative constancy that a measurable characteristic may have in a group of individuals over repeated observations (52). A number of methods may be used (53), and we used both the Pearson correlation coefficient and the comparison of quartile position between the two studies. Our findings are comparable to the findings of Sowers et al. (17) and Ahlborg et al. (48) and, therefore, supportive of those of Gilsanz and Nelson (54), who indicate that the morphologic traits that contribute to the strength of bone track throughout life, with values remaining in the same position relative to population percentiles. The high degree of tracking also indicates that one bone mineral density measure expresses a person's bone mineral density level and, as such, supports the notion that, except for patients with expected rapid bone loss or on bone mass treatment, there are rarely indications for frequent repeated bone mass measurements (55–59).

Notwithstanding the high degree of tracking, there is interindividual variation in bone loss estimates illustrated through both the confidence intervals and the distribution of participants into different "loss groups." As we used the notion of "minimal detectable difference," persons losing more than −3.14 percent annually at the distal site were identified as "fast losers," 1 percent of the women not using HRT. In the study of Sowers et al. (17), 30 percent of women aged 55–80 years lost at least 2 percent annually; the equivalent rate in our study would be 12.5 percent. We found, however, as did Sowers et al. and Nguyen et al. (60), that the rates of bone loss were not generally associated with baseline bone mineral density (or quartile positions).

In conclusion, our study is one of the first to describe bone mineral density changes in a longitudinal, population-based study comprising both sexes from the age of 45 years to well above 80 years. The frequency of fractures appears to be increasing in many countries (61), but the incidence of fractures varies (62). The Scandinavian countries, together with North America, have the highest incidence of hip and forearm fractures in the world (63, 64). Even if the study represents a northern population, the observed bone loss rates are not greater than those observed in other comparable populations.

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Paper IV

Cross-calibration in densitometry; can in vitro replace in vivo measures? The NOREPOS Study

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Abstract:

Background: Determination of bone mineral density (BMD) level and changes requires high-precision densitometry techniques. BMD measurements from different densitometers are not easily comparable. The purpose of this study was to investigate the agreement of densitometry between two types of densitometer phantoms and human measurements.

Methods: Bone densitometry was performed on the distal forearm with five similar SXA-devices on 17 persons with a wide variation in BMD level, bone size and body mass index (BMI). Each person was measured three times after full repositioning. Repeated measurements were also performed using equipment specific aluminium forearm phantoms (AFP) provided by the manufacturer, and the European forearm phantom (EFP) of semi-anthropomorphic calcium-hydroxyapatite. Data was analysed by pairwise comparison between densitometers, in addition to metaanalyses of the pairwise difference.

Results: One of the five densitometers measured at a higher level than the other four densitometers. Compared to AFP, there was better agreement between EFP and in vivo measurements, but EFP tended to overestimate the difference between the densitometers measurement level.

Conclusions: In vivo measurements remain the most valid tool for detection of densitometer differences. Densitometer performances are better captured by phantoms of calcium-hydroxyapatite than by aluminium phantoms. For follow-up and comparative studies, phantoms of calcium-hydroxyapatite are recommended for daily quality assessments.

Introduction

Osteoporotic fractures constitute a major health problem with substantial morbidity and costs [1;2]. The causation of fracture is complex, but bone fragility is an important contributor to fracture risk [3]. Bone mineral density (BMD) is a good surrogate measure of bone strength [4], and a strong relationship between BMD level and the probability of fracture has been documented [5]. Fracture risk differ between populations [6-8], but there are few studies comparing BMD levels across populations because the measurements are not easily comparable. BMD levels may vary as much as 18% between densitometers from different producers, and 5% between densitometers of same make and model [9]. Differences large enough to be clinically relevant may therefore occur even among devices from the same manufacturer [9].

Comparison of BMD measurement between populations is usually done by cross-calibrations of densitometers to a common scale by using standardized phantom measurements. This is a poorly documented praxis, and it is generally agreed that in vivo cross-calibration is the best [10;11] representing the gold-standard for calibration. Cross-calibration based on human measurements alone provides equivalency among the instruments in use, but could imply a lack of accuracy as we do not know which instrument is closest to the true value.

Conflicting results have been reported by the few studies comparing human and phantom measurements. Genant, using the European Spine Phantom (ESP), concluded that in vivo and in vitro were comparable [10], and so did Pearson using ESP, the Bona Fide Phantom and the GE Lunar Aluminium Spine Phantom

[11]. Blake, using the ESP and the Hologic Phantom, found however a significant mismatch between in vivo and in vitro cross calibration results [12].

Peripheral BMD measurements are associated with fracture risk at both peripheral and central sites [5;13-15]. Single x-ray absorptiometry (SXA) of the forearm has high precision, accuracy, ease of use, low radiation doses and moderate cost [16-21]. In a six-year longitudinal study, using two SXA devices, quality assessment procedures indicated that two types of phantoms identified changes in densitometer performance differently. The European Forearm phantom (EFP) (QRM-Germany) predicted BMD changes observed in a large population sample, whereas the equipment specific Aluminium Forearm Phantom (AFP) did not [22]. The aim of this study was to compare agreement between two phantoms (EFP and AFP) and in vivo densitometry of the distal forearm in a cross-calibration study.

Materials and methods

Study design and materials

The Norwegian Epidemiological Osteoporosis Studies (NOREPOS) comprise four large population-based multipurpose studies in the cities of Oslo (the Oslo Health Study, HUBRO, 2000-2001), Bergen (the Hordaland Health Study, HUSK, 1998 – 99), Tromsø (The Tromsø Study/Tromsø Osteoporosis Study, TROST, 1994-95 – 2001) and the county of Nord-Trøndelag (the Nord-Trøndelag Health Study, HUNT, 1995-1997) [23]. In 2003 the five SXA-devices (DTX-100; Osteometer MediTech, Inc., Hawthorne, California) formerly used in TROST [24-26], HUNT [27] and HUBRO [28] were brought together for a cross-calibration study.

Volunteers were recruited among employers at the University of Tromsø (UiTØ). In order to represent a wide range of characteristics which could influence BMD, initial selection of subjects was based on age, height, and weight as surrogates for bone mass, bone size and BMI. 20 participants underwent a preliminary DXA examination of total hip and were included into the study according to variation in BMD levels and bone size measured by DXA (total hip) and variation in BMI. The chosen range of variation was provided through a large population sample (TROMSØ V) with use of the three tertiles within the borders of the fifth and 95 percentile in the upper and lower part of the distribution. As displayed in Table 1, we had a total of 9 categories, and participants were included until a minimum of 3 participants fitted into each category. Each participant contributed to three categories. Finally a total of 17 participants were included into the study. Informed consent was obtained from all participants. The regional Committee of Medical Research Ethics recommended, and the Norwegian Data Inspectorate approved the study.

Human measurements

Bone densitometry was performed at the distal and ultradistal forearm sites on the five similar SXA-devices of the non-dominant arm. The distal site includes both the radius and ulna from the 8 mm-point (the point at which the ulna and radius are separated by 8 mm) and 24 mm proximally. The ultradistal site includes only the radius and stretches from the 8-mm point up to the radial endplate. Each of the 17 participants had three measurements done on each densitometer with full repositioning between each measurement. One trained technician performed the BMD measurements from the same protocol formerly used in NOREPOS sub-studies [28]. All scans were reviewed and reanalysed according to a rigorous quality control protocol [29]. Only measurements from the distal site are presented as the ultradistal measurements followed the same pattern.

Phantom measurements

From November 2003 to February 2004 measurements were performed regularly on all densitometers with the equipment specific AFP provided by the manufacturer, and the EFP [30-32] which is a semianthropomorphic phantom, comprising three hydroxyapatite bone imitations with different densities within the human range, 0,662 g/cm² (high), 0,415 g/cm² (medium) and 0,314 g/cm² (low). To keep the EFP in position for SXA measurements, a device was specially constructed in plastic. All EFP scans were analysed by the same person according to protocol using the special calculation option in the densitometer's software.

Statistical analysis

Short term precision error (σ_m) for each device with 95% confidence interval was estimated from the repeated measurements of the individuals. Coefficients of repeatability (CR) for each device were calculated by $CR_m = 1.96 \cdot \sqrt{2} \cdot \sigma_m$. We expect 95% of all differences (in absolute value) between two measurements on the same individual at the same machine to be less than the machine's CR value. The precision error is expressed by standard deviation and CV.

Evaluation of agreement between pairs of devices was performed by Bland-Altman analyses of the in vivo measurements [33]. Differences between means did not vary systematically over the range of BMD values and normal distribution assumption was valid, no transformation of the original data was necessary. The smallest detectable differences (SDD) [34] comparing measurements from machine i and machine j were calculated by the formula: $SDD_{i,j} = 1.96 \cdot \sqrt{\hat{\sigma}^2_{m_i} + \hat{\sigma}^2_{m_j}}$. The SDD is an estimate of the magnitude of inter-machine differences (absolute value) which is likely to occur when the same individuals are measured by two different machines. Computing an interval of length SDD around the mean difference in BMD between the two machines considered gave the limits of agreement (LOA) which cover about 95% of the differences observed on the actual material. If the interval is small enough and has no clinical importance, the two devices being investigated may be interchanged [33].

A meta-analysis approach was used in order to make a statistical comparison of in vivo data and phantom data with respect to the ability to identify differences in mean BMD between pairs of densitometers [35;35]]. Difference in mean BMD between two densitometers was scaled or standardised by the pooled standard deviation from the repeated measurements for each individual in the in vivo material. The standardised mean difference expresses the size of the machine differences for each individual relative to the variability observed for each individual. Hedges' adjustments to correct for small sample bias were applied to the standardised difference in mean BMD [35]. Further the standardised difference in mean BMD between the two densitometers were weighted by the inverse variance method giving a pooled estimate of the difference in mean for all individuals in the in vivo measurements. The weights used in the inverse variance method are the reciprocals of the squared standard error of the standardised difference. This method minimises the variability of the pooled estimate [35]. The pooled estimate of standardised difference in mean was calculated for all 10 pairs of densitometer based on the in vivo measurement. A similar procedure was applied on the phantom measurements. Finally the pooled estimate of standardised difference in mean of human and EFP measurements were compared by a Student T test.

Results

Human measurements

Seven participants were male, and the mean BMD level of the 17 participants was 491.3 mg/cm^2 (SD 90.6 mg/cm^2), with a range of variation from 269 to 619 mg/cm^2. The mean bone size was 34.7 mm^2 (SD 4.03 mm^2), with a range of variation from 29.0 to 42.0 mm^2. The mean BMI was 26.08 kg/m^2 (SD 3.21 kg/m^2), with a range of variation from 22.2 to 34.2 mm^2. BMD levels measured by the different densitometers are displayed in table 2 and the BMD differences from pair wise comparison between the densitometers in table 3. The measurement levels of four of the densitometers were similar, the mean BMD difference varying from 0 to 2.25 mg/cm^2. The fifth densitometer, SXA 3, reported BMD at a higher level compared to the other densitometers, with a mean difference varying between 5.53 and 7.78 mg/cm^2 (table 3).

Phantom measurements

Descriptive statistics from the phantom measurements according to the different densitometers are displayed in table 4. The AFP measurements indicated that

SXA 1 and 2 measured at an equal, but lower BMD level than SXA 3, 4 and 5. The AFP did not "recognise" SXA 3 to measure at a higher BMD level than SXA 4 and 5. The EFP measurements at the low density level, followed the same pattern as AFP. The EFP measurements at the mid density level, indicated a greater variance in BMD level between the densitometers, with SXA 3 measuring at the highest density level. The EFP measurements at the high density level, indicated, as the human measurements, that SXA 3 measured higher density. Although the mid and high density level reflected the densitometer differences measured in vivo, some heterogeneity in the estimated differences among the levels of the EFP phantom were present.

A presentation of the pooled estimate of the standardised difference in mean for each pair wise combination of the densitometers based on human and EFP measurements is shown in figure 1 and table 5. The figure illustrate what is also seen in table 5; the human measurements indicated different measurement levels only in the densitometer combinations involving SXA3, that is in four out of ten combinations. The direction of the differences was captured by the EFP in all four combinations, and by the AFP in three of four combinations. There were six combinations where the human measurements indicated no difference between the densitometer's measurement levels. The AFP indicated that the measurement level differed in five of these six combinations whereas the EFP followed the pattern of the human measurements. The differences between densitometers captured by the EFP followed the direction of the differences indicated by the human measurements in eight of 10 densitometer combinations, the differences were however overestimated in two of the combinations involving SXA 3 (SXA1-

SXA3 and SXA2 - SXA3). From the tables and the figure we can conclude that the differences in densitometers' measurement level in direction were generally captured by the EFP, the magnitude of the differences however tended to be overestimated.

Comparison of in vivo data and phantom data

Results of the meta-analyses are presented in table 5. The phantom measurements showed differences between all pairs of densitometers, while in vivo measurements identified significant differences for 4 out of the 10 pairs using 5% significance level. Comparing the pooled standardised mean differences estimated by in vivo data and phantom measurements showed that even if significant difference between pairs of densitometers are detected by each data set, there are significant difference in magnitude.

Discussion

In this cross-calibration study there was a better agreement between EFP and in vivo measurements compared to AFP. The EFP measurements followed the direction of the human measurements, however tending to overestimate the magnitude of differences in measurement level.

The strength of this study is the possibility to compare phantom measurements with human measurements (or in vivo) from a wide variety of BMD levels, measurements over a number of days giving the opportunity to estimate repeatability, and measurements of all densitometers performed by the same technician and location [11]. Initially we planned only to see how well the EFP revealed possible densitometer differences. As the results of our longitudinal study indicated that the EFP and AFP measurements predicted densitometer differences differently [36], we also included AFP measurements into this study. Because that was not planned initially, we only had daily AFP measurements available. Ideally the AFP measurements should have been performed in the same manner as the EFP measurements.

Genant et al tested standardised phantoms (the ESP, the European spine phantom prototype, the standard phantoms of Hologic, Lunar and Norland) with respect to similarity of results compared to humans on three types of DXA systems and concluded that area, BMC, and BMD values obtained on the three different systems were not directly comparable. The ESP demonstrated data that were very close to the patient data. After applying standardization formulas, the absolute average differences in patient's BMD between the three systems were significantly reduced [10]. Pearson et al compared three types of phantoms used for cross-calibration with in vivo cross-calibration (the Bona Fide Phantom, the ESP and the GE Lunar Aluminium Phantom) of two DXA systems, and reported no significant differences between the in vitro and in vivo calibration. The Bona Fide Phantom performed best compared to the human measurements, although the in vitro cross-calibrations were not significantly different from one another [11]. Pearson emphasised the importance of collecting data over a period of time to include day to day variation in densitometer performance [11], and recommended the use of calcium hydroxyapatite phantoms for cross-calibration of different DXA systems.

In a longitudinal study where a Hologenic QDR-2000 was upgraded to a QDR-2000plus, the new scanner was carefully cross-calibrated with the Hologic spine phantom, which is anthropomorphic in shape, and composed of calcium hydroxyapatite, but only represents a single density level [12]. The accuracy of this cross-calibration was checked by in vivo scans of patients in addition to the ESP. Blake reported that the in vivo study showed a significant mismatch between the two systems with systematic errors exceeding 2% at five out of 10 scan sites studied. The results from the ESP lay closer to the in vivo data than the Hologic spine phantom, but still the mismatch revealed was greater than anticipated. Blake therefore emphasised the importance of performing in vivo cross-calibration studies whenever DXA systems are replaced. The full explanation of the difference between phantom and in vivo cross-calibration between two systems is not clear [12].

Our study is based on SXA technology, but our findings are in concordance with Blake's; even if antropomorphic phantoms perform better than aluminium phantoms, in vitro cannot fully replace in vivo cross-calibration. The implication of our findings is, as other authors have concluded, that clinically relevant differences in measurement level may occur between densitometers of the same make and model [9;37]. In cross-sectional, single - or multi-centre studies, using different densitometers, in vivo cross-calibration still remain the best option to secure comparability of human BMD measured on different densitometers. If in vivo cross-calibration is not possible, like in longitudinal studies, in vitro cross-calibration with antropomorpic phantoms can replace human measurements, but one should be aware of influence on precision. Important differences in measurement level between densitometers, as well as changes in densitometer performance (due to maintenance, upgrading, long term drift etc) [38], might not be detected by aluminium phantoms, which are the phantoms provided by the manufacturers and usually integrated into the daily scanning procedures. In longitudinal or multi-centre studies where in vivo cross-calibrations are not obtainable, we recommend daily measurements with anthropomorphic phantoms of calcium hydroxyapatite in tissue-equivalent plastic on all participating densitometers in order to evaluate the stability of and differences in measuring levels of densitometers.

