Det helsevitenskapelige fakultet / Institutt for samfunnsmedisin

Age at menarche

The reproducibility of self-reported menarcheal age and the association between age at menarche and total- and cardiovascular mortality - The Tromsø Study

Reproduserbarheten til selv-rapportert menarkealder og assosiasjonen mellom alder ved menarke og total- og kardiovaskulær dødelighet - Tromsøundersøkelsen

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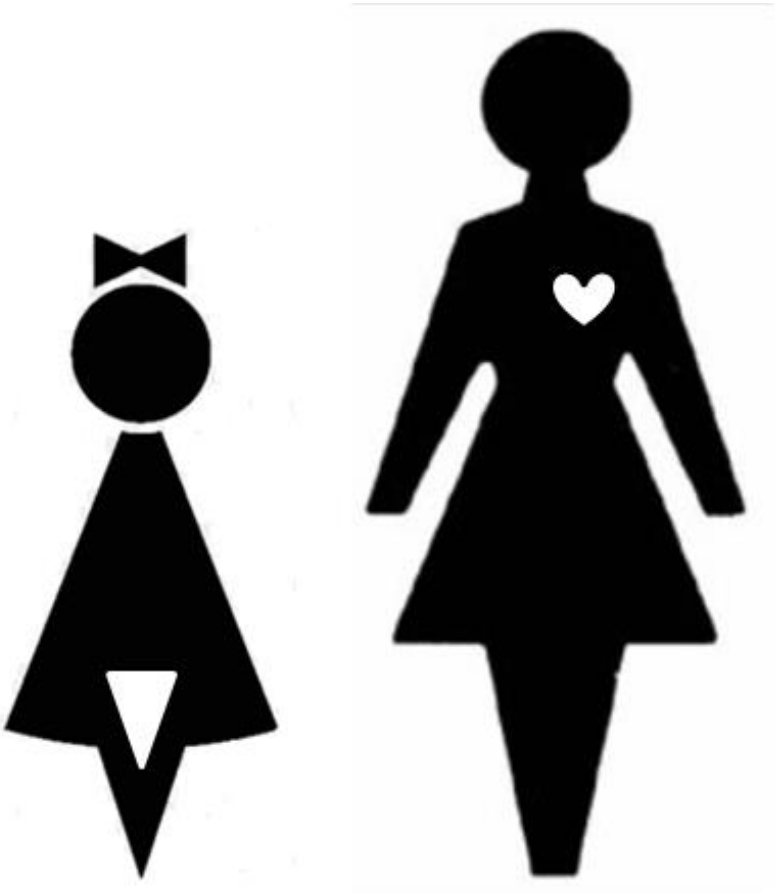

Preface

I started this master program with the hope of extending my knowledge regarding public health, research and preventive measures to help influence better conditions and health for the public as a whole. After the first master thesis seminar I asked Bjarne K. Jacobsen for tips regarding potential projects. Together we decided upon the present topic. I have worked with my thesis, while also taking courses, for approximately one year. It has been an exciting, challenging and very educational year. I have learned a lot, and my wishes and goals for my future are very different now, compared to when I started the master program. I now want to learn more, do more research and hopefully take a PhD. Many people have helped me succeed in finishing my master thesis earlier than first planned. First I want to thank Bjarne, my supervisor, for always making time for questions, providing amazing follow up and valuable help during the whole process. I could not have gotten a better supervisor! Thank you to my boyfriend Håvard, for supporting me in everything I do and for hanging in there while I have spent every evening of the last year in front of a computer. I also want to thank my 3 year old daughter who provides happiness and smiles during all necessary breaks from the thesis-writing. Thank you the rest of my family and friends for endless support, help and advice. A special thanks to my brother Eirik, who has proofread my writing and given tips during the process. I also want to thank Tonje Braaten for additional help with SPSS and our student consultant Tor-Gisle Lorentzen for always being helpful during the whole master-program. Last, but not least, I want to thank my co-student Anne Steigen for making a day at school like a cafe-visit!

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Abstract

Background: Previous research has observed a decreasing trend in menarcheal age since the 19th century. The reproducibility of self-reported age at menarche at two points in time is estimated by previous studies to have a moderate to high correlation, and self-reported menarcheal age is most often regarded as satisfactory for research purposes. Several previous studies have found that early menarche is associated with higher mortality and morbidity, e.g.; premature death from all-causes, higher prevalence of breast cancer, cardiovascular disease- and mortality and higher prevalence for metabolic syndrome.

Aim: The first aim of this thesis was to investigate the reproducibility of self-reported menarcheal age with a 7 year follow up, from 1986-1987 (Tromsø 3) to 1994-1995 (Tromsø 4). The second aim was to examine the association between age at menarche and cardiovascular- or all-cause mortality among the women in Tromsø. Cardiovascular disease is the leading cause of death in developed countries, and is of special interest.

Participants: In the reproducibility study, women who consented to research and reported menarcheal age in 1986-1987 (Tromsø 3) *and* in 1994-1995 (Tromsø 4) was included, a total of 6731 women with a mean age of 45.5 years.

In the investigation of all-cause and cardiovascular mortality, all attending females in Tromsø 4 who consented to research, reported menarcheal age and were < 25 years at menarche were included. A total of 12 409 women were eligible for analyses. The women were 25 - 94 years at start of follow-up in Tromsø 4 (1994), and mean age was 46.5 years.

Methods: This is a prospective cohort based on data from the large prospective Tromsø study. Follow-up for reproducibility purpose was 7 years. Pearson's correlation analysis and Bland-

Altman plot was used to investigate the reproducibility between self-reported age at menarche in Tromsø 3 and Tromsø 4. In the investigation of all-cause mortality follow-up was from date of attending Tromsø 4 and lasted until 30.06.2015; mean follow up was 18.7 years. Follow-up for cardiovascular disease mortality was until 31.12.2012; mean follow-up was 16.7 years. Multivariate Cox survival analysis was used to investigate the association between menarcheal age and both all-cause mortality and cardiovascular disease mortality. IBM SPSS Statistics 22 was the statistical program of choice.

Results: The reported menarcheal age in Tromsø 4 was significantly related to that reported in Tromsø 3 ($r = 0.84$, $p < 0.001$). The correlation was not weakened with increasing age of the respondents. A total of 62.5% of the women answered menarcheal age in Tromsø 4 with a 100% concordance with that reported in Tromsø 3. The mean difference in menarcheal age was negligible, 0.01 years, and the estimated limits of agreement according to the Bland-Altman analysis was -1.52 – 1.54 years, meaning that 95% of the difference in reported age at menarche between Tromsø 3 and Tromsø 4 are within these limits.

A total of 2203 women died during the follow up in the investigation of all-cause mortality. During the follow up of cardiovascular mortality, 654 women died from cardiovascular disease (184 from stroke, 250 from ischemic heart disease and 220 from other cardiovascular related causes). There was no association between age at menarche and total mortality after adjusting for confounding factors. For total cardiovascular mortality, however, there was an indication of a weak positive linear relationship after adjustments. One year increase in age at menarche was associated with 7 % increased cardiovascular mortality (HR: 1.07, 96% CI: 1.01 – 1.14, p = 0.03). Furthermore, women with menarcheal age 13 years and older had a significant higher

cardiovascular disease mortality compared to those with menarcheal age <13 years (HR: 1.40, 95% CI: 1.11 – 1.75, p=0.004).

Conclusion: Self-reported age at menarche in Tromsø 4 was strongly correlated with that reported in Tromsø 3, both when combined and in stratified age-groups. There was no association between menarcheal age and all-cause mortality among the women in Tromsø. A positive linear trend was observed between cardiovascular disease mortality and menarcheal age after adjusting for confounding factors. Further research should be emphasized. A reproducibility study with longer follow-up would have been very interesting.

Key words

Menarche

First menstruation

Maturation

Puberty

Cardiovascular disease

Stroke

Ischemic Heart Disease

Mortality

Death

Reproducibility

Content

Abbreviations

AAM	Age at menarche
BMI	Body Mass Index
CVD	Cardiovascular Disease
SD	Standard deviation
KS	Kolmogorov-Smirnov Test
IHD	Ischemic Heart Disease
Tr3	Tromsø 3
Tr4	Tromsø 4
HR	Hazard Ratio
TG	Triglyceride
FSH	Follicle Stimulation Hormone
LH	Luteinizing Hormone
GnRH	Gonadotropin-releasing hormone

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1.0 Introduction

1.1 Age at menarche and historical changes

Menarche is the first menstrual bleeding in females and represents the beginning of the reproductive life (1). Age at menarche (AAM) differs between girls and the current average menarcheal age worldwide is 12 years (2). A large secular trend in AAM have been observed since the 19th century when mean menarcheal age was approximately 17 years (3). This decrease is documented in several previous studies. A study from Taiwan observed a decrease in menarcheal age from generation to generation (from grandmothers to mothers and from mothers to daughters), where mean AAM (and standard deviation) for grandmothers was 15.16 (1.75) years, mean AAM for mothers was 14.50 (1.50) years and mean AAM for daughters was 13.0 (1.26) years (4). In recent years menarcheal age have been observed to stabilize in developed countries (5). The reason for this stabilization is unknown, but one previous study comparing menarcheal age in rural and urban areas, observed a more rapid decreasing trend in menarcheal age among the rural population compared to the urban (however the rural population had a higher median menarcheal age each year of the survey). This implies that the decrease in menarcheal age occur more rapidly in developing areas compared to developed (6). The difference between rural and urban menarcheal age got smaller during the study period, and improved living standards among the rural population was proposed as a potential explanation. They also found that higher Gross Domestic Product per capita and household consumption was linked to earlier menarche (6). More knowledge about diet, exercise and lifestyle related diseases have led to a growing focus on health among the public, especially among those with higher socio-economic status. As menarche is affected by nutrition and body mass index this change in socio-economic

status could be a potential explanation to why the decrease in menarcheal age has stabilized, and why this is mainly observed in developed countries.

1.2 Determinants of age at menarche

Puberty and its onset are mediated by several factors.

The physiology behind menarche is regulated in the female body through a hormonal connection between the hypothalamus, the adrenal gland and the ovaries (1). The pubertal event in females is characterized by the development of several secondary sexual characteristics and increased growth (7). Pubertal changes first occur at age 6-8 when a phase called adrenarche (the maturations of the adrenal gland) begins. The adrenal glands increase their secretion and production of adrenal androgens which are involved in the production of estrogen (estradiol) and testosterone (8). At the end of this phase girls could start to develop pubic- and axillary hairs, notice an adult body odor, get changes in the skin (e.g. acne) and experience mood-swings. The next phase in pubertal development is called gonadarche. In this phase the ovaries mature and the production of estradiol (estrogen) and progesterone increase. The production of estrogen and progesterone is regulated by the hypothalamus through a negative feedback system (pictured in figure 1), where Gonadotropin-releasing hormone (GnRH) from hypothalamus stimulates the production of Luteinizing Hormone (LH) and Follicle Stimulation Hormone (FSH) from the pituitary. This again stimulates the production of estradiol and the maturation of eggs in the

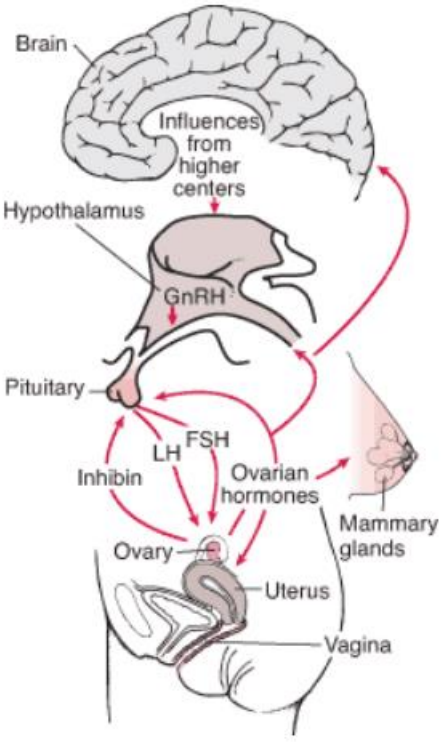


Figure 1: The hormonal pathways regulating the occurrence of menarche (1).

ovaries. Increased concentration of estrogen in the blood decreases the secretion of GnRH from the hypothalamus. This negative feedback system is fully functioning until the girl enters puberty and as the suppression of the activity from the hypothalamus (from mostly unknown reasons) decreases when approaching pubertal age, the secretion of GnRH increase (8). This eventually leads to the occurrence of menarche. The exact process of how this is regulated is not fully understood. More detailed explanations are given elsewhere (1, 8).

The mechanisms behind the decreased function of the negative feedback system when girls enter pubertal age, so that menarche can occur, remain unknown. It is well known that body mass index and fat distribution play a crucial role for the occurrence of menarche. This hypothesis was first presented by Rose Frisch as the "Frisch-Revelle Hypothesis" or "The critical weight hypothesis", saying that body weight has to increase to a certain level before changes in the metabolic rate occurs and triggers the occurrence of menarche (9). This hypothesis has been supported by several studies in later years. The association between body fat and menarche seems to be the protein leptin. Leptin is stored and secreted in the fat (especially in abdominal fat), and the concentration of leptin increases in parallel with the volume of body fat. The hypothalamus is sensitive to the concentration of leptin in the blood and the protein therefore work as a reflection of body fat, signaling to the hypothalamus when the body is ready to enter puberty and reproductive life (8). A study from 1997 showed that the amount of leptin in the blood was inversely associated with AAM (10). The hypothesis is that the female body has to contain approximately 17 % body fat for menarche to occur, and a distribution of 22 % body fat is necessary for achieving and maintaining a regular menstrual cycle (7). This hypothesis could explain why anorexia nervosa or having an exaggerated physical activity level delays menarcheal age and why higher childhood body mass index have been observed to be associated with earlier

menarcheal age. Obesity and lifestyle-related diseases have increased around the world and the "critical weight hypothesis" could also be one of the explanations for the observed secular trend in AAM.