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Table 1. Categories for inclusion of participants to the SXA cross-calibration study, the Norwegian Epidemiological Osteoporosis Studies

BMD total hip		**Bone size**		**BMI**	
(g/cm²)	N*	**(mm²)**	N*	**(kg/ m²)**	N*
0,680 – 0,861	4	29,8 – 33,5	5	20,7 – 24,5	8
0,862 – 0,995	8	33,6 – 37,4	8	24,6 – 28,2	4
0,996 – 1,202	5	37,5 – 42,6	4	28,3 – 34,1	5

* A total of 17 persons included, one person could contribute to more than one category.

Table 2. Results for 5 SXA densitometers in vivo. BMD at distal site (mg/cm²) of 17 subjects with 3 repeated measurements, the Norwegian Epidemiological Osteoporosis Studies

Machine m_i; i=1..5	Mean BMD (mg/cm²)	$\hat{\sigma}_{m_i}$ (short term precision error) (mg/cm²)	CV (%)	95% Confidence interval of $\hat{\sigma}_{m_i}$ (mg/cm²)	Coefficient of repeatability (CR): $1.96\sqrt{2}\,\hat{\sigma}_{m_i}$ (mg/cm²)
SXA1	491.08	5.84	1.2 %	4.97, 8.31	16.19
SXA2	489.92	4.57	0.9 %	3.89, 6.50	12.67
SXA3	496.61	4.16	0.8 %	3.54, 5.92	11.53
SXA4	489.92	2.99	0.6 %	2.54, 4.26	8.29
SXA5	488.82	5.20	1.1 %	4.42, 7.39	14.41
All machines	491.27	4.65	0.9 %	3.91, 4.75	12.89

Table 3. Pairwise comparison of BMD (mg/cm²) differences in vivo. Mean BMD, SDD (Smallest detectable difference) and LOA (Limits of agreement) for 17 individuals with 3 repeated measurements, the Norwegian Epidemiological Osteoporosis Studies

Pairs of SXA machines m_i, m_j; i,j=1..5	Mean difference	$\hat{\sigma}_{m_i,m_j} = \sqrt{\hat{\sigma}^2_{m_i} + \hat{\sigma}^2_{m_j}}$	SDD	LOA Lower	LOA Upper
SXA1-SXA2	1.16	7.41	14.53	-13.37	15.69
SXA1-SXA3	-5.53	7.17	14.05	-19.58	8.52
SXA1-SXA4	1.16	6.56	12.86	-11.70	14.01
SXA1-SXA5	2.25	7.82	15.32	-13.06	17.57
SXA2-SXA3	-6.69	6.18	12.11	-18.80	5.42
SXA2-SXA4	0	5.46	10.70	-10.70	10.70
SXA2-SXA5	1.10	6.92	13.56	-12.46	14.66
SXA3-SXA4	6.69	5.12	10.04	-3.35	16.73
SXA3-SXA5	7.78	6.66	13.05	-5.26	20.83
SXA4-SXA5	1.10	6.00	11.75	-10.65	12.85

Table 4. Descriptive statistics (mean ± sd) of phantom measurements (mg/cm²) where n=number of repeated measurements, the Norwegian Epidemiological Osteoporosis Studies

Phantom	True BMD	SXA Machine 1 (n=37)	SXA Machine 2 (n=37)	SXA Machine 3 (n=37)	SXA Machine 4 (n=37)	SXA Machine 5 (n=37)	Precision error $\hat{\sigma}$ (mg/cm²)
EFP	314	288.1 ± 2.3	286.6 ± 2.0	290.7 ± 1.9	290.2 ± 1.9	290.9 ± 2.5	2.12
	415	395.5 ± 1.6	392.1 ± 1.6	398.5 ± 2.1	394.5 ± 2.0	397.7 ± 2.1	1.86
	662	632.1 ± 2.4	632.4 ± 4.1	637.3 ± 1.5	631.8 ± 1.8	631.9 ± 1.9	2.50
AFP	(BMC= 3.535 g)	392.6 ± 1.7 (n=13)	392.2 ± 1.7 (n=11)	394.5 ± 1.1 (n=13)	394.4 ± 1.2 (n=12)	395.3 ± 0.9 (n=12)	1.25

Table 5. Meta-analyses of pair wise differences in BMD (mg/cm²). Pooled estimate of the standardised difference in mean , 95% CI of the pooled estimate and Student T-test statistics testing inequality in machine difference identified by in vivo and EFP measurements. In vivo measurements of 17 individuals and phantom measurements
at 3 levels, the Norwegian Epidemiological Osteoporosis Studies.

Pairs of SXA machines		Pooled estimate of standardised difference in mean	95% CI of pooled estimate		T-test statistics (In vivo-EFP)	Two-sided p-value
			Lower	Upper		
SXA1-SXA2	In vivo	0.30	-0.20	0.80	-5.4	<0.001
	EFP	1.14	0.77	1.52		
SXA1-SXA3	In vivo	-0.79	-1.35	-0.23	31.1	<0.001
	EFP	-6.54	-7.24	-5.84		
SXA1-SXA4	In vivo	0.01	-0.46	0.47	-2.9	0,010
	EFP	0.42	0.08	0,76		
SXA1-SXA5	In vivo	0.13	-0.35	0.60	9.5	<0.001
	EFP	-1.29	-1.67	-0.91		
SXA2-SXA3	In vivo	-0.86	-1.40	-0.31	40.4	<0.001
	EFP	-8.53	-9.42	-7.64		
SXA2-SXA4	In vivo	-0.10	-0.62	-0.43	5.3	<0.001
	EFP	-0.96	-1.38	-0.55		
SXA2-SXA5	In vivo	-0.25	-0.78	0.27	2.5	0.023
	EFP	-0.66	-1.10	-0.22		
SXA3-SXA4	In vivo	1.38	0.78	1,98	-4.2	<0.001
	EFP	2.16	1.71	2.61		
SXA3-SXA5	In vivo	1.02	0.49	1.56	1.5	0.153
	EFP	0.78	0.44	1.12		
SXA4-SXA5	In vivo	0.15	-0.31	0.61	8.7	<0.001
	EFP	-1.09	-3.00	-0,98		

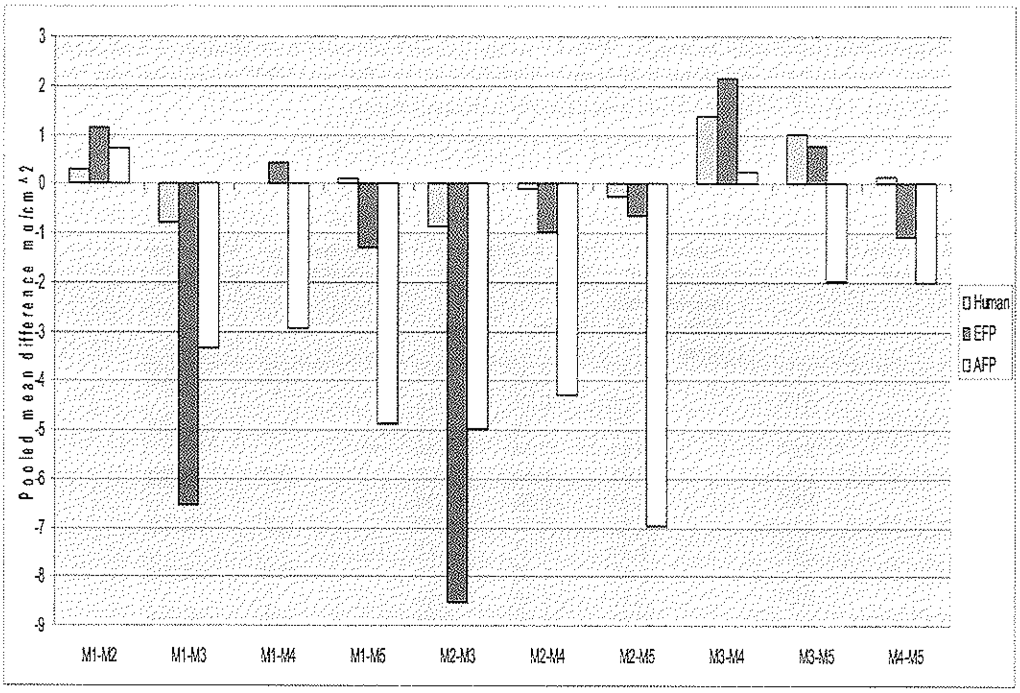
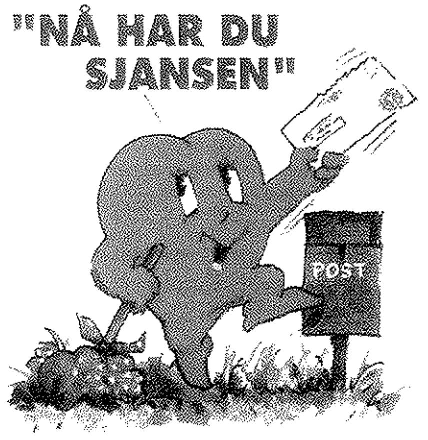


Fig 1. Pooled mean differences for all 10 pairs of densitometers. In vivo data, EFP measurements and AFP measurements, the Norwegian Epidemiological Osteoporosis Studies

Appendix 1

**First questionnaire,
Tromsø IV, 1994-95**

Innbydelse til
HELSEUNDERSØKELSEN



Fødselsdato Personnr. Kommune Kretsnr.

Velkommen til helseundersøkelsen i Tromsø!

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

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

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

Vennlig hilsen
Kommunehelsetjenesten
Fagområdet medisin, Universitetet i Tromsø
Statens helseundersøkelser

Sett bare ett kryss.

Dårlig 1
Ikke helt god 2
God 3
Svært god 4

	JA	NEI	Vet ikke
Hjerteinfarkt			
Angina pectoris (hjertekrampe)			
Hjerneslag/hjerneblødning			
Astma			
Diabetes (sukkersyke)			

Bruker du medisin mot høyt blodtrykk?

Nå 1
Før, men ikke nå 2
Aldri brukt 3

JA NEI

	Nei	Litt	En god del	Svært mye
Nervøs og urolig?				
Plaget av angst?				
Trygg og rolig?				
Irritabel?				
Glad og optimistisk?				
Nedfor/deprimert?				
Ensom?				
	1	2	3	4

JA NEI

JA NEI

Sett 0 hvis du ikke oppholder deg i røykfylt rom.

JA NEI

Sigaretter daglig? ....
Sigarer/sigarillos daglig? ....
Pipe daglig? ....

Hvor mange sigaretter røyker eller røykte du vanligvis daglig? ....

Hvor gammel var du da du begynte å røyke daglig? .... År

Hvor mange år tilsammen har du røykt daglig? .... Antall år

Tenk deg et ukentlig gjennomsnitt for året. Arbeidsvei regnes som fritid.

	Timer pr. uke			
	Ingen	Under 1	1-2	3 og mer
Lett aktivitet (ikke svett/andpusten)				
Hard fysisk aktivitet (svett/andpusten)				

Sett 0 hvis du ikke drikker kaffe daglig.

Kokekaffe .... Antall kopper
Annen kaffe .... Antall kopper

JA NEI

Regn ikke med lettøl.
Sett 0 hvis mindre enn 1 gang i mnd. .... Antall ganger

Øl glass	Vin glass	Brennevin glass

Regn ikke med lettøl.
Sett 0 hvis du ikke drikker alkohol.

Sett ett kryss.

Bruker ikke smør/margarin 1
Meierismør 2
Hard margarin 3
Bløt (soft) margarin 4
Smør/margarin blanding 5
Lettmargarin 6

Grunnskole, 7-10 år, framhaldsskole, folkehøgskole 1
Realskole, middelskole, yrkesskole, 1-2-årig videregående skole 2
Artium, øk.gymnas, allmennfaglig retning i videregående skole 3
Høgskole/universitet, mindre enn 4 år 4
Høgskole/universitet, 4 år eller mer 5

Lønnet arbeid ....
Heltids husarbeid ....
Utdanning, militærtjeneste ....
Arbeidsledig, permittert ....

Antall timer

Syketrygd (sykmeldt) ....
Attføring ....
Uførepensjon ....
Alderspensjon ....
Sosialstøtte ....
Arbeidsløshetstrygd ....

angina pectoris (hjertekrampe)? .... JA NEI Vet ikke

Appendix II

**Second questionnaire for subjects aged < 70 years,
Tromsø IV, 1994-95**

Helseundersøkelsen i Tromsø

Hovedformålet med Tromsøundersøkelsene er å skaffe ny kunnskap om hjerte-karsykdommer for å kunne forebygge dem. I tillegg skal undersøkelsen øke kunnskapen om kreftsykdommer og andre alminnelige plager som f.eks. allergier, smerter i muskulatur og nervøse lidelser. Vi ber deg derfor svare på noen spørsmål om forhold som kan ha betydning for risikoen for disse og andre sykdommer.

Skjemaet er en del av Helseundersøkelsen som er godkjent av Datatilsynet og av Regional komite for medisinsk forskningsetikk. Svarene brukes bare til forskning og behandles strengt fortrolig. Opplysningene kan senere bli sammenholdt med informasjon fra andre offentlige helseregistre etter de regler som Datatilsynet og Regional komite for medisinsk forskningsetikk gir.

Hvis du er i tvil om hva du skal svare, sett kryss i den ruten som du synes passer best.

Det utfylte skjema sendes i vedlagte svarkonvolutt. Portoen er betalt.

På forhånd takk for hjelpen!

Med vennlig hilsen

Fagområdet medisin
Universitetet i Tromsø — Statens helseundersøkelser

Hvis du ikke ønsker å besvare spørreskjemaet, sett kryss i ruten under og returner skjemaet. Da slipper du purring.

Jeg ønsker ikke å besvare spørreskjemaet ☐

Dato for utfylling av skjema: ..... / ..... / ..... (Dag Mnd År)

OPPVEKST

I hvilken kommune bodde du da du fylte 1 år?

....

Hvis du ikke bodde i Norge, oppgi land i stedet for kommune.

Hvordan var de økonomiske forhold i familien under din oppvekst?

- Meget gode ☐
- Gode ☐
- Vanskelige ☐
- Meget vanskelige ☐

Hvor mange av de første 3 årene av ditt liv
- bodde du i by? ______ år
- hadde dere katt eller hund i hjemmet? ______ år

Hvor mange av de første 15 årene av ditt liv
- bodde du i by? ______ år
- hadde dere katt eller hund i hjemmet? ______ år

BOLIG

Hvem bor du sammen med?
Sett ett kryss for hvert spørsmål og angi antall

	Ja	Nei	Antall
Ektefelle/samboer	☐	☐	
Andre personer over 18 år	☐	☐	____
Personer under 18 år	☐	☐	____

Hvor mange av barna har plass i barnehage? ....

Hvilken type bolig bor du i?
- Enebolig/villa ☐
- Gårdsbruk ☐
- Blokk/terrasseleilighet ☐
- Rekkehus/2-4 mannsbolig ☐
- Annen bolig ☐

Hvor stor er din boenhet? ______ m

I omtrent hvilket år ble boligen bygget? ______

	Ja	Nei
Er boligen isolert etter 1970?	☐	☐
Bor du i underetasje/kjeller?	☐	☐
Hvis "Ja", er gulvbelegget lagt på betong?	☐	☐

Hvordan er boligen hovedsakelig oppvarmet?
- Elektrisk oppvarming ☐
- Vedfyring ☐
- Sentralvarmeanlegg oppvarmet med:
  - Parafin ☐
  - Elektrisitet ☐

	Ja	Nei
Er det heldekkende tepper i stua?	☐	☐
Er det katt i boligen?	☐	☐
Er det hund i boligen?	☐	☐

ARBEID

Hvis du er i lønnet eller ulønnet arbeid, hvordan vil du beskrive ditt arbeid?
- For det meste stillesittende arbeid? ☐ 1
  (f.eks. skrivebordsarbeid, montering)
- Arbeid som krever at du går mye? ☐ 2
  (f.eks. ekspeditørarb., lett industriarb., undervisning)
- Arbeid hvor du går og løfter mye? ☐ 3
  (f.eks. postbud, pleier, bygningsarbeid)
- Tungt kroppsarbeid? ☐ 4
  (f.eks. skogsarb., tungt jordbruksarb., tungt bygn.arb.)

Kan du selv bestemme hvordan arbeidet ditt skal legges opp?
- Nei, ikke i det hele tatt ☐ 1
- I liten grad ☐ 2
- Ja, i stor grad ☐ 3
- Ja, det bestemmer jeg selv ☐ 4

	Ja	Nei
Har du skiftarbeid, nattarbeid eller går vakter?	☐	☐

Har du noen av følgende yrker (heltid eller deltid)?
Sett ett kryss for hvert spørsmål

	Ja	Nei
Sjåfør	☐	☐
Bonde/gårdbruker	☐	☐
Fisker	☐	☐

EGNE SYKDOMMER

Har du noen gang hatt:
Sett ett kryss for hvert spørsmål. Oppgi alderen ved hendelsen.
Hvis det har skjedd flere ganger, hvor gammel var du siste gang?

	Ja	Nei	Alder
Lårhalsbrudd	☐	☐	......
Brudd ved håndledd/underarm	☐	☐	......
Nakkesleng (whiplash)	☐	☐	......
Skade som førte til sykehusinnleggelse	☐	☐	......
Sår på magesekken	☐	☐	......
Sår på tolvfingertarmen	☐	☐	......
Magesår-operasjon	☐	☐	......
Operasjon på halsen	☐	☐	......

Har du eller har du hatt:
Sett ett kryss for hvert spørsmål.

	Ja	Nei
Kreftsykdom	☐	☐
Epilepsi (fallesyke)	☐	☐
Migrene	☐	☐
Kronisk bronkitt	☐	☐
Psoriasis	☐	☐
Benskjørhet (osteoporose)	☐	☐
Fibromyalgi/fibrositt/kronisk smertesyndrom	☐	☐
Psykiske plager som du har søkt hjelp for	☐	☐
Stoffskiftesykdom (skjoldbruskkjertel)	☐	☐
Sykdom i leveren	☐	☐
Nyrestein	☐	☐
Blindtarmsoperasjon	☐	☐
Allergi og overfølsomhet		
Atopisk eksem (f.eks. barneeksem)	☐	☐
Håndeksem	☐	☐
Høysnue	☐	☐
Matvareallergi	☐	☐
Annen overfølsomhet (ikke allergi)	☐	☐

Hvor mange ganger har du hatt forkjølelse, influensa, "ræksjuka" og lignende siste halvår? ...... ganger

	Ja	Nei
Har du hatt dette siste 14 dager?	☐	☐

SYKDOM I FAMILIEN

Kryss av for de slektningene som har eller har hatt noen av sykdommene:
Kryss av for "Ingen" hvis ingen av slektningene har hatt sykdommen

	Mor	Far	Bror	Søster	Barn	Ingen
Hjerneslag eller hjerneblødning	☐	☐	☐	☐	☐	☐
Hjerteinfarkt før 60 års alder	☐	☐	☐	☐	☐	☐
Kreftsykdom	☐	☐	☐	☐	☐	☐
Astma	☐	☐	☐	☐	☐	☐
Mage/tolvfingertarm-sår	☐	☐	☐	☐	☐	☐
Benskjørhet (osteoporose)	☐	☐	☐	☐	☐	☐
Psykiske plager	☐	☐	☐	☐	☐	☐
Allergi	☐	☐	☐	☐	☐	☐
Diabetes (sukkersyke)	☐	☐	☐	☐	☐	☐
- alder da de fikk diabetes	......	......	......	......	......	

SYMPTOMER

	Ja	Nei
Hoster du omtrent daglig i perioder av året?	☐	☐
Hvis "Ja":		
Er hosten vanligvis ledsaget av oppspytt?	☐	☐
Har du hatt slik hoste så lenge som i en 3 måneders periode i begge de to siste år?	☐	☐

	Ja	Nei
Har du hatt episoder med piping i brystet?	☐	☐
Hvis "Ja", har dette oppstått: *Sett ett kryss for hvert spørsmål.*		
Om natten	☐	☐
Ved luftveisinfeksjoner	☐	☐
Ved fysiske anstrengelser	☐	☐
Ved sterk kulde	☐	☐

	Ja	Nei
Har du merket anfall med plutselig endring i pulsen eller hjerterytmen siste år?	☐	☐

Hvor ofte er du plaget av søvnløshet?
- Aldri, eller noen få ganger i året ☐
- 1-2 ganger i måneden ☐
- Omtrent en gang i uken ☐
- Mer enn en gang i uken ☐

Hvis du er plaget av søvnløshet i perioder, når på året er du mest plaget?
- Ingen spesiell tid ☐
- Særlig i mørketiden ☐
- Særlig i midnattsoltiden ☐
- Særlig vår og høst ☐

	Ja	Nei
Har du det siste året vært plaget av søvnløshet slik at det har gått ut over arbeidsevnen?	☐	☐

Hvor ofte er du plaget av hodepine?
- Sjelden eller aldri ☐
- En eller flere ganger i måneden ☐
- En eller flere ganger i uken ☐
- Daglig ☐

Hender det at tanken på å få alvorlig sykdom bekymrer deg?
- Ikke i det hele tatt ☐
- Bare i liten grad ☐
- En del ☐
- Ganske mye ☐

BRUK AV HELSEVESENET

Hvor mange ganger har du siste året, på grunn av egen helse eller sykdom, vært:
Sett 0 hvis du ikke har hatt slik kontakt

	Antall ganger siste år
Hos vanlig lege/legevakt	......
Hos psykolog eller psykiater	......
Hos annen legespesialist utenfor sykehus	......
På poliklinikk	......
Innlagt i sykehus	......
Hos bedriftslege	......
Hos fysioterapeut	......
Hos kiropraktor	......
Hos akupunktør	......
Hos tannlege	......
Hos naturmedisiner (homøopat, soneterapeut e.l.)	......
Hos håndspålegger, synsk eller "leser"	......

LEGEMIDLER OG KOSTTILSKUDD

Har du det siste året periodevis brukt noen av de følgende midler daglig eller nesten daglig?
Angi hvor mange måneder du brukte dem.
Sett 0 hvis du ikke har brukt midlene

Legemidler
- Smertestillende .... mnd.
- Sovemedisin .... mnd.
- Beroligende midler .... mnd.
- Medisin mot depresjon .... mnd.
- Allergimedisin .... mnd.
- Astmamedisin .... mnd.

Kosttilskudd
- Jerntabletter .... mnd.
- Kalktabletter eller benmel .... mnd.
- Vitamin D-tilskudd .... mnd.
- Andre vitamintilskudd .... mnd.
- Tran eller fiskeoljekapsler .... mnd.

Har du de siste 14 dager brukt følgende legemidler eller kosttilskudd?
*Sett ett kryss for **hvert** spørsmål*

	Ja	Nei
Legemidler		
Smertestillende medisin	☐	☐
Febersenkende medisin	☐	☐
Migrenemedisin	☐	☐
Eksemsalve	☐	☐
Hjertemedisin (ikke blodtrykksmedisin)	☐	☐
Kolesterolsenkende medisin	☐	☐
Sovemedisin	☐	☐
Beroligende medisin	☐	☐
Medisin mot depresjon	☐	☐
Annen nervemedisin	☐	☐
Syrenøytraliserende midler	☐	☐
Magesårmedisin	☐	☐
Insulin	☐	☐
Tabletter mot diabetes (sukkersyke)	☐	☐
Tabletter mot lavt stoffskifte (thyroxin)	☐	☐
Kortisontabletter	☐	☐
Annen medisin	☐	☐
Kosttilskudd		
Jerntabletter	☐	☐
Kalktabletter eller benmel	☐	☐
Vitamin D-tilskudd	☐	☐
Andre vitamintilskudd	☐	☐
Tran eller fiskeoljekapsler	☐	☐

VENNER

Hvor mange gode venner har du som du kan snakke fortrolig med og gi deg hjelp når du trenger det? .... gode venner
Tell ikke med de du bor sammen med men ta med andre slektninger!

Hvor mange av disse gode vennene har du kontakt med minst en gang i måneden? ....

	Ja	Nei
Føler du at du har nok gode venner?	☐	☐

Hvor ofte tar du vanligvis del i foreningsvirksomhet som f.eks. syklubb, idrettslag, politiske lag, religiøse eller andre foreninger?
- Aldri, eller noen få ganger i året ☐
- 1-2 ganger i måneden ☐
- Omtrent en gang i uken ☐
- Mer enn en gang i uken ☐

KOSTVANER

Hvis du bruker smør eller margarin på brødet, hvor mange skiver rekker en liten porsjonspakning vanligvis til? Vi tenker på slik porsjonspakning som du får på fly, på kafé o.l. (10-12 gram).

Den rekker til omtrent .... skiver

Hva slags fett blir vanligvis brukt til **matlaging** (ikke på brødet) i din husholdning?
- Meierismør ☐
- Hard margarin ☐
- Bløt (Soft) margarin ☐
- Smør/margarin blanding ☐
- Oljer ☐

Hva slags type brød (kjøpt eller hjemmebakt) spiser du vanligvis?
Sett ett eller to kryss!

	Loff	Fint brød	Kneip-brød	Grov-brød	Knekke-brød
Brødtypen ligner mest på:	☐	☐	☐	☐	☐

Hvor mye (i **antall** glass, kopper, poteter eller brødskiver) spiser eller drikker du vanligvis **daglig** av følgende matvarer?
*Kryss av for **alle** matvarene.*

	0	Færre enn 1	1-2	3-4	5-6	Mer enn 6
Helmelk (søt eller sur) (glass)	☐	☐	☐	☐	☐	☐
Lettmelk (søt eller sur) (glass)	☐	☐	☐	☐	☐	☐
Skummet melk (søt eller sur) (glass)	☐	☐	☐	☐	☐	☐
Te (kopper)	☐	☐	☐	☐	☐	☐
Appelsinjuice (glass)	☐	☐	☐	☐	☐	☐
Poteter	☐	☐	☐	☐	☐	☐
Brødskiver totalt (inkl. knekkebrød)	☐	☐	☐	☐	☐	☐
Brødskiver med						
– fiskepålegg (f.eks. makrell i tomat)	☐	☐	☐	☐	☐	☐
– magert kjøttpålegg (f.eks. skinke)	☐	☐	☐	☐	☐	☐
– fetere kjøttpålegg (f.eks. salami)	☐	☐	☐	☐	☐	☐
– gulost	☐	☐	☐	☐	☐	☐
– brunost	☐	☐	☐	☐	☐	☐
– kaviar	☐	☐	☐	☐	☐	☐
– syltetøy og annet søtt pålegg	☐	☐	☐	☐	☐	☐

Hvor mange **ganger i uka** spiser du vanligvis følgende matvarer?
*Kryss av for **alle** matvarene*

	Aldri	Færre enn 1	1	2-3	4-6	Omtrent daglig
Yoghurt	☐	☐	☐	☐	☐	☐
Kokt eller stekt egg	☐	☐	☐	☐	☐	☐
Frokostblanding/havregryn o.l.	☐	☐	☐	☐	☐	☐
Middag med						
– rent kjøtt	☐	☐	☐	☐	☐	☐
– pølser/kjøttpudding/-kaker	☐	☐	☐	☐	☐	☐
– fet fisk (f.eks. laks/sild)	☐	☐	☐	☐	☐	☐
– mager fisk (f.eks. torsk)	☐	☐	☐	☐	☐	☐
– fiskeboller/-pudding/-kaker	☐	☐	☐	☐	☐	☐
– grønnsaker	☐	☐	☐	☐	☐	☐
Majones, remulade o.l.	☐	☐	☐	☐	☐	☐
Gulrøtter	☐	☐	☐	☐	☐	☐
Blomkål/kål/brokkoli	☐	☐	☐	☐	☐	☐
Epler/pærer	☐	☐	☐	☐	☐	☐
Appelsiner, mandariner o.l.	☐	☐	☐	☐	☐	☐
Sukkerholdige leskedrikker	☐	☐	☐	☐	☐	☐
Sukkerfrie («Light») leskedrikker	☐	☐	☐	☐	☐	☐
Sjokolade	☐	☐	☐	☐	☐	☐
Vafler, kaker o.l.	☐	☐	☐	☐	☐	☐

ALKOHOL

Hvor ofte pleier du å drikke	øl?	vin?	brennevin?
Aldri, eller noen få ganger i året	☐	☐	☐
1-2 ganger i måneden	☐	☐	☐
Omtrent 1 gang i uken	☐	☐	☐
2-3 ganger i uken	☐	☐	☐
Omtrent hver dag	☐	☐	☐

Omtrent hvor ofte har du i løpet av siste år drukket alkohol tilsvarende minst 5 halvflasker øl, en helflaske vin eller 1/4 flaske brennevin?

- Ikke siste år ☐
- Noen få ganger ☐
- 1 - 2 ganger per måned ☐
- 1 - 2 ganger i uken ☐
- 3 eller flere ganger i uken ☐

I omtrent hvor mange år har ditt alkoholforbruk vært slik du har svart i spørsmålene over? ____ år

SLANKING

Omtrent hvor mange ganger har du bevisst prøvd å slanke deg? Sett 0 hvis ingen forsøk.

- før 20 år ______ ganger
- senere ______ ganger

Hvis du har slanket deg, omtrent hvor mange kilo har du på det meste gått ned i vekt?

- før 20 år ______ kg
- senere ______ kg

Hvilken vekt ville du være tilfreds med (din "trivselsvekt")? ______ kg

UFRIVILLIG URINLEKKASJE

Hvor ofte har du ufrivillig urinlekkasje?

- Aldri ☐
- Ikke mer enn en gang i måneden ☐
- To eller flere ganger i måneden ☐
- Ukentlig eller oftere ☐

Dine kommentarer:

BESVARES BARE AV KVINNER

MENSTRUASJON

Hvor gammel var du da du fikk menstruasjon første gang? ______ år

Hvis du ikke lenger har menstruasjon, hvor gammel var du da den sluttet? ______ år

Når du ser bort fra svangerskap og barselsperiode, har du noen gang vært blødningsfri i minst 6 måneder? Ja ☐ Nei ☐

Hvis "Ja", hvor mange ganger? ______ ganger

Hvis du fremdeles har menstruasjon eller er gravid: dag/mnd/år

Hvilken dato startet din siste menstruasjon? ____/____/____

Bruker du vanligvis smertestillende legemidler for å dempe menstruasjonsplager? Ja ☐ Nei ☐

SVANGERSKAP

Hvor mange barn har du født? ______ barn

Er du gravid nå? Ja ☐ Nei ☐ Usikker ☐

Har du i forbindelse med svangerskap hatt for høyt blodtrykk og/eller eggehvite (protein) i urinen? Ja ☐ Nei ☐

Hvis "Ja", i hvilket svangerskap?

	Svangerskap Første	Senere
For høyt blodtrykk	☐	☐
Eggehvite i urinen	☐	☐

Hvis du har født, fyll ut for hvert barn barnets fødselsår og omtrent antall måneder du ammet barnet.

Barn	Fødselsår	Antall måneder med amming
1	______	______
2	______	______
3	______	______
4	______	______
5	______	______
6	______	______

PREVENSJON OG ØSTROGEN

Bruker du, eller har du brukt:	Nå	Før	Aldri
P-pille (også minipille)	☐	☐	☐
Hormonspiral	☐	☐	☐
Østrogen (tabletter eller plaster)	☐	☐	☐
Østrogen (krem eller stikkpiller)	☐	☐	☐

Hvis du bruker p-pille, hormonspiral eller østrogen: hvilket merke bruker du nå?

Hvis du bruker eller har brukt p-pille:

- Alder da du begynte med P-piller? ______ år
- Hvor mange år har du tilsammen brukt P-piller? ______ år
- Dersom du har født: hvor mange år brukte du P-piller før første fødsel? ______ år
- Hvis du har sluttet å bruke P-piller: Alder da du sluttet? ______ år

Takk for hjelpen! Husk å postlegge skjemaet idag!

Helseundersøkelsen i Tromsø

Appendix III

**Second questionnaire for subjects aged > 70 years,
Tromsø IV, 1994-95**

Helseundersøkelsen i Tromsø

for dem som er 70 år og eldre.

Hovedformålet med Tromsøundersøkelsene er å skaffe ny kunnskap om hjerte-karsykdommer for å kunne forebygge dem. De skal også øke kunnskapen om kreftsykdommer og alminnelige plager som f.eks. allergier, smerter i muskulatur og nervøse lidelser. Endelig skal de gi kunnskap om hvorledes den eldste delen av befolkningen har det. Vi ber deg derfor svare på spørsmålene nedenfor.