There is a strong genetic component in the determination of AAM (57 - 82 %). There is usually an association between mothers menarcheal age and timing of daughters menarche, but other factors have also been discovered to be influential (3). A review that investigated determinants of AAM found a significant effect of the following factors on menarcheal age; nutrition and childhood body mass index (a high-energy-diet and high childhood body mass index are associated with earlier menarche), psychological stress in childhood (e.g. conflict, divorce, fathers absence and mothers mood disorders is associated with earlier menarcheal age) and socioeconomic status (higher socioeconomic status is associated with earlier menarcheal age) in addition to environmental toxins (11). Normally, socioeconomic status does not have a large influence on AAM in developed countries. However, one Norwegian study found an association between socioeconomic status and AAM; before the 1950's high socioeconomic status was associated with low menarcheal age, while after the 1950's low socioeconomic status was associated with low AAM (12). These results were related to findings regarding body weight in the different groups of socioeconomic status; before the 1950s high socioeconomic status was associated with a higher body weight while after the 1950s low socioeconomic status was associated with a higher body weight. Again, the association between body mass index and AAM is underscored.

1.3 Cardiovascular disease; definition and status

Cardiovascular disease (CVD) is a group-term of disorders that affect the heart and/or the blood vessels. A number of conditions are included in this term. The most common are ischemic heart

disease (IHD) and stroke, which often occur acute and as result of the development of atherosclerosis (13). Atherosclerosis is a condition where plaque develops inside the wall of the blood vessel, leading the diameter inside the vessel to narrow. The circulation of blood is inhibited and so is the transportation of oxygen to heart or the brain. Lack of oxygen in these organs can lead to several serious conditions, e.g.; heart attack, ischemia or stroke (14). IHD and stroke was ranked as the two leading causes of death worldwide in 2012, accounting for 7.4 million and 6.7 million deaths, respectively (13). CVD is the leading cause of death in Europe and approximately 46 % of all deaths (> 4 million deaths per year) can be attributed to CVD. Approximately 20 % of these deaths are due to cardiovascular heart disease (CHD). The proportion of cardiovascular related deaths are higher among females (51 %) compared to men (46 %). CVD is ranked as the leading cause of death in Norway. However, in 2012 both Norway and Denmark had the lowest age adjusted CVD death rates in Europe with < 120 deaths per 100 000 (15). CVD mortality is decreasing in most developed countries. However, from 2013 to 2014 there was a small increase in CVD death rates among women in Norway. CHD death rates remained stable (15).

1.3.1 Risk factors for cardiovascular disease

Several risk factors for cardiovascular disease have been identified and are well documented. Both genetic and behavioral characteristics could lead to an increased risk for cardiovascular disease and death. Some risk factors are not possible to influence, e.g. gender, family history of CVD, age and ethnicity. Other risk factors could be mediated through lifestyle-changes or medical treatment. These include; hypertension, high cholesterol and low HDL cholesterol, smoking, secondary tobacco exposure, excessive use of alcohol, obesity, unhealthy diets, physical inactivity and diabetes (16).

1.4 Potential effects of age at menarche on adult health: previous research

The age at when menarche occur have been linked to several health issues that develops later in life, and the determinants of this event is therefore of interest. Previous studies have shown contrasting results for different conditions. To sum it up, early AAM have been associated with the following conditions; higher all-cause mortality (17) and cardiovascular disease mortality (18-20), higher risk of breast cancer (21), cardiovascular disease (2, 20), diabetes (22-24), obesity (25) and metabolic syndrome (26, 27). Early menarcheal occurrence has also been linked to psychological disorders, depression, smoking and alcohol use in adolescence and early sexual behavior (28-30).

1.4.1 Previous research of AAM and mortality, morbidity and risk factors for disease

All-cause mortality: Charalampopoulos et al. (17), observed in a systematic review and meta-analysis a significant inverse association between menarcheal age and all-cause mortality where one year increase in menarcheal age was associated with a 3 % lower all-cause mortality (HR = 0.97, 95% CI: 0.96 - 0.98). Correspondingly, Xiaoyan et al. (22), (not included in the review) found a significant association between earlier AAM and increased all-cause mortality.

CVD and CVD mortality: The review did not identify a significant association between menarcheal age and CVD mortality in combined results from the included studies, presented in a meta-analysis (17). Two of the studies included in the meta-analysis did however report a significant association between AAM and CVD mortality. One of the studies, by Mueller et al. (31), observed an inverse association between AAM and CVD mortality only among never smokers and the other study, by Lakshman et al. (20), found that women who reported early menarche (<12 years of age) had an increased risk of hypertension, CVD and CVD-related

mortality, coronary heart disease, all-cause mortality and cancer mortality after adjusting for potential confounders.

The review by Charalampopoulos et al. (17), found that the relative risk for IHD (among non-smokers only) was 24% higher in the youngest menarcheal age group compared to the median menarcheal age group. They found no association between menarcheal age and stroke. An association between early AAM and stroke was found by Xiaoyan et al. (22), who concluded that earlier AAM was linked to increased mortality from both stroke and diabetes.

A possible explanation for the observed association between earlier AAM and CVD mortality is that early AAM have been linked to high body mass index and waist circumference, elevated blood lipids and metabolic syndrome, which all are risk factors for CVD (32, 33). Several studies support this hypothesis. Feng et al. (32), showed an inverse association between AAM and body composition, insulin sensitivity and blood lipid levels. Correspondingly, Remsberg et al. (33), found that girls with early menarche (<12 years of age) more often had hypertension and glucose intolerance compared to girls who experienced menarche at a later stage. A study from Finland investigated the association between AAM and cardiovascular risk and found no independent effect of AAM on cardiovascular risk factors (26). Rather they reported that increased pre-menarcheal body mass index was associated with earlier AAM. Pre-menarcheal body mass index and earlier AAM were together associated with increased body mass index in adulthood, which further was linked to multiple risk factors for cardiovascular disease (26).

Cancer: There is conclusive evidence of an inverse association between AAM and breast cancer incidence (in addition to other types of cancer). This association is well documented and the main explanation for the increased risk of breast cancer with early menarcheal age is the prolonged

exposure to estrogen when experiencing early menarche. The production of estrogen increases around the time of menarche. One of the effects of estrogen is to increase cell-division in the breast tissue (34). The length of reproductive years (from menarche to menopause) has been hypothesized to be the cause for the elevated risk for breast cancer as the women experience prolonged exposure to estrogen. A review from the Collaborative Group on Hormonal Factors in Breast Cancer presented that one year younger AAM was associated with a higher risk for breast cancer compared to one year older age at menopause (21). They stress that the length of reproductive life is not the only explanation for the observed increase in breast cancer (21). Correspondingly, a Norwegian study found a larger impact from one-year difference in AAM on all-cause mortality, compared to one-year difference in age at menopause in the same population. They state that an explanation might be linked to the biological age of the woman rather than her actual age (35).

1.5 Self-reported age at menarche

AAM is an important variable for several research-purposes; in analysis of menarcheal trend and to examine how menarche differs between areas, cohorts or ethnicities. Also, research of associations between menarcheal age and mortality and morbidity later in life depend on reported AAM. It is challenging to ensure accurate information regarding AAM without extensive monitoring. Without any gold standard for determining menarcheal age most research relies on self-reported menarcheal age or menarcheal age reported by the parents. The validity and reproducibility of the menarcheal information (how accurately women remember their menarcheal age and to what extent they give consistent information) is crucial. The correlation between reported AAM at two points in time does not validate the actual menarcheal age, but illustrates how consistent the women are when reporting AAM. Despite the importance of self-

reported menarcheal age, there are few studies focusing on the reliability of self-reported AAM over time (36).

1.5.1 Validity

Previous studies focusing on the validity of self-reported AAM have found a moderate to strong correlation between actual AAM and self-reported AAM later in life, with various lengths of follow-ups (37-39). Must et al. (38), found a strong correlation between recorded AAM and self-reported AAM. In a prospective birth cohort, Cooper et al. (37), observed a moderate correlation between menarcheal age and self-reported AAM at age 48. They state that researchers should be aware of the potential limitations when using self-reported menarcheal age from middle-aged women in research (37). Casey et al. (40), observed that 84% of the included females remembered their menarcheal age within 1 year of the actual event. Koprowski et al. (39), found a strong correlation between actual menarcheal age and self-reported menarcheal age after approximately 5 years of follow-up. They did however conclude that the validity of recalled menarcheal age decreased with time.

1.5.2 Reproducibility

Previous studies on the reproducibility between self-reported menarcheal age at two different points in time observed a satisfactory to strong correlation (41, 42). An article from the Bogalusa Heart Study report a moderate correlation between reported menarcheal age at two points in time (*r*: 0.57) (43). They state that lack of specific information, like month of occurrence, could be the reason to why they only observed a moderate correlation. They did however find that 84 % of the girls reported menarcheal age within one year difference between the two points in time (43). The moderate reliability corresponded with another study who found an interclass correlation (ICC) of 0.64 (36). The latter also investigated how the interview method affected the reliability of

reported menarche. They found that menarcheal ages reported at in-person interviews had a strong correlation ((*ICC*): 0.77) compared to menarcheal ages reported at phone-interviews which had a moderate correlation ((*ICC*): 0.64) (36). Both studies include adolescents, which one could hypothesize have a stronger recollection of menarcheal age compared to older women because it is a more recent event. Madrigal et al. (44), investigated the reliability of recalled menarcheal age among a study sample of older women (50 years and older). They found a strong correlation between self-reported menarcheal age at two points in time (*r:* 0.81). However, few women were included in the follow-up survey for comparison (28 women) and there was a short duration of follow-up (9 months).

1.6 Relevance to the field of public health

It is of interest for the field of public health to investigate the association between AAM and total mortality as it involves important information concerning all women. The potential association with cardiovascular disease is of particular interest (and more narrowly IHD and stroke) as it is the leading cause(s) of death both in developed and developing countries and leads to a significant burden on both health and economy (14). In addition, examining the reproducibility of self-reported menarcheal age is important for research purposes, as many studies rely on self-reported AAM.

1.7Aim of the study:

Previous studies recommend more research concerning the relationship between AAM and mortality. The first aim of my master thesis is to investigate the reproducibility of information concerning self-reported AAM between Tromsø 3 and Tromsø 4. The second aim is to investigate the association between menarcheal age and all-cause- and cardiovascular (total, IHD and stroke) mortality among women living in Tromsø.

2.0 Methods and Materials

2.1 Tromsø and the Tromsø study

Tromsø is the largest city in the North of Norway with a total of 72 681 inhabitants by January 1st 2015 (45, 46). The Tromsø Study, which is a prospective cohort study, first started in 1974 and is now one of the largest epidemiological studies in Norway. The initial focus was on CVD and mostly focused on middle-aged men, as CVD was previously understood as a male disease. In the 1970's men in Norway had a 20% risk of dying from myocardial infarction before the age of 75 (46). Myocardial infarction mortality was even higher in Northern Norway (46). The motivation behind the development of the Tromsø Study was to identify risk factors, prevent CVD and study the etiology of disease in Northern Norway. The Tromsø study has, during the last 41 years, expanded to include a large part of the population and a number of diseases. The main focus is; diabetes mellitus, fractures, osteoporosis, mental health, renal disease, eye disease, musculoskeletal problems, chronic pain, health service- and medicine consumption etc. (46). A total of 6 surveys have been conducted since 1974, and a 7th survey is currently ongoing. The participants receive a questionnaire by post (including a large number of questions) together with information regarding the Tromsø study and a written consent form, approximately 2 weeks before suggested time of an appointment for physical examination. The written consent is to be signed and submitted before the clinical examination. In addition to the questionnaire received at baseline and the physical examination, there has been included an additional physical examination visit since Tromsø 4 (1994-1995) (further information is reported elsewhere) (46).

2.2 Study population/selection

This master thesis is based on data collected in Tromsø 4. The variable AAM from Tromsø 3 was also included, for the purpose of investigating the reproducibility of self-reported AAM.

Tromsø 3 was conducted in 1986-87, and was based on self-administered questionnaires in addition to physical examinations. A total of 13 745 women were invited to participate in Tromsø 3. The response was 79% and a total of 10 863 women participated. A total of 6731 of these women answered the question regarding AAM in both Tromsø 3 and Tromsø 4, and were included in the reproducibility study.

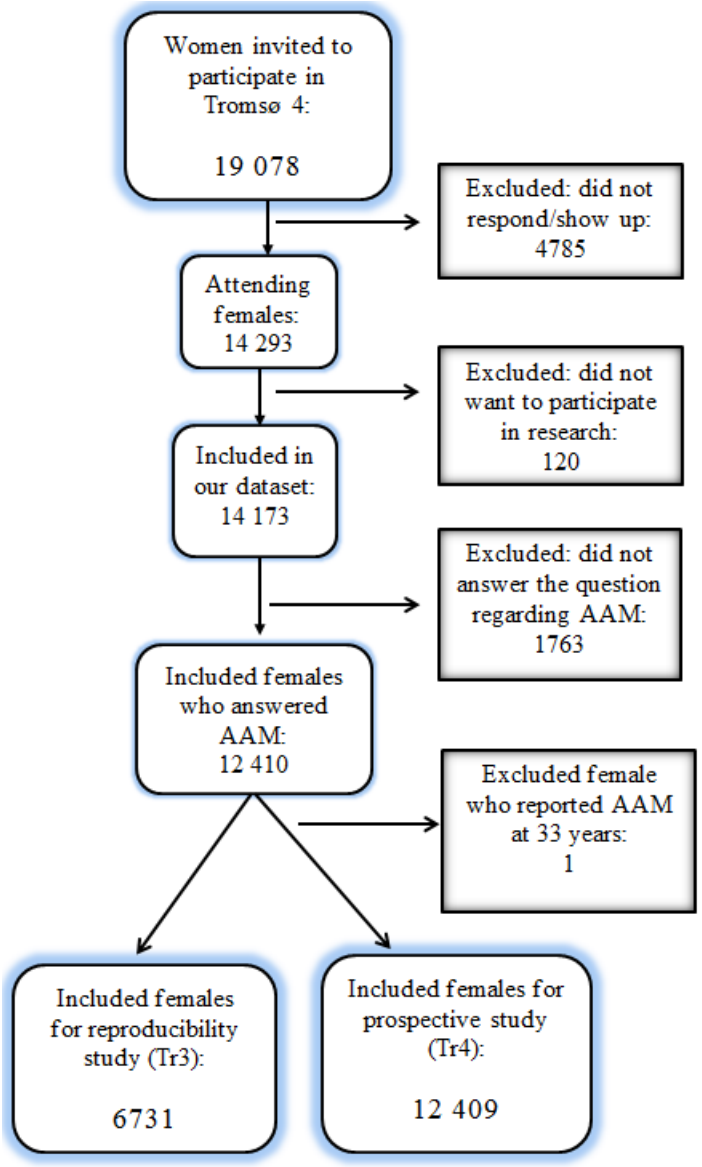


Figure 2: Flow diagram of the data material (inclusion/exclusion)

Tromsø 4 is the largest of all the surveys with a total of 27 158 participating men and women. The response rate was 77%.