Skjemaet er en del av Helseundersøkelsen som er godkjent av Datatilsynet og av Regional komite for medisinsk forskningsetikk. Svarene brukes bare til forskning og behandles strengt fortrolig. Opplysningene kan senere bli sammenholdt med informasjon fra andre offentlige helseregistre etter de regler som Datatilsynet og Regional komite for medisinsk forskningsetikk gir.

Hvis du er i tvil om hva du skal svare, sett kryss i den ruten som du synes passer best.

Det utfylte skjema sendes i vedlagte svarkonvolutt. Portoen er betalt.

På forhånd takk for hjelpen!

Med vennlig hilsen

Fagområdet medisin
Universitetet i Tromsø — Statens helseundersøkelser

Hvis du ikke ønsker å besvare spørreskjemaet, sett kryss i ruten under og returner skjemaet. Da slipper du purring.

Jeg ønsker ikke å besvare spørreskjemaet ❑

Dato for utfylling av skjema: Dag ..../ Mnd ..../ År ....

OPPVEKST

I hvilken kommune bodde du da du fylte 1 år?

....

Hvis du ikke bodde i Norge, oppgi land i stedet for kommune.

Hvordan var de økonomiske forhold i familien under din oppvekst?

- Meget gode ❑ 1
- Gode ❑ 2
- Vanskelige ❑ 3
- Meget vanskelige ❑ 4

Hvor gamle ble dine foreldre?

- Mor ble ______ år
- Far ble ______ år

BOLIG

Hvem bor du sammen med?

Sett ett kryss for hvert spørsmål og angi antall.

	Ja	Nei	Antall
Ektefelle/samboer	❑	❑	
Andre personer over 18 år	❑	❑	______
Personer under 18 år	❑	❑	______

Hvilken type bolig bor du i?

- Enebolig/villa ❑ 1
- Gårdsbruk ❑ 2
- Blokk/terrasseleilighet ❑ 3
- Rekkehus/2-4 mannsbolig ❑ 4
- Annen bolig ❑ 5

Hvor lenge har du bodd i boligen du bor i nå? ______ år

	Ja	Nei
Er boligen tilpasset til dine behov?	❑	❑
Hvis "Nei", er det problemer med:		
Plassen i boligen	❑	❑
Ujevn, for høy eller for lav temperatur	❑	❑
Trapper	❑	❑
Toalett	❑	❑
Bad/dusj	❑	❑
Vedlikehold	❑	❑
Annet (spesifiser)	❑	❑
Ønsker du å flytte til en eldrebolig?	❑	❑

TIDLIGERE ARBEID OG ØKONOMI

Hvordan vil du beskrive det arbeidet du hadde de siste 5-10 årene før du ble pensjonist?

- For det meste stillesittende arbeid? ❑ 1
  (f.eks. skrivebordsarbeid, montering)
- Arbeid som krever at du går mye? ❑ 2
  (f.eks. ekspeditørarbeid, husmor, undervisning)
- Arbeid hvor du går og løfter mye? ❑ 3
  (f.eks. postbud, pleier, bygningsarbeid)
- Tungt kroppsarbeid? ❑ 4
  (f.eks. skogsarb., tungt jordbruksarb., tungt bygn.arb.)

Har du hatt noen av følgende yrker (heltid eller deltid)?

Sett ett kryss for hvert spørsmål.

	Ja	Nei
Sjåfør	❑	❑
Bonde/gårdbruker	❑	❑
Fisker	❑	❑

Hvor gammel var du da du ble pensjonert? ______ år

Hva slags pensjon har du?

- Minstepensjon ❑
- Tilleggspensjon ❑

Hvordan er din økonomi nå?

- Meget god ❑ 1
- God ❑ 2
- Vanskelig ❑ 3
- Meget vanskelig ❑ 4

HELSE OG SYKDOM

Er helsen din blitt forandret det siste året?

- Ja, dårligere ☐ 1
- Nei, uforandret ☐ 2
- Ja, bedre ☐ 3

Hvordan synes du at helsen din er nå i forhold til andre på samme alder?

- Mye dårligere ☐ 1
- Litt dårligere ☐ 2
- Omtrent lik ☐ 3
- Litt bedre ☐ 4
- Mye bedre ☐ 5

EGNE SYKDOMMER

Har du noen gang hatt:
Sett ett kryss for hvert spørsmål. Oppgi alderen ved hendelsen.
Hvis det har skjedd flere ganger, hvor gammel var du siste gang?

	Ja	Nei	Alder
Lårhalsbrudd	☐	☐	______
Brudd ved håndledd/underarm	☐	☐	______
Nakkesleng (whiplash)	☐	☐	______
Skade som førte til sykehusinnleggelse	☐	☐	______
Sår på magesekken	☐	☐	______
Sår på tolvfingertarmen	☐	☐	______
Magesår-operasjon	☐	☐	______
Operasjon på halsen	☐	☐	______

Har du eller har du hatt:
Sett ett kryss for hvert spørsmål.

	Ja	Nei
Kreftsykdom	☐	☐
Epilepsi (fallesyke)	☐	☐
Migrene	☐	☐
Parkinsons sykdom	☐	☐
Kronisk bronkitt	☐	☐
Psoriasis	☐	☐
Benskjørhet (osteoporose)	☐	☐
Fibromyalgi/fibrositt/kronisk smertesyndrom	☐	☐
Psykiske plager som du har søkt hjelp for	☐	☐
Stoffskiftesykdom (skjoldbruskkjertel)	☐	☐
Sykdom i leveren	☐	☐
Gjentatt, ufrivillig urinlekkasje	☐	☐
Grønn stær	☐	☐
Grå stær	☐	☐
Slitasjegikt (artrose)	☐	☐
Leddgikt	☐	☐
Nyrestein	☐	☐
Blindtarmsoperasjon	☐	☐
Allergi og overfølsomhet		
Atopisk eksem (f.eks. barneeksem)	☐	☐
Håndeksem	☐	☐
Høysnue	☐	☐
Matvareallergi	☐	☐
Annen overfølsomhet (ikke allergi)	☐	☐

Hvor mange ganger har du hatt forkjølelse, influensa, "ræksjuka" og lignende siste halvår? ______ ganger

	Ja	Nei
Har du hatt dette de siste 14 dager?	☐	☐

SYKDOM I FAMILIEN

Kryss av for de slektningene som har eller har hatt noen av sykdommene:
Kryss av for "Ingen" hvis ingen av slektningene har hatt sykdommen.

	Mor	Far	Bror	Søster	Barn	Ingen
Hjerneslag eller hjerneblødning	☐	☐	☐	☐	☐	☐
Hjerteinfarkt før 60 års alder	☐	☐	☐	☐	☐	☐
Kreftsykdom	☐	☐	☐	☐	☐	☐
Høyt blodtrykk	☐	☐	☐	☐	☐	☐
Astma	☐	☐	☐	☐	☐	☐
Benskjørhet (osteoporose)	☐	☐	☐	☐	☐	☐
Slitasjegikt (artrose)	☐	☐	☐	☐	☐	☐
Psykiske plager	☐	☐	☐	☐	☐	☐
Alderdomssløvhet	☐	☐	☐	☐	☐	☐
Diabetes (sukkersyke)	☐	☐	☐	☐	☐	☐
– alder da de fikk diabetes	___	___	___	___	___	

SYMPTOMER

	Ja	Nei
Hoster du omtrent daglig i perioder av året?	☐	☐
Hvis "Ja":		
Er hosten vanligvis ledsaget av oppspytt?	☐	☐
Har du hatt slik hoste så lenge som i en 3 måneders periode i begge de to siste år?	☐	☐
Har du hatt episoder med piping i brystet?	☐	☐
Hvis "Ja", har dette oppstått: *Sett ett kryss for hvert spørsmål.*		
Om natten	☐	☐
Ved luftveisinfeksjoner	☐	☐
Ved fysiske anstrengelser	☐	☐
Ved sterk kulde	☐	☐
Har du merket anfall med plutselig endring i pulsen eller hjerterytmen siste år?	☐	☐
Har du gått ned i vekt siste året?	☐	☐

Hvis "Ja":
Hvor mange kilo? ________ kg

Hvor ofte er du plaget av søvnløshet?

- Aldri, eller noen få ganger i året ☐ 1
- 1-2 ganger i måneden ☐ 2
- Omtrent en gang i uken ☐ 3
- Mer enn en gang i uken ☐ 4

Hvis du er plaget av søvnløshet i perioder, når på året er du mest plaget?

- Ingen spesiell tid ☐ 1
- Særlig i mørketiden ☐ 2
- Særlig i midnattsoltiden ☐ 3
- Særlig vår og høst ☐ 4

	Ja	Nei
Pleier du å ta en lur på dagen?	☐	☐
Føler du at du vanligvis får nok søvn?	☐	☐

Er du plaget av:	Nei	Litt	I stor grad
Svimmelhet	☐	☐	☐
Dårlig hukommelse	☐	☐	☐
Kraftløshet	☐	☐	☐
Forstoppelse	☐	☐	☐

Hender det at tanken på å få alvorlig sykdom bekymrer deg?

- Ikke i det hele tatt ☐
- Bare i liten grad ☐
- En del ☐
- Ganske mye ☐

LEGEMLIGE FUNKSJONER

Klarer du selv disse gjøremålene i det daglige uten hjelp fra andre?

	Ja	Med noe hjelp	Nei
Gå innendørs i samme etasje	☐	☐	☐
Gå i trapper	☐	☐	☐
Gå utendørs	☐	☐	☐
Gå ca. 500 meter	☐	☐	☐
Gå på toalettet	☐	☐	☐
Vaske deg på kroppen	☐	☐	☐
Bade eller dusje	☐	☐	☐
Kle på og av deg	☐	☐	☐
Legge deg og stå opp	☐	☐	☐
Spise selv	☐	☐	☐
Lage varm mat	☐	☐	☐
Gjøre lett husarbeid (f.eks. oppvask)	☐	☐	☐
Gjøre tyngre husarbeid (f.eks. gulvvask)	☐	☐	☐
Gjøre innkjøp	☐	☐	☐
Ta bussen	☐	☐	☐

	Ja	Vanskelig	Nei
Kan du høre vanlig tale (evt. med høreapparat)?	☐	☐	☐
Kan du lese (evt. med briller)?	☐	☐	☐

Er du avhengig av noen av disse hjelpemidlene?

	Ja	Nei
Stokk	☐	☐
Krykke	☐	☐
Gåstol (rullator)	☐	☐
Rullestol	☐	☐
Høreapparat	☐	☐
Trygghetsalarm	☐	☐

BRUK AV HELSEVESENET

Hvor mange ganger har du siste året, på grunn av egen helse eller sykdom, vært:
Sett 0 hvis du ikke har hatt slik kontakt.

	Antall ganger siste år
Hos vanlig lege/legevakt	______
Hos psykolog eller psykiater	______
Hos annen legespesialist utenfor sykehus	______
På poliklinikk	______
Innlagt i sykehus	______
Hos fysioterapeut	______
Hos kiropraktor	______
Hos akupunktør	______
Hos tannlege	______
Hos fotterapeut	______
Hos naturmedisiner (homøopat, soneterapeut o.l.)	______
Hos håndspålegger, synsk eller "leser"	______

Har du hjemmehjelp?

	Ja	Nei
Privat	☐	☐
Kommunal	☐	☐

Har du hjemmesykepleie? ☐ ☐

Er du fornøyd med helse- og hjemmetjenesten i kommunen?

	Ja	Nei	Vet ikke
Prinsippet med fast lege	☐	☐	☐
Hjemmesykepleien	☐	☐	☐
Hjemmehjelpen	☐	☐	☐

Er du trygg på at du kan få hjelp av helse- og hjemmetjenesten hvis du trenger det?

- Trygg ☐ 1
- Ikke trygg ☐ 2
- Svært utrygg ☐ 3
- Vet ikke ☐ 4

LEGEMIDLER OG KOSTTILSKUDD

Har du det siste året periodevis brukt noen av de følgende midler daglig eller nesten daglig?
Angi hvor mange måneder du brukte dem.
Sett 0 hvis du ikke har brukt midlene.

Legemidler

- Smertestillende ______ mnd.
- Sovemedisin ______ mnd.
- Beroligende midler ______ mnd.
- Medisin mot depresjon ______ mnd.
- Allergimedisin ______ mnd.
- Astmamedisin ______ mnd.
- Hjertemedisin (ikke blodtrykksmedisin) ______ mnd.
- Insulin ______ mnd.
- Tabletter mot diabetes (sukkersyke) ______ mnd.
- Tabletter mot lavt stoffskifte (thyroxin) ______ mnd.
- Kortisontabletter ______ mnd.
- Midler mot forstoppelse ______ mnd.

Kosttilskudd

- Jerntabletter ______ mnd.
- Vitamin D-tilskudd ______ mnd.
- Andre vitamintilskudd ______ mnd.
- Kalktabletter eller benmel ______ mnd.
- Tran eller fiskeoljekapsler ______ mnd.

FAMILIE OG VENNER

	Ja	Nei
Har du nær familie som kan gi deg hjelp og støtte når du trenger det?	☐	☐

Hvis "Ja": Hvem kan gi deg hjelp?

- Ektefelle/samboer ☐
- Barn ☐
- Andre ☐

Hvor mange gode venner har du som du kan snakke fortrolig med og gi deg hjelp når du trenger det? ______ gode venner
Tell ikke med dem du bor sammen med, men ta med andre slektninger!

	Ja	Nei
Føler du at du har nok gode venner?	☐	☐

Føler du at du hører med i et fellesskap (gruppe av mennesker) som stoler på hverandre og føler forpliktelse overfor hverandre (f.eks. i politisk parti, religiøs gruppe, slekt, naboskap, arbeidsplass eller organisasjon)?

- Sterk tilhørighet ☐ 1
- Noe tilhørighet ☐ 2
- Usikkert ☐ 3
- Liten eller ingen tilhørighet ☐ 4

Hvor ofte tar du vanligvis del i foreningsvirksomhet som f.eks. syklubb, idrettslag, politiske lag, religiøse eller andre foreninger?

- Aldri, eller noen få ganger i året ☐ 1
- 1-2 ganger i måneden ☐ 2
- Omtrent en gang i uken ☐ 3
- Mer enn en gang i uken ☐ 4

KOSTVANER

	Antall
Hvor mange måltider spiser du vanligvis daglig (middag og brødmåltid)?	______
Hvor mange ganger i uken spiser du varm middag?	______

Hva slags type brød (kjøpt eller hjemmebakt) spiser du vanligvis?

Sett ett eller to kryss.

	Loff	Fint brød	Kneip-brød	Grov-brød	Knekke-brød
Brødtypen ligner mest på:	☐	☐	☐	☐	☐

Hva slags fett blir til vanligvis brukt til *matlaging* (ikke på brødet) i din husholdning?

- Meierismør ☐
- Hard margarin ☐
- Bløt (Soft) margarin ☐
- Smør/margarin blanding ☐
- Oljer ☐

Hvor mye (i antall glass, poteter eller brødskiver) spiser/drikker du vanligvis daglig av følgende matvarer?

Kryss av for alle matvarene.

	Ingen	Mindre enn 1	1-2	3 og mer
Melk alle sorter (glass)	☐	☐	☐	☐
Appelsinjuice (glass)	☐	☐	☐	☐
Poteter	☐	☐	☐	☐
Brødskiver totalt (inkl. knekkebrød)	☐	☐	☐	☐
Brødskiver med				
– fiskepålegg (f.eks. makrell i tomat)	☐	☐	☐	☐
– gulost	☐	☐	☐	☐
– kaviar	☐	☐	☐	☐
	1	2	3	4

Hvor mange ganger i uka spiser du vanligvis følgende matvarer?

Kryss av for alle matvarene.

	Aldri	Sjeldnere enn 1	1	2 og mer
Yoghurt	☐	☐	☐	☐
Kokt eller stekt egg	☐	☐	☐	☐
Frokostblanding/havregryn o.l.	☐	☐	☐	☐
Middag med				
– rent kjøtt	☐	☐	☐	☐
– feit fisk (f.eks. laks/uer)	☐	☐	☐	☐
– mager fisk (f.eks. torsk)	☐	☐	☐	☐
– grønnsaker (rå eller kokte)	☐	☐	☐	☐
Gulrøtter (rå eller kokte)	☐	☐	☐	☐
Blomkål/kål/brokkoli	☐	☐	☐	☐
Epler/pærer	☐	☐	☐	☐
Appelsiner, mandariner o.l.	☐	☐	☐	☐
	1	2	3	4

TRIVSEL

Hvordan trives du med å bli gammel - alt i alt?