A total of 19 078 women were invited in 1994-1995 to participate in Tromsø 4. With a response rate of 74.9%, 14 293 women participated in the survey (46).

2.3 Inclusion/exclusion

The exclusion and inclusion of participants is described in figure 2. A total of 4785 women did not attend the Tromsø 4 survey. Those who did not want to participate in research (120 women) and those who did not answer the question regarding AAM in Tromsø 4 (1763 women) were

excluded. Only those who reported menarcheal age between 8 and 25 years were included. One participant was excluded, as she reported menarcheal age on 33 years. This was considered a mistake or reflecting a medical condition which leads to delayed menarche. Thus, 12 409 women remained eligible for analyses in the study sample.

2.4 Variables

2.4.1 Independent variables

The main independent variable is AAM in Tromsø 4**.** The women were asked "How old were you when you started menstruating (age)?" The variable AAM was recoded from *one* continuous variable into the following groups; < 12 years, 12, 13, 14, 15 and >15 years. Only 1.3 % reported to being 10 years or younger at time of menarche and the youngest menarcheal group was therefore set to <12 years. The AAM variable was also split into low menarcheal age (<13 years) vs. high menarcheal age (13 + years), to look for potential differences in survival.

The main dependent variable in the analyses was all-cause or cardiovascular death, with sub-variables; death from stroke or ischemic heart disease (IHD).

2.4.2 Follow-up

2.4.2.1 All-cause mortality

Start of follow-up in the prospective study of all-cause mortality was the date the participant attended the examination in Tromsø 4. The follow-up lasted until 30.06.2015 or until date of emigration or date of death, whichever came first. Mean duration of follow up was 18.7 years. During this time, 2203 women died and 140 emigrated.

2.4.2.2 Cardiovascular death (stroke, IHD and other)

Information regarding cause-specific (including cardiovascular) mortality was available until 31.12.2012. Follow-up period for cardiovascular mortality was from the date of examination until 31.12.2012 or until date of emigration or date of death, whichever came first. Mean years of follow-up were 16.7 years. During the time of follow up, 1838 women died, among these, 654 died from cardiovascular disease (184 from stroke, 250 from IHD and 220 from other cardiovascular related causes). A total of 131 women emigrated during these years of follow up.

2.4.3 Other dependent variables, covariates and possible confounders

Possible confounders were identified through previous literature and from present knowledge regarding risk factors for cardiovascular disease and premature death. The identified confounders were as following; age (*age in years per 31.12.1994)*, blood pressure (systolic and diastolic) and blood pressure treatment (currently, previously, never). A hypertension variable was created, where presence of the following was regarded as being hypertensive; those who had mean systolic blood pressure >150 mmHg or diastolic blood pressure > 95 mmHg or currently used blood pressure lowering drugs.

Body mass index (BMI) was used as a continuous variable in addition to being recoded into; *underweight; BMI <18.5 kg/m^2, normal; BMI 18.5-24.99 kg/m^2, overweight; BMI 25-29.99 kg/m^2 and obesity; BMI ≥ 30.0 kg/m^2)*. Serum cholesterol (mmol/l), triglycerides (mmol/l) and high density lipoprotein (HDL) (mmol/l) was included.

Prior heart attack, angina pectoris, stroke or diabetes was included as potential confounders. If occurrence of any of the prior conditions were answered yes, then age at first event was included. Also smoking status (never, previously or current smoker) and alcohol consumption

(*times/month*) or teetotaler status (yes/no) was included. The two latter were combined into one variable (those who were teetotalers were missing in the alcohol-variable).

Hours of physical activity (PA) per week (*Sedate; light PA < 1 hour/week, Moderate; hard PA < 1 hour/week or light PA 1, 2 or 3 hours and more per week, Active; hard PA 1, 2 or 3 hours and more per week).* Additionally, a variable regarding occurrence of cardiovascular disease in closest family (*heart attack or angina among parents or siblings*) was included, together with parity/number of children and age at menopause (if menopause had occurred).

All newly created variables were thoroughly checked to ensure that they were created correctly and matched their purpose. Variables recorded as currently, previously or never was recoded to be included in linear analysis (never, previously, currently).

2.5 Data analysis

2.5.1 General

The variables were checked by frequency counts, descriptives etc. to identify obvious outliers.

The variables were checked for normal distribution by visual inspection of histograms. In addition, the Kormogorov-Smirnov (KS) test was used for testing normal distribution. KS was significant for most of the variables included. It is known that the KS is sensitive to small variations in large study-samples, which probably is the explanation for the significant results in this sample. For those variables that were significant in the KS test (and therefore categorized as non-normally distributed), skewness and kurtosis was examined. If the variables ranged between -2 and 2 they were considered normally distributed.

Descriptive analyses were performed for all included variables by using cross tabulation and comparison of means with AAM. Linear regression (for continuous variables) and binary logistic regression (for categorical yes/no answers) was used in order to determine p-values for linear trend. Age was included as a covariate in the model in order to provide age-adjusted p-values for linear trend in the descriptive of potential confounders (table 3 and 4).

There was some item non-response/missing in the variables, but these accounted for a small percentage of the total dataset and were not expected to influence the end-result.

2.5.2 Reproducibility study

The overall reproducibility of self-reported AAM was assessed by performing correlation analysis between the two continuous variables AAM according to Tromsø 3 and Tromsø 4. The Pearson correlation coefficient was chosen because menarcheal age is a continous variable. To investigate this correlations further, stratified analyses were performed according to age groups in Tromsø 4: 25-34 years, 35-44 years, 45-54 years, 55-64 years, 65-74 years and 75 + years. The correlation coefficient have some weaknesses when it comes to describing agreement between two measurements (47). Several problems with the correlation model when comparing two methods or measurements at two points in time is presented by Bland and Altman (48) in an article from 1986. For the purpose of investigating the agreement between self-reported AAM in Tromsø 3 and Tromsø 4, we therefore included a Bland-Altman plot where the difference between AAM in Tromsø 3 and Tromsø 4 is indicated on the ordinate and the mean of the two AAMs on the abscissa. This is regarded as an appropriate method to apply when investigating the agreement between reported menarcheal age at two points in time. The Bland Altman gives information in addition to the correlation coefficient. It show the agreement between two variables by presenting the limits of agreement which is calculated from the means and standard

deviation of the difference between recorded AAM in Tromsø 3 and 4. Other characteristics in the data could also be observed in a Bland-Altman Plot, e.g. if there is systematic differences between the two measurements it could indicate systematic bias.

2.5.3 Survival analysis

To clarify if the condition for performing Cox regression was satisfied in this dataset, the proportional hazard assumption (PH-assumption) was checked. The PH-assumption is that the effect of the different variables on survival remains constant over the time variable in the Cox regression (here: years of follow-up). This was checked by performing time dependent covariate survival analysis. The PH assumption was met for all variables and Cox regression survival analysis could be performed.

The following procedure was used to identify variables that should be included in the final survival analysis. First, all variables that were significantly associated with the menarcheal age groups after age adjustment (linear regression for continuous variables, and logistic regression for binary variables) were considered eligible for survival analysis. One by one these variables were included, together with age and AAM, in Cox regression to examine if they were significantly associated with survival. P-value <0.05 made the variables candidates for the final survival analysis. Step two was to include all the variables that had a significant effect on mortality, together with age and AAM in Tromsø 4 in a multivariate Cox regression survival analysis. Variables that were non-significant in this multivariable survival analysis were removed, until all remaining variables in the analyses were significant ($p<0.05$). Potential interaction between total cholesterol, triglycerides and HDL was examined. There was significant interaction between the three variables. These variables were not the main focus in the final analysis and the most significant was kept while the others were removed. This procedure was performed for both all-

cause mortality analysis and CVD mortality analysis. Triglyceride was the most significant variable in analyses of all-cause mortality and was included there. HDL was most significant for both total CVD mortality and IHD mortality, and was included in survival analyses regarding these causes of death. None of the three variables (triglyceride, HDL and total cholesterol) were significantly associated with mortality from stroke and none of them were included in final analyses for stroke mortality.

Other elimination methods could have been used for the same purpose; variables that significantly changed the risk estimate for AAM could have been included in the survival analysis. However, none of the variables in this data (except for age) had a large effect on the risk estimates for mortality by menarcheal age groups.

Separate survival analyses were performed for those aged >59 years in Tromsø 4 and those younger than 60 years, to examine if there were differences in the relationship between AAM and survival between these two age-groups. Similar stratified analyses were performed for current, former and never smokers. We also performed separate analysis using AAM with the following cut-off; low vs. high menarcheal age (< 13 years vs. 13 years and older). These analyses were performed for both all-cause and CVD mortality.

In survival analysis the reference for AAM was set to mean menarcheal age: 13 years. Normal body mass index (18.5 – 24.99 kg/m^2) was the reference for body mass index. Sedate activity level was reference when examining physical activity and the never smokers were the reference for smoking. HR was interpreted as relative risk. 95 % confidence intervals are given. A two-sided p-value < 0.05 was considered statistically significant. We used IBM SPSS statistics 22 to analyze the data.

2.6 Ethics and permission

Approval was given from the Data and Publication committee for the Tromsø-study and access to a data-file containing all chosen variables (described above) was received. The Tromsø Study is approved by the Regional Committee for Medical Research Ethics (REK) and the investigation is covered by this approval. All included subjects also provided written consent.

3.0 Results

3.1 The reproducibility of reported age at menarche

The reproducibility study included 6731 women which reported menarcheal age in both 1986-1987 (Tromsø 3) and 1994-1995 (Tromsø 4). Mean age in Tromsø 4 for the females included in the analyses was 45.3 years. Mean menarcheal age according to the information in Tromsø 4 and Tromsø 3 was 13.2 years (SD 1.30) and 13.2 (SD 1.28) respectively.

Analysis showed a strong correlation between self-reported menarcheal age in Tromsø 3 and Tromsø 4 (Pearson's $r = 0.84$, $p < 0.001$) (Table 1). The correlation held for all age groups and did not get weaker with increasing age. On the contrary it got stronger. Among those in the youngest (25-34 year) age-group the Pearson's r was 0.81 ($p < 0.001$). The strongest correlation for self-reported AAM was observed in the oldest age-group eligible for comparison (65-74 years) ($r = 0.91$, $p < 0.001$). In the youngest age group (25-34 years), 58.9 % answered menarcheal age in Tromsø 4 with a 100% concordance with their answer in Tromsø 3. This is compared to a 73.8 % perfect concordance for the women in the oldest age-group (65-74 years). Among those who reported menarcheal age with more than one year difference (in either direction), the highest percentage (6.9 %) was in the youngest age group (25-34 years) compared to the lowest percentage of 4.5% in the age group 55-64 years. For all age-groups combined, 62.4 % reported menarcheal age within the same year in Tromsø 3 and Tromsø 4. A total of 5.4 % reported menarcheal age with more than one year difference in Tromsø 4 than that reported in Tromsø 3. Mean difference of reported menarcheal age in Tromsø 3 and Tromsø 4 was 0.01 (SD: 0.78) and mean absolute difference was 0.44 (SD: 0.64). The mean absolute difference, in one direction or the other, in self-reported AAM ranged from 0.35 years in the oldest age group (65-74 years) to 0.49 years in the youngest age group (25-34 years) (Table 1).

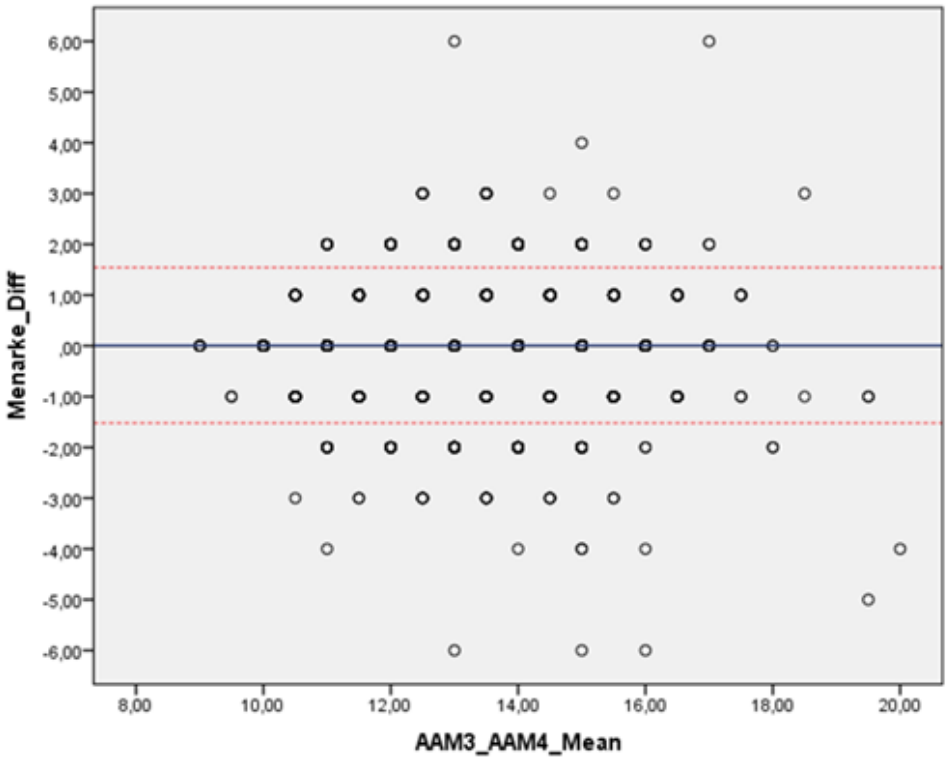
Figure 3 shows the agreement between self-reported menarcheal age in Tromsø 3 and Tromsø 4. The blue line represents the mean difference between reported menarcheal ages at two points in time. The red dotted lines show the limits of agreement, which is calculated from the mean difference ± 1.96 SD. The limits of agreement display how dispersed reported AAM at two time-periods is likely to be for most women. Here the limits of agreement range from -1.52 – 1.54 years, meaning that approximately 95 % of the women will have differences in reported menarcheal age within these limits. All dots are approximately scattered around the line of no difference (0) and there is no systematic error (which would be represented by dots systematically located above or beneath the line of no difference: 0).

The outliers observed in the plot are the women who reported menarcheal age with a high discrepancy between Tromsø 3 and Tromsø 4. These are observed as dots located away from the cloud of dots in the center (e.g. 5 women reported menarcheal age in Tromsø 4 with a 6 year difference from that reported in Tromsø 3, these are observed at the bottom and the top of the plot).