- Godt ☐ 1
- Ganske bra ☐ 2
- Opp og ned ☐ 3
- Dårlig ☐ 4

Hvordan ser du på livet fremover?

- Lyst ☐ 1
- Ikke så verst ☐ 2
- Noksa bekymret ☐ 3
- Mørkt ☐ 4

BESVARES BARE AV KVINNER

MENSTRUASJON

Hvor gammel var du da du fikk menstruasjon første gang? ______ år

Hvor gammel var du da menstruasjonen sluttet? ______ år

SVANGERSKAP

Hvor mange barn har du født? ______ barn

Hvis du har født, fyll ut for hvert barn barnets fødselsår og omtrent antall måneder du ammet barnet.

Hvis du har født mer enn 6 barn, noter fødselsår og antall måneder med amming for dem nederst på siden.

Barn:	Fødselsår:	Antall måneder med amming:
1	______	______
2	______	______
3	______	______
4	______	______
5	______	______
6	______	______

	Ja	Nei
Har du i forbindelse med svangerskap hatt for høyt blodtrykk og/eller eggehvite (protein) i urinen?	☐	☐

Hvis "Ja", i hvilket svangerskap?

	Svangerskap Første	Senere
For høyt blodtrykk	☐	☐
Eggehvite i urinen	☐	☐

ØSTROGEN-MEDISIN

Bruker du, eller har du brukt, østrogen-medisin?

	Nå	Før	Aldri
Tabletter eller plaster	☐	☐	☐
Krem eller stikkpiller	☐	☐	☐

Hvis du bruker østrogen, hvilket merke bruker du nå?

....

Dine kommentarer:

Takk for hjelpen! Husk å postlegge skjemaet idag!

Helseundersøkelsen i Tromsø

Appendix IV

First questionnaire, Tromsø V, 2001

Helse-
undersøkelsen

Personlig innbydelse

1. EGEN HELSE

1.1 Hvordan er helsen din nå? *(Sett bare ett kryss)*

Dårlig	Ikke helt god	God	Svært god
☐ 1	☐ 2	☐ 3	☐ 4

1.2 Har du, eller har du hatt?:

	JA	NEI	Alder første gang
Astma	☐	☐	
Høysnue	☐	☐	
Kronisk bronkitt/emfysem	☐	☐	
Diabetes (sukkersyke)	☐	☐	
Benskjørhet (osteoporose)	☐	☐	
Fibromyalgi/kronisk smertesyndrom	☐	☐	
Psykiske plager som du har søkt hjelp for	☐	☐	
Hjerteinfarkt	☐	☐	
Angina pectoris (hjertekrampe)	☐	☐	
Hjerneslag/hjerneblødning	☐	☐	

1.3 Har du merket anfall med plutselig endring i pulsen eller hjerterytmen siste året? JA ☐ NEI ☐

1.4 Får du smerter eller ubehag i brystet når du:

Går i bakker, trapper eller fort på flat mark? JA ☐ NEI ☐

1.5 Hvis du får slike smerter, pleier du da å:

Stoppe?	Saktne farten?	Fortsette i samme takt?
☐ 1	☐ 2	☐ 3

1.6 Dersom du stopper, forsvinner smertene da etter mindre enn 10 minutter? JA ☐ NEI ☐

1.7 Kan slike smerter opptre selv om du er i ro? JA ☐ NEI ☐

2. MUSKEL OG SKJELETTPLAGER

2.1 Har du vært plaget med smerter og/eller stivhet i muskler og ledd i løpet av de siste 4 ukene?
(Varighet angis bare hvis du har hatt plager)

	Ikke plaget	En del plaget	Sterkt plaget	Varighet: Inntil 2 uker	Varighet: 2 uker eller mer
Nakke/skuldre	☐	☐	☐	☐	☐
Armer, hender	☐	☐	☐	☐	☐
Øvre del av ryggen	☐	☐	☐	☐	☐
Korsryggen	☐	☐	☐	☐	☐
Hofter, ben, føtter	☐	☐	☐	☐	☐
Andre steder	☐	☐	☐	☐	☐
	1	2	3	1	2

2.2 Har du noen gang hatt:

	JA	NEI	Alder siste gang
Brudd i håndledd/underarm?	☐	☐	
Lårhalsbrudd?	☐	☐	

3. ANDRE PLAGER

3.1 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 mye	Veldig mye
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, tungsindig	☐	☐	☐	☐
Følelse av å være unyttig, lite verd	☐	☐	☐	☐
Følelse av at alt er et slit	☐	☐	☐	☐
Følelse av håpløshet mht. framtida	☐	☐	☐	☐
	1	2	3	4

4. BRUK AV HELSETJENESTER

4.1 Hvor mange ganger de siste 12 månedene har du selv brukt:
(Sett ett kryss for hver linje)

	Ingen	1-3 ganger	4 eller flere
Allmennpraktiserende lege	☐	☐	☐
Bedriftslege	☐	☐	☐
Psykolog eller psykiater *(privat eller på poliklinikk)*	☐	☐	☐
Annen spesialist *(privat eller på poliklinikk)*	☐	☐	☐
Legevakt *(privat eller offentlig)*	☐	☐	☐
Sykehusinnleggelse	☐	☐	☐
Hjemmesykepleie	☐	☐	☐
Fysioterapeut	☐	☐	☐
Kiropraktor	☐	☐	☐
Tannlege	☐	☐	☐
Alternativ behandler	☐	☐	☐

5. OPPVEKST OG TILHØRIGHET

5.1 Hvor lenge har du samlet bodd i fylket?
(Sett 0 hvis mindre enn et halvt år)

5.2 Hvor lenge har du samlet bodd i kommunen?
(Sett 0 hvis mindre enn et halvt år)

5.3 Hvor bodde du det meste av tiden før du fylte 16 år?
(kryss av for ett alternativ og spesifiser)

Samme kommune ☐ 1

Annen kommune i fylket ☐ 2 Hvilken: ____________

Annet fylke i Norge ☐ 3 Hvilket: ____________

Utenfor Norge ☐ 4 Land: ____________

5.4 Har du flyttet i løpet av de siste fem årene?

Nei	Ja, en gang	Ja, flere ganger
☐ 1	☐ 2	☐ 3

6. VEKT

6.1 Anslå din vekt da du var 25 år gammel: hele kg

7. MAT OG DRIKKE

7.1 Hvor ofte spiser du vanligvis disse matvarene? *(Sett ett kryss pr. linje)*

	Sjelden /aldri	1-3 g. pr.mnd	1-3 g. pr.uke	4-6 g. pr.uke	1-2 g. pr.dag	3 g. el. mer pr.dag
Frukt, bær	☐	☐	☐	☐	☐	☐
Ost *(alle typer)*	☐	☐	☐	☐	☐	☐
Poteter	☐	☐	☐	☐	☐	☐
Kokte grønnsaker	☐	☐	☐	☐	☐	☐
Rå grønnsaker/salat	☐	☐	☐	☐	☐	☐
Fet fisk *(f.eks. laks, ørret, makrell, sild)*	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

7.2 Hva slags fett bruker du oftest? *(Sett ett kryss pr. linje)*

	Bruker ikke	Meierismør	Hard margarin	Myk/lett margarin	Oljer	Annet
På brødet	☐	☐	☐	☐	☐	☐
I matlagingen	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

7.3 Bruker du følgende kosttilskudd:

	Ja, daglig	Iblant	Nei
Tran, trankapsler, fiskeoljekapsler?	☐	☐	☐
Vitamin- og/eller mineraltilskudd?	☐	☐	☐

7.4 Hvor mye drikker du vanligvis av følgende? *(Sett ett kryss pr. linje)*

	Sjelden /aldri	1-6 glass pr.uke	1 glass pr.dag	2-3 glass pr.dag	4 glass el. mer pr.dag
Helmelk, kefir, yoghurt	☐	☐	☐	☐	☐
Lettmelk, cultura, lettyoghurt	☐	☐	☐	☐	☐
Skummet melk (sur/søt)	☐	☐	☐	☐	☐
Ekstra lettmelk	☐	☐	☐	☐	☐
Fruktjuice	☐	☐	☐	☐	☐
Vann	☐	☐	☐	☐	☐
Farris, Ramlosa e.l.	☐	☐	☐	☐	☐
Cola-holdig leskedrikk	☐	☐	☐	☐	☐
Annen brus/leskedrikk	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

7.5 Drikker du vanligvis brus/cola: Med sukker ☐ 1 Uten sukker ☐ 2

7.6 Hvor mange kopper kaffe og te drikker du daglig? *Antall kopper*
(Sett 0 for de typene du ikke drikker daglig)

Filterkaffe ....

Kokekaffe/trykkanne ....

Annen kaffe ....

Te ....

7.7 Omtrent hvor ofte har du i løpet av det siste året drukket alkohol? *(Lettøl og alkoholfritt øl regnes ikke med)*

Har aldri drukket alkohol ☐ 1 Har ikke drukket alkohol siste år ☐ 2 Noen få ganger siste år ☐ 3 Omtrent 1 gang i måneden ☐ 4

2-3 ganger pr. måned ☐ 5 ca. 1 gang i uka ☐ 6 2-3 ganger i uka ☐ 7 4-7 ganger i uka ☐ 8

Til dem som har drukket siste år:

7.8 Når du har drukket alkohol, hvor mange glass eller drinker har du vanligvis drukket? *Antall*

7.9 Omtrent hvor mange ganger i løpet av det siste året har du drukket så mye som minst 5 glass eller drinker i løpet av ett døgn? *Antall ganger*

7.10 Når du drikker, drikker du da vanligvis: *(Sett ett eller flere kryss)*

Øl ☐ Vin ☐ Brennevin ☐

8. RØYKING

8.1 Hvor lenge er du vanligvis daglig tilstede i røykfylt rom? *Antall hele timer*

	JA	NEI
8.2 Røykte noen av de voksne hjemme da du vokste opp?	☐	☐
8.3 Bor du, eller har du bodd, sammen med noen dagligrøykere etter at du fylte 20 år?	☐	☐

8.4 Har du røykt/røyker du daglig? Ja, nå ☐ Ja, tidligere ☐ Aldri ☐
Hvis ALDRI: Hopp til spørsmål 9 (UTDANNING OG ARBEID)

8.5 Hvis du røyker daglig nå, røyker du:

	JA	NEI
Sigaretter?	☐	☐
Sigarer/sigarillos?	☐	☐
Pipe?	☐	☐

8.6 Hvis du har røykt daglig tidligere, hvor lenge er det siden du sluttet? *Antall år*

8.7 Hvis du røyker daglig nå eller har røykt tidligere:

Hvor mange sigaretter røyker eller røykte du vanligvis daglig? *Antall sigaretter*

Hvor gammel var du da du begynte å røyke daglig? *Alder i år*

Hvor mange år til sammen har du røykt daglig? *Antall år*

9. UTDANNING OG ARBEID

9.1 Hvor mange års skolegang har du gjennomført? *Antall år*
(Ta med alle år du har gått på skole eller studert)

9.2 Er du i inntektsgivende arbeid?

Ja, full tid ☐ 1 Ja, deltid ☐ 2 Nei ☐ 3

9.3 Beskriv virksomheten på det arbeidsstedet (avdelingen) der du utførte inntektsgivende arbeid i lengst tid de siste 12 mnd. *(F.eks. regnskapsbyrå, ungdomsskole, barneavd. på sykehus, snekkerverksted, bilverksted, bank, dagligvarehandel e.l.)*

Virksomhet: ____________
Hvis pensjonert, skriv tidligere hovedvirksomhet og yrke. Gjelder også 9.4

9.4 Hvilket yrke/tittel har eller hadde du på dette arbeidsstedet? *(F.eks. sekretær, lærer, industriarbeider, barnepleier, møbelsnekker, avdelingsleder, selger, sjåfør e.l.)*

Yrke: ____________

9.5 Arbeider du i ditt hovedyrke som selvstendig, som ansatt eller som familiemedlem uten fast avtalt lønn?

Selvstendig ☐ Ansatt ☐ Familiemedlem ☐

	JA	NEI
9.6 Mener du at du står i fare for å miste ditt nåværende arbeid eller inntekt de nærmeste 2 årene?	☐	☐

9.7 Mottar du noen av følgende ytelser?

	JA	NEI
Sykepenger (er sykmeldt)	☐	☐
Alderstrygd, førtidspensjon (AFP) eller etterlattepensjon	☐	☐
Rehabiliterings-/attføringspenger	☐	☐
Uførepensjon (hel eller delvis)	☐	☐
Dagpenger under arbeidsledighet	☐	☐
Sosialhjelp/-stønad	☐	☐
Overgangsstønad for enslige forsørgere	☐	☐

10. MOSJON OG FYSISK AKTIVITET

10.1 Hvordan har din fysiske aktivitet i fritiden vært det siste året?
Tenk deg et ukentlig gjennomsnitt for året. Arbeidsvei regnes som fritid. Besvar begge spørsmålene.

	Timer pr. uke			
	Ingen	Under 1	1-2	3 og mer
Lett aktivitet (*Ikke svett/andpusten*)............	☐	☐	☐	☐
Hard fysisk aktivitet (*Svett/andpusten*)..................	☐	☐	☐	☐
	1	2	3	4

10.2 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 stillesittende beskjeftigelse?.. ☐ 1

Spaserer, sykler eller beveger deg på annen måte minst 4 timer i uka?.. ☐ 2
(Her skal du også regne med gang eller sykling til arbeidsstedet, søndagsturer m.m.)

Driver mosjonsidrett, tyngre hagearbeid e.l.? .... ☐ 3
(Merk at aktiviteten skal vare minst 4 timer i uka)

Trener hardt eller driver konkurranseidrett regelmessig og flere ganger i uka?.................................... ☐ 4

11. FAMILIE OG VENNER

11.1 Bor du sammen med: JA NEI
Ektefelle/samboer? .... ☐ ☐

11.2 Hvor mange gode venner har du? *Antall venner*
Regn med de du kan snakke fortrolig med og som kan gi deg hjelp dersom du trenger det. Tell ikke med de du bor sammen med, men ta med andre slektninger.

11.3 Hvor stor interesse viser folk for det du gjør?
(Sett bare ett kryss)

Stor interesse	Noe interesse	Litt interesse	Ingen interesse	Usikkert
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

11.4 Hvor mange foreninger, lag, grupper, kirkesamfunn e.l. deltar du i på fritiden? *Antall*
(Skriv 0 hvis ingen)

11.5 Føler du at du kan påvirke det som skjer i lokalsamfunnet der du bor? *(Sett bare ett kryss)*

Ja, i stor grad	Ja, en del	Ja, i liten grad	Nei	Har ikke forsøkt
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

12. SYKDOM I FAMILIEN

12.1 Har en eller flere av dine foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)? .... JA ☐ NEI ☐ VET IKKE ☐

12.2 Kryss av for de slektningene som har eller har hatt noen av sykdommene: *(Sett kryss for hver linje)*

	Mor	Far	Bror	Søster	Barn	Ingen av disse
Hjerneslag eller hjerneblødning............	☐	☐	☐	☐	☐	☐
Hjerteinfarkt før 60 års alder..........................	☐	☐	☐	☐	☐	☐
Astma.........................	☐	☐	☐	☐	☐	☐
Kreftsykdom...............	☐	☐	☐	☐	☐	☐
Diabetes (sukkersyke).	☐	☐	☐	☐	☐	☐

12.3 Hvis noen slektninger har diabetes, i hvilken alder fikk de diabetes (hvis for eks. flere søsken, før opp den som fikk det tidligst i livet):

Vet ikke, ikke aktuelt	Mors alder	Fars alder	Brors alder	Søsters alder	Barns alder
☐					

13. BRUK AV MEDISINER

Med medisiner mener vi her medisiner kjøpt på apotek. Kosttilskudd og vitaminer regnes ikke med her.

13.1 Bruker du?

	Nå	Før, men ikke nå	Aldri brukt
Medisin mot høyt blodtrykk	☐	☐	☐
Kolesterolsenkende medisin	☐	☐	☐

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

	Ikke brukt siste 4 uker	Sjeldnere enn hver uke	Hver uke, men ikke daglig	Daglig
Smertestillende uten resept	☐	☐	☐	☐
Smertestillende på resept.........	☐	☐	☐	☐
Sovemedisin	☐	☐	☐	☐
Beroligende medisin	☐	☐	☐	☐
Medisin mot depresjon	☐	☐	☐	☐
Annen medisin på resept..........	☐	☐	☐	☐
	1	2	3	4

13.3 For de medisinene som du har krysset av for i pkt. 13.1 og 13.2 og som du har brukt i løpet av de siste 4 ukene:
Angi navnet og hvilken grunn det er til at du tar/har tatt disse (sykdom eller symptom):
(Kryss av for hvor lenge du har brukt medisinen)

Navn på medisinen: (*ett navn pr. linje*):	Grunn til bruk av medisinen:	Hvor lenge har du brukt medisinen? Inntil 1 år	Ett år eller mer
		☐	☐
		☐	☐
		☐	☐
		☐	☐
		☐	☐
		☐	☐
		☐	☐

Dersom det ikke er nok plass her, kan du fortsette på eget ark som du legger ved.

14. RESTEN AV SKJEMAET SKAL BARE BESVARES AV KVINNER

14.1 Hvor gammel var du da du fikk menstruasjon aller første gang? *Alder i år*

14.2 Hvis du ikke lenger får menstruasjon, hvor gammel var du da den sluttet? *Alder i år*

14.3 Er du gravid nå?

Ja	Nei	Usikker	Over fruktbar alder
☐ 1	☐ 2	☐ 3	☐ 4

14.4 Hvor mange barn har du født? *Antall barn*

14.5 Bruker du, eller har du brukt?
(Sett ett kryss for hver linje)

	Nå	Før, men ikke nå	Aldri
P-pille/minipille/p-sprøyte...........	☐	☐	☐
Hormonspiral (*ikke vanlig spiral*)	☐	☐	☐
Østrogen (*tabletter eller plaster*)	☐	☐	☐
Østrogen (*krem eller stikkpiller*)	☐	☐	☐

14.6 Hvis du bruker/har brukt reseptpliktig østrogen:
Hvor lenge har du brukt dette? *Antall år*

14.7 Hvis du bruker p-pille, minipille, p-sprøyte, hormonspiral eller østrogen; hvilket merke bruker du?

Appendix V

Second questionnaire for subjects aged < 70 years, Tromsø V, 2001

Tilleggsspørsmål til helseundersøkelsen i Troms og Finnmark 2001-2002

Hovedformålet med Helseundersøkelsen er å skaffe ny kunnskap om hjerte-karsykdommer for å kunne forebygge dem. I tillegg skal undersøkelsen øke kunnskapen om kreftsykdommer og plager som f.eks allergier, smerter i muskulatur og nervøse lidelser. Vi ber deg derfor svare på noen spørsmål om forhold som kan ha betydning for risikoen for disse og andre sykdommer.
Skjemaet er en del av Helseundersøkelsen som er godkjent av Datatilsynet og forelagt Regional komité for medisinsk forskningsetikk. Svarene brukes bare til forskning og behandles strengt fortrolig.

Opplysningene kan senere bli sammenholdt med informasjon fra andre offentlige helseregistre etter de regler som Datatilsynet og Regional komité for medisinsk forskningsetikk gir.

Hvis du er i tvil om hva du skal svare, sett kryss i den ruten du synes passer best.

Det utfylte skjemaet sendes i vedlagte svarkonvolutt. Portoen er betalt. På forhånd takk for hjelpen!

Med vennlig hilsen
Institutt for samfunnsmedisin Statens helseundersøkelser
Universitetet i Tromsø

Hvis du ikke ønsker å besvare dette spørreskjemaet, sett kryss i ruten under og returner skjemaet. Da slipper du å bli purret på!

Jeg ønsker ikke å besvare spørreskjemaet ☐

Dato for utfylling:
Dag Måned År

T1. LOKALMILJØ OG BOLIG

1.1 I hvilken kommune bodde du da du fylte 1 år?
(Hvis du ikke bodde i Norge, oppgi hvilket land i stedet for kommune)

____

1.2 Hvilken type bolig bor du i? *(Sett bare ett kryss)*

- Enebolig/villa ☐ 1
- Gårdsbruk ☐ 2
- Blokk/terrasseleilighet ☐ 3
- Rekkehus/2-4 mannsbolig ☐ 4
- Institusjon/omsorgsbolig ☐ 5
- Annen bolig ☐ 6

1.3 Hvor stor er din boenhet? ____ *kvm (brutto)*

1.4 Er du plaget av: *(Sett ett kryss for hver linje)*

	Ikke plaget	En del plaget	Sterkt plaget
Fukt, trekk eller kulde i din bolig	☐	☐	☐
Andre former for dårlig inneklima	☐	☐	☐
Trafikkstøy (biltrafikk eller fly)	☐	☐	☐
Annen støy (bedrift, byggeplass e.l.)	☐	☐	☐
Nabostøy	☐	☐	☐
Dårlig drikkevann	☐	☐	☐
Luftforurensning fra trafikk	☐	☐	☐
Luftforurensning fra ved-, oljefyring, fabrikk e.l.	☐	☐	☐

1.5 Hvilket hjemmespråk hadde dine besteforeldre?
(Kryss av for ett eller flere alternativ)

	Norsk	Samisk	Kvensk/ finsk	Annet språk
Mormor	☐	☐	☐	☐
Morfar	☐	☐	☐	☐
Farmor	☐	☐	☐	☐
Farfar	☐	☐	☐	☐

T1. LOKALMILJØ OG BOLIG (forts.)

1.6 Hva regner du deg selv som?
(Kryss av for ett eller flere alternativ)

Norsk	Samisk	Kvensk/ finsk	Annet
☐	☐	☐	☐

	JA	NEI
1.7 Føler du at du har nok gode venner?	☐	☐

1.8 Hvor ofte tar du vanligvis del i foreningsvirksomhet som f.eks. syklubb, idrettslag, politiske lag eller andre foreninger?
(Sett bare ett kryss)

- Aldri, eller noen få ganger i året ☐ 1
- 1-3 ganger i måneden ☐ 2
- Omtrent 1 gang i uken ☐ 3
- Mer enn en gang i uken ☐ 4

T2. LØNNET OG ULØNNET ARBEID

2.1 Hvis du er i lønnet eller ulønnet arbeid, hvordan vil du beskrive ditt arbeid? *(Sett bare ett kryss)*

- For det meste stillesittende arbeid? *(f.eks. skrivebordsarbeid, montering)* ☐ 1
- Arbeid som krever at du går mye? *(f.eks. ekspeditørarb., lett industriarb., undervisning)* ☐ 2
- Arbeid hvor du går og løfter mye? *(f.eks. postbud, pleier, bygningsarbeider)* ☐ 3
- Tungt kroppsarbeid? *(f.eks. skogsarb., tungt jordbruksarb., tungt bygn.arb.)* ☐ 4

2.2 Kan du selv bestemme hvordan arbeidet ditt (lønnet eller ulønnet) skal legges opp? *(Sett bare ett kryss)*

- Nei, ikke i det hele tatt ☐ 1
- I liten grad ☐ 2
- Ja, stort sett ☐ 3
- Ja, det bestemmer jeg selv ☐ 4

	JA	NEI
2.3 Har du skiftarbeid, nattarbeid eller går vakter?	☐	☐

T3. TOBAKK

3.1 Røyker du?

Ja, daglig ☐1 Ja, av og til ☐2 Nei, aldri ☐3

Hvis "Ja, av og til",
Hva røyker du?

☐ Sigaretter ☐ Pipe ☐ Sigar/sigarillos

3.2 Har du brukt, eller bruker du snus daglig?

Ja, nå ☐ Ja, tidligere ☐ Aldri ☐

Hvis JA:
Hvor mange år har du til sammen brukt snus? år

T4. ALKOHOL

	JA	NEI
4.1 Er du totalavholdsmann/-kvinne?	☐	☐

4.2 Hvor mange ganger i måneden drikker du vanligvis alkohol? Antall ganger
(Regn ikke med lettøl.
Sett 0 hvis mindre enn 1 gang i måneden)

4.3 Hvor mange glass øl, vin eller brennevin drikker du vanligvis i løpet av 2 uker?

Øl Vin Brennevin

(Regn ikke med lettøl.
Sett 0 hvis du ikke drikker alkohol)

4.4 I omtrent hvor mange år har ditt alkoholforbruk vært slik du har svart i spørsmålene over? år

4.5 Har du i en eller flere perioder de siste 5 årene drukket så mye alkohol at det har hemmet deg i yrkeslivet eller sosialt?

Ja, i yrkeslivet ☐1 Ja, sosialt ☐2 Ja, både i yrkeslivet og sosialt ☐3 Nei, aldri ☐4

T5. MAT OG KOSTTILSKUDD

	JA	NEI
5.1 Spiser du vanligvis frokost hver dag?	☐	☐

5.2 Hvor mange ganger i uken spiser du varm middag? ganger

5.3 Hvor stor vekt legger du på å ha et sunt kosthold?

Stor ☐1 Middels ☐2 Liten ☐3 Ingen ☐4

5.4 Bruker du følgende kosttilskudd?

	Ja, daglig	Iblant	Nei
Jerntabletter	☐	☐	☐
Kalk eller benmel	☐	☐	☐
Vitamin D	☐	☐	☐
Tran	☐	☐	☐

T6. VEKTEN

6.1 Gjør du for tiden noe forsøk på å endre kroppsvekten din?

Nei ☐1 Ja, jeg forsøker å legge på meg ☐2 Ja, jeg forsøker å slanke meg ☐3

6.2 Hvilken vekt vil du være tilfreds med (din "trivselsvekt")? kg

T7. SYKDOMMER OG SKADER

7.1 Har du noen gang hatt:
Sett ett kryss for hvert spørsmål. Oppgi også alderen ved hendelsen. Hvis det har skjedd flere ganger, hvor gammel var du siste gang?

	JA	NEI	Alder siste gang
Alvorlig skade som førte til sykehusinnleggelse	☐	☐	år
Ankelbrudd	☐	☐	år
Magesår	☐	☐	år
Magesår-operasjon	☐	☐	år
Operasjon på halsen	☐	☐	år
Prostata-operasjon	☐	☐	år

7.2 Har du, eller har du hatt?
(Sett ett kryss for hvert spørsmål)

	JA	NEI
Kreftsykdom	☐	☐
Psoriasis	☐	☐
Stoffskiftesykdom (skjoldbruskkjertel)	☐	☐
Grønn stær	☐	☐
Grå stær	☐	☐
Slitasjegikt (artrose)	☐	☐
Krokete fingre	☐	☐
Hudstramninger i håndflatene	☐	☐
Nyrestein	☐	☐
Blindtarmsoperasjon	☐	☐
Brokkoperasjon	☐	☐
Operasjon/behandling for urinlekkasje	☐	☐
Epilepsi	☐	☐
Poliomyelitt ("Polio")	☐	☐
Parkinsons sykdom	☐	☐
Migrene	☐	☐
Leggsår	☐	☐
Allergi og overfølsomhet:	JA	NEI
Atopisk eksem (f.eks. barneeksem)	☐	☐
Håndeksem	☐	☐
Matvareallergi	☐	☐
Annen overfølsomhet (ikke allergi)	☐	☐

	JA	NEI
7.3 Har du hatt forkjølelse, influensa, "ræksjuka" eller lignende siste 14 dager?	☐	☐
7.4 Har du i løpet av de siste 3 ukene vært forkjølet, hatt influensa, bronkitt, lungebetennelse, bihulebetennelse eller annen luftveisinfeksjon?	☐	☐
7.5 Har du noen gang hatt bronkitt eller lungebetennelse?	☐	☐

7.6 Har du i løpet av de siste 2 årene hatt bronkitt eller lungebetennelse? *(Sett bare ett kryss)*

Nei ☐1 1-2 ganger ☐2 Mer enn 2 ganger ☐3

T8. SYMPTOMER

8.1 Har du de siste to ukene følt deg:
(Sett ett kryss for hvert spørsmål)

	Nei	Litt	En god del	Svært mye
Nervøs og urolig	☐	☐	☐	☐
Plaget av angst	☐	☐	☐	☐
Trygg og rolig	☐	☐	☐	☐
Irritabel	☐	☐	☐	☐
Glad og optimistisk	☐	☐	☐	☐
Nedfor/deprimert	☐	☐	☐	☐
Ensom	☐ 1	☐ 2	☐ 3	☐ 4

	JA	NEI
8.2 Hoster du omtrent daglig i perioder av året?	☐	☐
Hvis JA: Er hosten vanligvis ledsaget av oppspytt?	☐	☐
Har du hatt slik hoste så lenge som i en 3 måneders periode i begge de to siste år?	☐	☐
8.3 Har du hatt episoder med piping i brystet?	☐	☐

Hvis JA:
Har dette oppstått: *(Sett ett kryss for hvert spørsmål)*

	JA	NEI
Om natten	☐	☐
Ved luftveisinfeksjon	☐	☐
Ved fysisk anstrengelse	☐	☐
Ved sterk kulde	☐	☐

	JA	NEI
8.4 Får du smerter i tykkleggen når du går	☐	☐

Hvis JA:
Hvor langt kan du gå for du får smerter? .... *meter*

8.5 Blir du tungpusten i følgende situasjoner?
(Sett ett kryss for hvert spørsmål)

	JA	NEI
Når du går hurtig på flatmark eller svak oppoverbakke	☐	☐
Når du spaserer i rolig tempo på flatmark	☐	☐
Når du vasker deg eller kler på deg	☐	☐
Når du er i hvile	☐	☐

	JA	NEI
8.6 Må du stoppe på grunn av tung pust når du går i eget tempo på flatmark?	☐	☐
8.7 Har du i løpet av det siste året vært plaget med smerter og/eller stivhet i muskler og ledd som har vart i minst 3 måneder sammenhengende?	☐	☐
Hvis JA: Har plagene ført til redusert aktivitet i fritida?	☐	☐

Hvor lenge har plagene vart totalt?

ca .... *år og* .... *måneder*

Har plagene redusert din arbeidsevne det siste året?
(Gjelder også hjemmearbeidende og pensjonister. (Sett ett kryss)

Nei/ubetydelig	I noen grad	I betydelig grad	Vet ikke
☐ 1	☐ 2	☐ 3	☐ 4

	JA	NEI	Ikke i arbeid
Har du vært sykmeldt pga. disse plagene det siste året?	☐	☐	☐

T8. SYMPTOMER (fortsettelse)

8.8 Hvor ofte er du plaget av søvnløshet?
(Sett bare ett kryss)

Aldri, eller noen få ganger i året	☐ 1
1-3 ganger i måneden	☐ 2
Omtrent 1 gang i uken	☐ 3
Mer enn en gang i uken	☐ 4

8.9 Hvis du er plaget av søvnløshet månedlig eller hyppigere, når på året er du mest plaget?

Ingen spesiell tid	☐ 1
Særlig i mørketiden	☐ 2
Særlig i midnattsoltiden	☐ 3
Særlig vår og høst	☐ 4

	JA	NEI
8.10 Har du det siste året vært plaget av søvnløshet slik at det har gått ut over arbeidsevnen?	☐	☐
8.11 Pleier du sove om dagen?	☐	☐

8.12 Hvor ofte har du ufrivillig urinlekkasje?

Aldri	☐ 1
Ikke mer enn en gang i måneden	☐ 2
To eller flere ganger i måneden	☐ 3
Ukentlig eller oftere	☐ 4

	JA	NEI
8.13 Kan du gå ned 10 trappetrinn uten å holde deg i noe (f.eks. et gelender)	☐	☐
8.14 Bruker du briller?	☐	☐
8.15 Bruker du høreapparat?	☐	☐

8.16 Hvordan er hukommelsen?
(Sett ett kryss for hvert spørsmål)

	JA	NEI
Glemmer du ting du akkurat har hørt eller lest?	☐	☐
Glemmer du hvor du har lagt ting?	☐	☐
Er det vanskeligere å huske nå enn før?	☐	☐
Skriver du huskelapper oftere nå enn før?	☐	☐
Hvis "JA" på ett av disse spørsmålene; Er det et problem i hverdagen?	☐	☐

T9. MEDISINER

9.1 Bruker du, eller har du brukt noen av følgende medisiner:

	Nå	Før, men ikke nå	Alder ved bruk 1. gang	Aldri brukt
Medisin mot osteoporose (benskjørhet)	☐	☐	år	☐
Tabletter mot sukkersyke	☐	☐	år	☐
Tabletter mot lavt stoffskifte (thyroxin)	☐	☐	år	☐

	JA	NEI
9.2 Bruker du noen medisin som du får som sprøyte (injeksjon)?	☐	☐

Hvis JA:
Oppgi navn på medisinen (til sprøyte):
(ett navn pr. linje):