		Age at Menarche (years)					Percentage of reported difference (year)	
Age (Tromsø 4)	**N (%)**	**Tromsø 3**	**Tromsø 4**	**Difference**	**Absolute difference**	**Correlation coefficient***	**% perfect**	**% > 1 year**
25-34	1058 (15.7)	13.04 (1.32)	13.05 (1.35)	0.01 (0.83)	0.49 (0.67)	0.806	58.9	6.9
34-44	2154 (32.0)	13.07 (1.29)	13.11 (1.32)	0.04 (0.76)	0.44 (0.62)	0.832	61.9	5.5
45-54	2131 (31.7)	13.20 (1.32)	13.19 (1.38)	-0.01 (0.77)	0.43 (0.64)	0.838	63.6	5.2
55-64	1323 (19.7)	13.56 (1.38)	13.56 (1.36)	-0.01 (0.76)	0.42 (0.64)	0.844	63.3	4.5
65-73	65 (1.0)	14.12 (1.87)	14.08 (1.60)	-0.05 (0.80)	0.35 (0.72)	0.905	73.8	6.1
Total	6731 (100.0)	13.21 (1.28)	13.22 (1.30)	0.01 (0.78)	0.44 (0.64)	0.836	62.4	5.4

Table 1: AAM in Tromsø 3 and Tromsø 4 according to age-groups (difference and correlation): AAM, difference and absolute difference between reported menarcheal age is presented as means with standard deviations according to age. The correlation coefficient (Pearson's *r*) is presented for all age-groups. % perfect relates to that percentage who answered the question regarding AAM within the same year in Tromsø 3 and Tromsø 4. % >1 year represent that percentage which answered the question regarding AAM with more than 1 year difference in either direction (younger or older).

*All correlations were significant with $p < 0.001$



Mean Difference (SD): 0.01 (0.78)

Mean difference + 1.96 SD: 1.54

Mean difference – 1.96 SD: -1.52

Figure 3: Bland-Altman plot of agreement in reported menarcheal age (Tromsø 3 and Tromsø 4)

*The red dotted lines present the limits of agreement; ranged from -1.52 – 1.54 years.

*The blue line represents the mean difference between reported menarcheal age in Tromsø 3 and Tromsø 4.

3.2 Descriptive and characteristics of participants included in the prospective study

3.2.1 General information regarding participants

The analyses of AAM and mortality included 12 409 women. Mean age for females included in Tromsø 4 was 46.5 years.

There were few missing-values in the dataset. One variable had 3 % missing (this was the maximum missing-value). This was regarded as having no impact on the analyses.

Among the 12 409 females in Tromsø 4, 36.4 % were daily smokers, 40.6 % never smoked and the remaining 23 % were ex-smokers. The mean intake of alcohol was 2.08 times/month. Mean body mass index was 24.75 kg/m^2 and more than half (55.8 %) of the women were moderately active, 24.9 % were active and 19.2 % had a sedate physical activity level. There was 1.4 % (175 women) who had experienced a heart attack and mean age at event was 62.6 years. A total of 45.3 % (5619 women) of the women reported that someone in their close family had a heart attack or angina, while 49 % (6076) had no family history of heart disease (the remaining 5.8 % did not know). There was 1.2 % (146 women) who had experienced a stroke (infarction or brain hemorrhage) with mean age of 54.8 years at first event. Among the 12 409 women, one out of five (20.1 % (2490 women)) suffered from hypertension.

A total of 2203 women died during the mean follow-up of 18.7 years in the investigation of AAM and all-cause mortality. During the mean follow up of 16.7 years in the investigation of CVD mortality, 1838 women died.

3.2.2 Characteristics within menarcheal age groups <12 - >15 years.

The majority of the females in Tromsø 4 were 13 and 14 years old at menarcheal occurrence (27.6 % and 24.9 % respectively). Consequently, a higher mean AAM was observed the older the women were at the examination (Table 2). The p-value for linear trend was significant ($p < 0.001$). In Tromsø 4, the mean age in the youngest menarcheal age group (<12 years) was 41.84 years and the mean age among the oldest menarcheal age group (>15) was 52.81 years. Among the youngest participants in Tromsø 4 (age-group 25-34 years), 11.3 % had menarcheal age of <12 years and 23.2 % had menarcheal age of 12 years. Among the oldest participants in Tromsø 4 (age-group 75+ years), 3.4 % reported menarcheal age <12 years and 10.5 % a menarcheal age of 12 years. Correspondingly, 12.3% in the oldest age-group (75 + years) reported menarcheal age > 16 years, compared to 4.0% in the youngest age group (25-34 years) ($p < 0.001$) (results not presented in tables).

Age (group)	N (%)	Age at menarche Tr4 years
25-34	3212 (25.9)	13.06 (1.35)
35-44	3137 (25.3)	13.15 (1.35)
45-54	2589 (20.9)	13.22 (1.39)
55-64	1524 (12.3)	13.54 (1.36)
65-74	1274 (10.3)	13.87 (1.35)
75-94	673 (5.4)	13.96 (1.42)
Total	12 409 (100)	13.30 (1.32)
P-value for trend		< 0.001

Table 2: Mean age at menarche (standard deviation) according to age-groups in Tromsø 4.

Table 3 present descriptives of the dependent variables by menarcheal age groups. Unadjusted and age-adjusted p-values are for linear trend. Age-adjusted p-values showed the following variables to be significantly different according to menarcheal age groups: systolic blood pressure (p=0.002), diastolic blood pressure (p <0.001), current hypertension (p=0.006) body mass index (p <0.001), triglycerides (p=0.001), HDL (p <0.001) and use of blood pressure treatment (p=0.001). Before adjusting for age, mean systolic and diastolic blood pressure was positively associated with menarcheal age. These observations were statistically significant. After adjusting for age, the association between menarcheal age and both diastolic and systolic blood pressure was reversed. Unadjusted binary regression analysis demonstrated a significant increase in hypertension with increasing menarcheal age. Age-adjustment, however, reversed the results, and presented a significant decrease in hypertension with increasing menarcheal age (OR: 0.94, 95% CI: 0.90 – 0.98, p=0.006). Across all menarcheal ages (except the youngest) >50 % of the women had a normal body mass index. A larger proportion of females were underweight (according to body mass index) in the oldest menarcheal age group (4.6% (32 women)) compared to the youngest menarcheal age group (1.0 % (11 women)). In addition, in the youngest menarcheal age group 16.1 % (180 women) of the women were obese, compared to 9.5 % (66 women) in the oldest menarcheal age group. Regression analysis showed a significant decrease in body mass index on 0.28 kg/m^2 by each year increase in AAM. The p-value for linear trend was highly significant (p < 0.001) before and after adjusting for age.

Mean total cholesterol was positively associated with menarcheal age. This association was no longer present after adjusting for age. Mean triglyceride levels increased with 0.02 mmol/l for each year older AAM. This association was significant after adjusting for age (p=0.001). Also HDL was positively associated with AAM and one category increase in AAM was associated

with an increase of HDL of 0.01 mmol/l. The linear trend was significant before and after adjusting for age ($p < 0.001$).

Descriptive for disease characteristics according to AAM are displayed in table 4. The relationship between AAM and previous heart attack, angina pectoris and stroke was not significant after adjusting for age.