____

____

T10. SYKDOM I FAMILIEN

10.1 Kryss av for de slektningene som har eller har hatt noen av sykdommene: *(Sett kryss for hver linje)*

	Mor	Far	Bror	Søster	Barn	Ingen av disse
Hjerteinfarkt (sår på hjertet)	☐	☐	☐	☐	☐	☐
Angina pectoris (hjertekrampe)	☐	☐	☐	☐	☐	☐
Høyt blodtrykk	☐	☐	☐	☐	☐	☐
Utvidet hovedpulsåre i magen	☐	☐	☐	☐	☐	☐
Mage-/tolvfingertarm-sår	☐	☐	☐	☐	☐	☐
Lårhalsbrudd	☐	☐	☐	☐	☐	☐
Psykiske plager	☐	☐	☐	☐	☐	☐
Allergi	☐	☐	☐	☐	☐	☐
Slitasjegikt (artrose)	☐	☐	☐	☐	☐	☐
Aldersdemens	☐	☐	☐	☐	☐	☐

10.2 Hvor mange søsken og barn har du?

	Brødre	Søstre	Barn
Antall			

10.3 Fører sykdom e.l. hos noen i nær familie til at du vanligvis utfører ekstra omsorgsarbeid?

Ja, stor sett daglig ☐1 Ja, av og til ☐2 Nei ☐3

10.4 Har du/din familie hjemmehjelp eller hjemmesykepleie? .... JA ☐ NEI ☐

	JA	NEI	Evt. alder ved død
10.5 Lever din mor?	☐	☐	år
10.6 Lever din far?	☐	☐	år

T11. MOBILTELEFON

11.1 Disponerer du (eier, leier e.l.) mobiltelefon?

Ja, hele tiden ☐1 Ja, av og til ☐2 Nei ☐3

Hvis JA:
Hva bruker du mobiltelefonen til, og hvor ofte bruker du den? *(Sett ett kryss for hver linje)*

Antall ganger per døgn	30 eller flere	10-29	2-9	1 eller mindre	Aldri
Samtaler	☐	☐	☐	☐	☐
Tekstmeldinger	☐	☐	☐	☐	☐
	1	2	3	4	5

T12. RESTEN BESVARES BARE AV KVINNER

12.1 Hvis du har født barn, fyll ut hvert barns fødselsår, og hvor mange måneder du ammet etter fødselen.

(Hvis du ikke ammet, skriv 0)

Barn:	*Fødselsår:*	*Antall mnd med amming:*
1. barn		
2. barn		
3. barn		
4. barn		
5. barn		
6. barn		

(Hvis flere barn, bruk ekstra ark)

T12. RESTEN BESVARES BARE AV KVINNER

12.2 Hvis du fremdeles har menstruasjon eller er gravid: Hvilken dato startet din siste menstruasjon?

Dag Måned År

12.3 Hvis du ikke lenger har menstruasjon; hvorfor mistet du menstruasjonen? *(Sett ett kryss)*

- Den stoppet av seg selv .... ☐1
- Operasjon på livmoren .... ☐2
- Operert bort begge eggstokkene .... ☐3
- Annen grunn (f.eks. stråling, cellegift-behandling) ☐4

12.4 Bruker du eller har du brukt reseptpliktig østrogen (tabletter eller plaster)? .... JA ☐ NEI ☐

Hvis JA:
Hvor gammel var du da du begynte med østrogen? .... år

Hvis du har sluttet å bruke østrogen,
Hvor gammel var du da du sluttet med østrogen? .... år

12.5 Bruker du eller har du brukt p-piller? .. JA ☐ NEI ☐

Hvis JA:
Hvor gammel var du da du begynte med p-piller? .... år

Hvor mange år har du til sammen brukt p-piller? .... *Antall år*

Dersom du har født:
Hvor mange år brukte du p-piller for første fødsel? .... *Antall år*

Hvis du sluttet å bruke p-piller:
Hvor gammel var du da du sluttet? ...... år

12.6 Når du ser bort fra svangerskap og barselsperiode, har du noen gang vært blødningsfri i minst 6 måneder? JA ☐ NEI ☐

Hvis JA:
Hvor mange ganger? .. .. *ganger*

12.7 Hvordan er blødningsforholdene for deg nå?

- Jeg har ikke hatt blødninger det siste året ☐1
- Jeg har regelmessige blødninger .... ☐2
- Jeg har uregelmessige blødninger .... ☐3

12.8 Da du var i 25-29 årsalderen, hvor mange dager var det vanligvis mellom starten på to blødninger?

Minimum *dager* Maksimum *dager* Vet ikke ☐

Pågikk selve blødningen omtrent like mange dager hver gang? .. .. JA ☐ NEI ☐

Hvor mange dager varte en typisk menstruasjonsblødning? .... *dager*

Takk for hjelpen!
Husk å postlegge skjemaet i dag!

Appendix VI

Second questionnaire for subjects aged > 70 years, Tromsø V, 2001

E

Helse-
undersøkelsen

Personlig innbydelse

Ikke skriv her:

F13 (Kommune)   (Fylke)   (Land)   E15 (Merke)

E1 EGEN HELSE

Hvordan er helsen din nå? *(Sett bare ett kryss)*

Dårlig	Ikke helt god	God	Svært god
☐ 1	☐ 2	☐ 3	☐ 4

Har du, eller har du hatt?:

	JA	NEI	Alder første gang
Astma	☐	☐	
Kronisk bronkitt/emfysem	☐	☐	
Diabetes (sukkersyke)	☐	☐	
Benskjørhet (osteoporose)	☐	☐	
Fibromyalgi/kronisk smertesyndrom	☐	☐	
Psykiske plager som du har søkt hjelp for	☐	☐	
Hjerteinfarkt	☐	☐	
Angina pectoris (hjertekrampe)	☐	☐	
Hjerneslag/hjerneblødning	☐	☐	

Får du smerter eller ubehag i brystet når du:

	JA	NEI
Går i bakker, trapper eller fort på flat mark?	☐	☐

Hvis du får slike smerter, pleier du da å:

Stoppe?	Sakne farten?	Fortsette i samme takt?
☐ 1	☐ 2	☐ 3

	JA	NEI
Dersom du stopper, forsvinner smertene da etter mindre enn 10 minutter?	☐	☐
Kan slike smerter opptre selv om du er i ro?	☐	☐

E2. SYKDOM I FAMILIEN

Har en eller flere av dine foreldre eller søsken hatt:

	JA	NEI	Vet ikke
Hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)?	☐	☐	☐

Kryss av for de slektningene som har eller har hatt noen av sykdommene: *(Sett kryss for hver linje)*

	Mor	Far	Bror	Søster	Barn	Ingen av disse
Hjerneslag eller hjerneblødning	☐	☐	☐	☐	☐	☐
Hjerteinfarkt før 60 års alder	☐	☐	☐	☐	☐	☐
Astma	☐	☐	☐	☐	☐	☐
Kreftsykdom	☐	☐	☐	☐	☐	☐
Diabetes (sukkersyke)	☐	☐	☐	☐	☐	☐

Hvis noen slektninger har diabetes, i hvilken alder fikk de diabetes (hvis for eks. flere søsken, før opp den som fikk det tidligst i livet):

Vet ikke, ikke aktuelt	Mors alder	Fars alder	Brors alder	Søsters alder	Barns alder
☐					

E3. PLAGER

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 linje)

	Ikke plaget	Litt plaget	Ganske mye	Veldig mye
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, tungsindig	☐	☐	☐	☐
Følelse av å være unyttig, lite verd	☐	☐	☐	☐
Følelse av at alt er et slit	☐	☐	☐	☐
Følelse av håpløshet mht. framtida	☐ 1	☐ 2	☐ 3	☐ 4

E4. TENNER, MUSKEL OG SKJELETT

Hvor mange tenner har du mistet/trukket? *Antall tenner*
(Se bort fra melketenner og visdomstenner)

Har du vært plaget med smerter og/eller stivhet i muskler og ledd i løpet av de siste 4 ukene?

	Ikke plaget	En del plaget	Alvorlig plaget
Nakke/skuldre	☐	☐	☐
Armer, hender	☐	☐	☐
Øvre del av ryggen	☐	☐	☐
Korsryggen	☐	☐	☐
Hofter, ben, føtter	☐	☐	☐
Andre steder	☐	☐	☐

Har du noen gang hatt:

	JA	NEI	Alder siste gang
Brudd i håndledd/underarm?	☐	☐	
Lårhalsbrudd?	☐	☐	

Har du falt i løpet av det siste året? *(Sett bare ett kryss)*

Nei	Ja, 1-2 ganger	Ja, mer enn 2 ganger
☐ 1	☐ 2	☐ 3

E5. MOSJON OG FYSISK AKTIVITET

Hvordan har din fysiske aktivitet vært det siste året?
Tenk deg et ukentlig gjennomsnitt for året.
Besvar begge spørsmålene.

Timer pr. uke

	Ingen	Under 1	1-2	3 og mer
Lett aktivitet *(ikke svett/andpusten)*	☐	☐	☐	☐
Hard fysisk aktivitet *(svett/andpusten)*	☐ 1	☐ 2	☐ 3	☐ 4

E6. VEKT

Anslå din vekt da du var 25 år gammel: hele k

E7. UTDANNING

Hvor mange års skolegang har du gjennomført? *Antall år*
(Ta med alle år du har gått på skole eller studert)

E8. MAT OG DRIKKE

Hvor ofte spiser du vanligvis disse matvarene?
(Sett ett kryss for hver linje)

	Sjelden /aldri	1-3 g pr.mnd	1-3 g. pr.uke	4-6 g. pr.uke	1-2 g. pr.dag	3 g. el. mer pr.dag
Frukt, bær	☐	☐	☐	☐	☐	☐
Ost *(alle typer)*	☐	☐	☐	☐	☐	☐
Poteter	☐	☐	☐	☐	☐	☐
Kokte grønnsaker	☐	☐	☐	☐	☐	☐
Rå grønnsaker/salat	☐	☐	☐	☐	☐	☐
Feit fisk *(f.eks. laks, ørret, makrell, sild)*	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

Bruker du kosttilskudd:

	Ja, daglig	Iblant	Nei
Tran, trankapsler, fiskeoljekapsler	☐	☐	☐
Vitamin- og/eller mineraltilskudd	☐	☐	☐

Hvor mye drikker du vanligvis av følgende?
(Sett ett kryss for hver linje)

	Sjelden /aldri	1-6 glass pr.uke	1 glass pr.dag	2-3 glass pr.dag	4 glass el. mer pr.dag
Helmelk, kefir, yoghurt	☐	☐	☐	☐	☐
Lettmelk, cultura, lettyoghurt	☐	☐	☐	☐	☐
Skummet melk (sur/søt)	☐	☐	☐	☐	☐
Ekstra lettmelk	☐	☐	☐	☐	☐
Fruktjuice	☐	☐	☐	☐	☐
Vann	☐	☐	☐	☐	☐
Brus, mineralvann	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

Hvor mange kopper kaffe og te drikker du daglig?
(Sett 0 for de typene du ikke drikker daglig) *Antall kopper*

Filterkaffe ....

Kokekaffe/trykkanne ....

Annen kaffe ....

Te ....

Omtrent hvor ofte har du i løpet av det siste året drukket alkohol? *(Lettøl og alkoholfritt øl regnes ikke med)*

Har aldri drukket alkohol	Har ikke drukket alkohol siste år	Noen få ganger siste år	Omtrent 1 gang i måneden
☐ 1	☐ 2	☐ 3	☐ 4
2-3 ganger pr. måned	**ca. 1 gang i uka**	**2-3 ganger i uka**	**4-7 ganger i uka**
☐ 5	☐ 6	☐ 7	☐ 8

Til dem som har drukket siste år:
Når du har drukket alkohol, hvor mange glass eller drinker har du vanligvis drukket? *Antall*

Omtrent hvor mange ganger i løpet av det siste året har du drukket så mye som minst 5 glass eller drinker i løpet av ett døgn? *Antall ganger*

E9. RØYKING

Hvor lenge er du vanligvis daglig tilstede i et røykfylt rom? *Antall hele timer*

	JA	NEI
Røykte noen av de voksne hjemme da du vokste opp?	☐	☐
Bor du, eller har du bodd, sammen med noen dagligrøykere etter at du fylte 20 år?	☐	☐

	Ja, nå	Ja, tidligere	Aldri
Har du røykt/røyker du daglig?	☐	☐	☐

Hvis du ALDRI har røykt daglig;
Hopp til spørsmål E11 (FUNKSJON OG TRYGGHET)

Hvis du røyker daglig nå, røyker du:

	JA	NEI
Sigaretter?	☐	☐
Sigarer/sigarillos?	☐	☐
Pipe?	☐	☐

Hvis du har røykt daglig tidligere, hvor lenge er det siden du sluttet? *Antall år*

Hvis du røyker daglig nå eller har røykt tidligere:

Hvor mange sigaretter røyker eller røykte du vanligvis daglig? *Antall sigaretter*

Hvor gammel var du da du begynte å røyke daglig? *Alder i år*

Hvor mange år til sammen har du røykt daglig? *Antall år*

E10. FUNKSJON OG TRYGGHET

Ville du føle deg trygg ved å ferdes alene på kveldstid i nærområdet der du bor?

Ja	Litt utrygg	Svært utrygg
☐ 1	☐ 2	☐ 3

Når det gjelder førlighet, syn og hørsel, kan du:
(Sett ett kryss for hver linje)

	Uten problemer	Med litt problemer	Med store problemer	Nei
Gå en 5 minutters tur i noenlunde raskt tempo?	☐	☐	☐	☐
Lese vanlig tekst i aviser, evt. med briller?	☐	☐	☐	☐
Høre hva som blir sagt i en normal samtale?	☐ 1	☐ 2	☐ 3	☐ 4

Har du på grunn av varige helseproblemer vansker med å: *(Sett ett kryss for hver linje)*

	Ingen vansker	Noen vansker	Store vansker
Bevege deg rundt i egen bolig?	☐	☐	☐
Komme deg ut av boligen på egen hånd?	☐	☐	☐
Delta i foreningsliv eller andre fritidsaktiviteter?	☐	☐	☐
Bruke offentlige transportmidler?	☐	☐	☐
Utføre nødvendige daglige ærend?	☐	☐	☐

E11. BRUK AV HELSETJENESTER

Hvor mange ganger de siste 12 månedene har du selv brukt:
(Sett ett kryss for hver linje)

	Ingen	1-3 ganger	4 eller flere
Allmennpraktiserende lege	☐	☐	☐
Spesialist *(privat eller på poliklinikk)*	☐	☐	☐
Legevakt *(privat eller offentlig)*	☐	☐	☐
Sykehusinnleggelse	☐	☐	☐
Hjemmesykepleie	☐	☐	☐
Fysioterapeut	☐	☐	☐
Kiropraktor	☐	☐	☐
Kommunal hjemmehjelp	☐	☐	☐
Tannlege	☐	☐	☐
Alternativ behandler	☐	☐	☐

Er du trygg på at du kan få hjelp av helseog hjemmetjenesten hvis du trenger det? JA ☐1 NEI ☐2 Vet ikke ☐3

E12. FAMILIE OG VENNER

Bor du: Hjemme? ☐1 Institusjon/bofellesskap? ☐2

Bor du sammen med:

	JA	NEI
Ektefelle/samboer?	☐	☐
Andre personer?	☐	☐

Hvor mange gode venner har du?
Regn med de du kan snakke fortrolig med og som kan gi deg hjelp når du trenger det. Tell ikke med de du bor sammen med, men ta med barn og andre slektninger. *Antall venner*

Hvor stor interesse viser folk for det du gjør?
(Sett bare ett kryss)

Stor interesse ☐1 Noe interesse ☐2 Litt interesse ☐3 Ingen interesse ☐4 Usikkert ☐5

Hvor mange foreninger, lag, grupper, kirkesamfunn e.l. deltar du i ? *Antall*
(Skriv 0 hvis ingen)

E13. OPPVEKST OG TILHØRIGHET

Hvor lenge har du samlet bodd i fylket? år

Hvor lenge har du samlet bodd i kommunen? år

Hvor bodde du det meste av tiden for du fylte 16 år?
(Kryss av for ett alternativ og spesifiser)

Samme kommune ☐1

Annen kommune i fylket ☐2 Hvilken:__________

Annet fylke i Norge ☐3 Hvilket:__________

Utenfor Norge ☐4 Land:__________

Har du flyttet i løpet av de siste fem årene?

Nei ☐1 Ja, en gang ☐2 Ja, flere ganger ☐3

E14. BRUK AV MEDISINER

Med medisiner mener vi her medisiner kjøpt på apotek. Kosttilskudd og vitaminer regnes ikke med her.

Bruker du?
(Sett ett kryss for hver linje)

	Nå	Før, men ikke nå	Aldri brukt
Medisin mot høyt blodtrykk	☐	☐	☐
Kolesterolsenkende medisin	☐	☐	☐
Medisin mot osteoporose (benskjørhet)	☐	☐	☐
Insulin	☐	☐	☐
Tabletter mot sukkersyke	☐	☐	☐

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

	Ikke brukt siste 4 uker	Sjeldnere enn hver uke	Hver uke, men ikke daglig	Daglig
Smertestillende uten resept	☐	☐	☐	☐
Smertestillende på resept	☐	☐	☐	☐
Sovemedisin	☐	☐	☐	☐
Beroligende medisin	☐	☐	☐	☐
Medisin mot depresjon	☐	☐	☐	☐
Annen medisin på resept	☐	☐	☐	☐
	1	2	3	4

Angi navnet på de medisinene du bruker nå, og hva grunne er til at du tar medisinene (sykdom eller symptom):
(Kryss av for hvor lenge du har brukt medisinen)

Navn på medisinen: (ett navn pr. linje):	Grunn til bruk av medisinen:	Hvor lenge har brukt medisinen: Inntil 1 år	Ett å eller m
		☐	☐
		☐	☐
		☐	☐
		☐	☐
		☐	☐
		☐	☐
		☐	☐

Dersom det ikke er nok plass her, kan du fortsette på eget ark som du legger ved

E15. RESTEN AV SKJEMAET SKAL BARE BESVARES AV KVINNER

Hvor gammel var du da du fikk menstruasjon aller første gang? *Alder i år*

Hvor gammel var du da menstruasjonen sluttet? *Alder i år*

Hvor mange barn har du født? *Antall barn*

Bruker du, eller har du brukt østrogenmedisin? *I antall år totalt*

	Aldri	Før	Nå
Tabletter eller plaster	☐	☐	☐
Krem eller stikkpiller	☐	☐	☐

Hvis du bruker østrogen; hvilket merke bruker du nå?

____

Har du noen gang brukt P-pille? JA ☐ NEI ☐

ISM SKRIFTSERIE - FØR UTGITT:

1. Bidrag til belysning av medisinske og sosiale forhold i Finnmark fylke, med særlig vekt på forholdene blant finskættede i Sør-Varanger kommune.
Av Anders Forsdahl, 1976. (nytt opplag 1990)

2. Sunnhetstilstanden, hygieniske og sosiale forhold i Sør-Varanger kommune 1869-1975 belyst ved medisinal-beretningene.
Av Anders Forsdahl, 1977.

3. Hjerte-karundersøkelsen i Finnmark - et eksempel på en populasjonsundersøkelse rettet mot cardiovasculære sykdommer. Beskrivelse og analyse av etterundersøkelsesgruppen.
Av Jan-Ivar Kvamme og Trond Haider, 1979.

4. D. The Tromsø Heart Study: Population studies of coronary risk factors with special emphasis on high density lipoprotein and the family occurrence of myocardial infarction.
Av Olav Helge Førde og Dag Steinar Thelle, 1979.

5. D. Reformer i distriktshelsetjenesten III: Hypertensjon i distriktshelsetjenesten.
Av Jan-Ivar Kvamme, 1980.

6. Til professor Knut Westlund på hans 60-års dag, 1983.

7.* Blodtrykksovervåkning og blodtrykksmåling.
Av Jan-Ivar Kvamme, Bernt Nesje og Anders Forsdahl, 1983.

8.* Merkesteiner i norsk medisin reist av allmennpraktikere - og enkelte utdrag av medisinalberetninger av kulturhistorisk verdi.
Av Anders Forsdahl, 1984.

9. "Balsfjordsystemet." EDB-basert journal, arkiv og statistikksystem for primærhelsetjenesten.
Av Toralf Hasvold, 1984.

10. D. Tvunget psykisk helsevern i Norge. Rettsikkerheten ved slikt helsevern med særlig vurdering av kontrollkommisjonsordningen.
Av Georg Høyer, 1986.

11. D. The use of self-administered questionnaires about food habits. Relationships with risk factors for coronary heart disease and associations between coffee drinking and mortality and cancer incidence.
Av Bjarne Koster Jacobsen, 1988.

12.* Helse og ulikhet. Vi trenger et handlingsprogram for Finnmark.
Av Anders Forsdahl, Atle Svendal, Aslak Syse og Dag Thelle, 1989.

13. D. Health education and self-care in dentistry - surveys and interventions.
Av Anne Johanne Søgaard, 1989.

14. Helsekontroller i praksis. Erfaringer fra prosjektet helsekontroller i Troms 1983-1985.
Av Harald Siem og Arild Johansen, 1989.

15. Til Anders Forsdahls 60-års dag, 1990.

16. D. Diagnosis of cancer in general practice. A study of delay problems and warning signals of cancer, with implications for public cancer information and for cancer diagnostic strategies in general practice.
Av Knut Holtedahl, 1991.

17. D. The Tromsø Survey. The family intervention study. Feasibility of using a family approach to intervention on coronary heart disease. The effect of lifestyle intervention of coronary risk factors.
Av Synnøve Fønnebø Knutsen, 1991.

18. Helhetsforståelse og kommunikasjon. Filosofi for klinikere.
Av Åge Wifstad, 1991.

19. D. Factors affecting self-evaluated general health status - and the use of professional health care services.
Av Knut Fylkesnes, 1991.

20. D. Serum gamma-glutamyltransferase: Population determinants and diagnostic characteristics in relation to intervention on risk drinkers.
Av Odd Nilssen, 1992.

21. D. The Healthy Faith. Pregnancy outcome, risk of disease, cancer morbidity and mortality in Norwegian Seventh-Day-Adventists.
Av Vinjar Fønnebø, 1992.

22. D. Aspects of breast and cervical cancer screening.
Av Inger Torhild Gram, 1992.

23. D. Population studies on dyspepsia and peptic ulcer disease: Occurrence, aetiology, and diagnosis. From The Tromsø Heart Study and The Sørreisa Gastrointestinal Disorder Studie.
Av Roar Johnsen, 1992.

24. D. Diagnosis of pneumonia in adults in general practice.
Av Hasse Melbye, 1992.

25. D. Relationship between hemodynamics and blood lipids in population surveys, and effects of n-3 fatty acids.
Av Kaare Bønaa, 1992.

26. D. Risk factors for, and 13-year mortality from cardiovascular disease by socioeconomic status. A study of 44690 men and 17540 women, ages 40-49.
Av Hanne Thürmer, 1993.

27. Utdrag av medisinalberetninger fra Sulitjelma 1891-1990.
Av Anders Forsdahl, 1993.

28. Helse, livsstil og levekår i Finnmark. Resultater fra Hjerte-karundersøkelsen i 1987-88. Finnmark III.
Av Knut Westlund og Anne Johanne Søgaard, 1993.

29. D. Patterns and predictors of drug use. A pharmacoepidemiologic study, linking the analgesic drug prescriptions to a population health survey in Tromsø, Norway.
Av Anne Elise Eggen, 1994.

30. D. ECG in health and disease. ECG findings in relation to CHD risk factors, constitutional variables and 16-year mortality in 2990 asymptomatic Oslo men aged 40-49 years in 1972.
Av Per G. Lund-Larsen, 1994.

31. D. Arrhythmia, electrocardiographic signs, and physical activity in relation to coronary heart risk factors and disease. The Tromsø Study.
Av Maja-Lisa Løchen, 1995.

32. D. The Military service: mental distress and changes in health behaviours among Norwegian army conscript.
Av Edvin Schei, 1995.

33. D. The Harstad injury prevention study: Hospital-based injury recording and community-based intervention.
Av Børge Ytterstad, 1995.

34.* D. Vilkår for begrepsdannelse og praksis i psykiatri. En filosofisk undersøkelse.
Av Åge Wifstad, 1996. (utgitt Tano Aschehoug forlag 1997)

35. Dialog og refleksjon. Festskrift til professor Tom Andersen på hans 60-års dag, 1996.

36. D. Factors affecting doctors´ decision making.
Av Ivar Sønbø Kristiansen, 1996.

37. D. The Sørreisa gastrointestinal disorder study. Dyspepsia, peptic ulcer and endoscopic findings in a population.
Av Bjørn Bernersen, 1996.

38. D. Headache and neck or shoulder pain. An analysis of musculoskeletal problems in three comprehensive population studies in Northern Norway.
Av Toralf Hasvold, 1996.

39. Senfølger av kjernefysiske prøvespreninger på øygruppen Novaya Semlya i perioden 1955 til 1962. Rapport etter programmet "Liv". Arkangelsk 1994.
Av A.V. Tkatchev, L.K. Dobrodeeva, A.I. Isaev, T.S. Podjakova, 1996.

40. Helse og livskvalitet på 78 grader nord. Rapport fra en befolkningsstudie på Svalbard høsten 1988. **Av Helge Schirmer, Georg Høyer, Odd Nilssen, Tormod Brenn og Siri Steine, 1997.**

41.* D. Physical activity and risk of cancer. A population based cohort study including prostate, testicular, colorectal, lung and breast cancer.
Av Inger Thune, 1997.

42. The Norwegian - Russian Health Study 1994/95. A cross-sectional study of pollution and health in the border area.
Av Tone Smith-Sivertsen, Valeri Tchachtchine, Eiliv Lund, Tor Norseth, Vladimir Bykov, 1997.

43. D. Use of alternative medicine by Norwegian cancer patients
Av Terje Risberg, 1998.

44 D. Incidence of and risk factors for myocardial infarction, stroke, and diabetes mellitus in a general population. The Finnmark Study 1974-1989.
Av Inger Njølstad, 1998.

45. D. General practitioner hospitals: Use and usefulness. A study from Finnmark County in North Norway.
Av Ivar Aaraas, 1998.

45B Sykestuer i Finnmark. En studie av bruk og nytteverdi.
Av Ivar Aaraas, 1998.

46. D. No går det på helsa laus. Helse, sykdom og risiko for sykdom i to nord-norske kystsamfunn.
Av Jorid Andersen, 1998.

47. D. The Tromsø Study: Risk factors for non-vertebral fractures in a middle-aged population.
Av Ragnar Martin Joakimsen, 1999.

48. D. The potential for reducing inappropriate hospital admissions: A study of health benefits and costs in a department of internal medicine.
Av Bjørn Odvar Eriksen, 1999.

49. D. Echocardiographic screening in a general population. Normal distribution of echocardiographic measurements and their relation to cardiovascular risk factors and disease. The Tromsø Study.
Av **Henrik Schirmer, 2000.**

50. D. Environmental and occupational exposure, life-style factors and pregnancy outcome in artic and subartic populations of Norway and Russia.
Av Jon Øyvind Odland, 2000.

50B Окружающая и профессиональная экспозиция, факторы стиля жизни и исход беременности у населения арктической и субарктической частей Норвегии и России
Юн Ойвин Удлан 2000

51. D. A population based study on coronary heart disease in families. The Finnmark Study 1974-1989.
Av Tormod Brenn, 2000.

52 D. Ultrasound assessed carotid atherosclerosis in a general population. The Tromsø Study.
Av Oddmund Joakimsen, 2000.

53. D. Risk factors for carotid intima-media thickness in a general population. The Tromsø Study 1979-1994.
Av Eva Stensland-Bugge, 2000.

54. D. The South Asian cataract management study.
Av Torkel Snellingen, 2000.

55. D. Air pollution and health in the Norwegian-Russian border area.
Av Tone Smith-Sivertsen, 2000.

56. D. Interpretation of forearm bone mineral density. The Tromsø Study.
Av Gro K. Rosvold Berntsen, 2000.

57. D. Individual fatty acids and cardiovascular risk factors.
Av Sameline Grimsgaard, 2001.

58. Finnmarkundersøkelsene
Av Anders Forsdahl, Fylkesnes K, Hermansen R, Lund E, Lupton B, Selmer R, Straume E, 2001.

59. D. Dietary data in the Norwegian women and cancer study. Validation and analyses of health related aspects.
Av Anette Hjartåker, 2001.

60. D. The stenotic carotid artery plaque. Prevalence, risk factors and relations to clinical disease. The Tromsø Study.
Av Ellisiv B. Mathiesen, 2001.

61. D. Studies in perinatal care from a sparsely populated area.
Av Jan Holt, 2001.

62. D. Fragile bones in patients with stroke? Bone mineral density in acute stroke patients and changes during one year of follow up.
Av Lone Jørgensen, 2001.

63. D. Psychiatric morbidity and mortality in northern Norway in the era of deinstitutionalisation. A psyhiatric case register study.
Av Vidje Hansen, 2001.

64. D. Ill health in two contrasting countries.
Av Tom Andersen, 1978/2002.

65. D. Longitudinal analyses of cardiovascular risk factors.
Av Tom Wilsgaard, 2002.

66. Helseundersøkelsen i Arkangelsk 2000.
Av Odd Nilssen, Alexei Kalinin, Tormod Brenn, Maria Averina et al.,2003.

67. D. Bio-psycho-social aspects of severe multiple trauma.
Av Audny G. W. Anke, 2003.

68. D. Persistent organic pollutants in human plasma from inhabitants of the artic.
Av Torkjel Manning Sandanger, 2003.

69. D. Aspects of women's health in relation to use of hormonal contraceptives and pattern of child bearing.
Av Merethe Kunmle, 2003.

70. Pasienterfaringer i primærlegetjenesten før og etter fastlegereformen.
Av Olaug Lian, 2003.

71. D. Vitamin D security in northern Norway in relation to marine food traditions.
Av Magritt Brustad, 2004.

72. D. Intervensjonsstudien i Finnmark. Evaluering av lokalsamfunns basert hjerte- og kar forebygging i kystkommunene Båtsfjord og Nordkapp.
Av Beate Lupton, 2004.

73. D. Environmental factors, metabolic profile, hormones and breast and endiometrial cancer risk.
Av Anne-Sofie Furberg, 2004.

74. D. Det skapende mellomrommet i møtet mellom pasient og lege.
Av Eli Berg, 2004.

75. Kreftregisteret i Arkhangelsk oblast i nordvest Russland. Med en sammenligning av kreftforekomst i Arkhangelsk oblast og Norge 1993 - 2001.
Av Vaktskjold Arild, Lebedintseva Jelena, Korotov Dmitrij, Tkatsjov Anatolij, Podjakova Tatjana, Lund Eiliv, 2004

76. D. Characteristics and prognosis of long-term stroke survivors. The Tromsø Study.
Av Torgeir Engstad, 2004

77. D. Withdrawal and exclusion. A study of the spoken word as means of understanding schizophrenic patients.
Av Geir Fagerjord Lorem, 2005.

78. "Søkelys på safunnsmedisinene." Evaluering av kommunal samfunnsmedisinsk legetjeneste, offentlig legearbeid og de forebyggende oppgaver i Fastlegeordningen.
Av Betty Pettersen og Roar Johnsen, 2005.

1. **Prosjekt egenmelding Kristiansand kommune.** Evaluering av kontrollert intervensjonsforsøk i stor skala, med utvidet rett til egenmelding i kombinasjon med økt og formalisert samhandling mellom arbeidstaker og arbeidsplassen ved sykefravær.
Av Nils Fleten og Roar Johnsen, 2005.

80. D. Abdominal aortic aneurysms:Diagnosis and epidemiology. The Tromsø study.
Av Kulbir Singh, 2005.

81. D. A population based study on cardiovascular diseases in Northwest Russia.The Arkhangelsk study 2000.
Av Maria Averina, 2005.

82. D. Exposure to exogenous hormones in women: risk factors for breast cancer and molecular signature.
Av Vanessa Dumeaux, 2005.

83. D. Repeated ultrasound measurements of carotid artery plaques in a general population. The Tromsø Study 1994-2001.
Av Stein Harald Johnsen, 2005.

84. D. Risk Factors For Fractures In Tromsø. The Tromsø Study.
Av Luai Awad Ahmed, 2005.

85. D. The quality and use of two health registries in Russia. The Arkhangelsk Cancer Registry and the Kola Birth Registry
Качество и использование двух медицинских регистров в России. Архангельск регистр рака и Кольский регистр родов
Av Arild Vaktskjold, 2005.

86. D. Haemoglobin, anaemia and haematological malignancies.
Av Tove Skjelbakken, 2006

87. D. The sick-listed – an under-recognised resource in handling sickness absence.
Av Nils Fleten, 2006.

De som er merket med D er doktorgradsarbeid.
De som er merket med * har vi dessverre ikke flere eksemplar av.