Age adjusted regression analysis of family history of CVD showed a significant inverse association with AAM. One year increase in menarcheal age reduced the odds of having a family member with CVD history, OR=0.92, CI: 0.89 – 0.95. After age-adjustment, one year increase in menarcheal age reduced the odds of being menopausal by 0.92, CI: 0.88 – 0.98. To sum it up: After adjustment for age, the probability of being menopausal or having a family member with CVD decreases with increasing menarcheal age.

	Age at menarche							
	< 12	12	13	14	15	> 15	P-value for linear trend	P-value for linear trend (age adjust.)
N	9.0 (1120)	19.6 (2428)	27.6 (3429)	24.9 (1646)	13.3 (1645)	5.6 (694)		
Age (years)	41.84 (12.12)	43.49 (13.66)	45.22 (14.58)	48.36 (15.56)	50.68 (16.02)	52.81 (16.83)	<0.001	
Systolic blood pressure (mmHg)	128.55 (18.72)	129.57 (20.47)	130.39 (21.17)	132.72 (23.02)	135.04 (24.47)	137.34 (24.56)	<0.001	0.002
Diastolic blood pressure (mmHg)	75.28 (11.73)	75.68 (11.97)	75.39 (12.24)	76.37 (12.73)	77.16 (13.26)	78.17 (13.66)	<0.001	<0.001
Blood pressure treatment								
- **Never**	92.9 (1041)	92.5 (2245)	91.9 (3139)	91.2 (2812)	89.5 (1466)	90.2 (624)	<0.001	0.001
- **Previously**	2.9 (32)	2.5 (61)	2.6 (89)	2.6 (79)	2.7 (44)	2.5 (17)		
- **Currently**	4.2 (47)	4.9 (120)	5.5 (189)	6.2 (191)	7.8 (128)	7.4 (51)		
Current hypertension* :	85.3 (955)	84.1 (2041)	81.5 (2787)	78.1 (2409)	74.5 (1221)	69.2 (478)		
- **No**	14.7 (165)	15.9 (385)	18.5 (631)	21.9 (677)	25.5 (419)	30.8 (213)	<0.001	0.006
- **Yes**								
BMI (kg/m^2)	25.81 (4.64)	25.13 (4.33)	24.67 (4.14)	24.47 (4.07)	24.40 (3.97)	24.24 (4.10)	<0.001	<0.001
BMI								
- **Underweight**	1.0 (11)	1.4 (34)	1.9 (64)	2.8 (86)	2.5 (41)	4.6 (32)		
- **Normal-weight**	49.0 (547)	55.2 (1338)	58.7 (2007)	59.5 (1837)	59.2 (974)	58.4 (405)		
- **Overweight**	33.9 (378)	30.6 (742)	28.5 (975)	27.7 (855)	29.2 (480)	27.4 (190)	<0.001	<0.001
- **Obesity**	16.1 (180)	12.8 (309)	10.9 (371)	10.1 (311)	9.1 (150)	9.5 (66)		
Total cholesterol (mmol/l)	5.81 (1.32)	5.94 (1.34)	5.93 (1.36)	6.12 (1.40)	6.23 (1.40)	6.29 (1.48)	<0.001	0.052
Triglycerides (mmol/l)	1.33 (0.83)	1.33 (0.85)	1.29 (0.83)	1.35 (0.85)	1.35 (0.87)	1.44 (1.01)	0.004	0.001

HDL (mmol/l)	1.60 (0.39)	1.62 (0.40)	1.64 (0.40)	1.66 (0.41)	1.67 (0.41)	1.65 (0.42)	<0.001	<0.001
Alcohol (times/month)	2.09 (2.76)	2.12 (2.99)	2.12 (3.05)	2.12 (3.23)	1.96 (2.92)	1.83 (3.32)	0.042	0.62
Smoking								
- **Never**	39.7 (432)	39.3 (924)	41.1 (1376)	40.4 (1226)	42.4 (687)	40.9 (274)		
- **Previously**	21.9 (238)	22.2 (521)	22.6 (758)	23.3 (708)	24.3 (394)	24.5 (164)	0.008	0.67
- **Currently**	38.5 (419)	38.5 (904)	36.3 (1215)	36.3 (1101)	33.3 (539)	34.6 (232)		
Nulliparity								
- **No**	17.2 (189)	16.4 (391)	16.7 (560)	15.5 (473)	14.4 (232)	13.0 (88)		
- **Yes**	82.8 (913)	83.6 (1992)	83.3 (2802)	84.5 (2572)	85.6 (1383)	87.0 (588)	0.003	0.10
Parity	1.90 (1.31)	1.96 (1.33)	1.97 (1.41)	2.12 (1.51)	2.21 (1.54)	2.31 (1.63)	<0.001	0.26
Physical activity								
- **Sedate**	17.1 (190)	17.7 (425)	18.7 (633)	19.5 (598)	21.2 (344)	25.0 (173)		
- **Moderate**	53.2 (591)	56.5 (1357)	55.3 (1878)	56.0 (1718)	57.5 (935)	55.4 (383)	<0.001	0.64
- **Active**	29.6 (329)	25.8 (619)	26.0 (882)	24.5 (751)	21.3 (346)	19.5 (135)		

Table 3: Descriptive of independent variables according to menarcheal age groups. The descriptive are presented as percentage with number (% (N)) or mean with standard deviation. All variables are presented with p-values and age adjusted p-values for linear trend.

*Hypertension: the combined variable consisting of systolic blood pressure >150 mmHg and/or diastolic blood pressure > 95 and/or currently use of blood pressure lowering drugs.

	Age at menarche							
	< 12	12	13	14	15	>15	P-value for linear trend	P-value for linear trend (age adjust).
Heart attack								
- **No**	99.2 (1107)	99.1 (2404)	98.7 (3382)	98.1 (3027)	98.2 (1614)	97.8 (676)	<0.001	0.57
- **Yes**	0.8 (9)	0.9 (21)	1.3 (43)	1.9 (58)	1.8 (29)	2.2 (15)		
Age at first event (years)	62.88 (7.62)	61.50 (14.29)	62.88 (9.02)	60.43 (12.60)	66.34 (10.55)	62.86 (14.92)	0.47	0.56
Angina Pectoris								
- **No**	98.4 (1099)	98.0 (2375)	96.8 (3315)	96.0 (2963)	95.4 (1571)	94.4 (653)	<0.001	0.54
- **Yes**	1.6 (18)	2.0 (49)	3.2 (110)	4.0 (123)	4.6 (75)	5.6 (39)		
Age at first event (years)	60.12 (11.25)	60.79 (10.08)	60.14 (10.94)	60.92 (10.30)	60.75 (12.76)	61.18 (11.67)	0.68	0.23
Stroke								
- **No**	99.5 (1109)	99.2 (2406)	98.8 (3381)	98.5 (3042)	98.6 (1620)	98.1 (680)	0.001	0.69
- **Yes**	0.5 (6)	0.8 (19)	1.2 (40)	1.5 (45)	1.4 (23)	1.9 (13)		
Age at stroke (years)	65.40 (10.0)	46.41 (22.50)	53.85 (19.13)	56.64 (18.52)	55.39 (19.43)	58.85 (17.67)	0.31	0.40
Diabetes								
- **No**	98.7 (1104)	98.5 (2389)	98.5 (3369)	98.0 (3020)	1612 (98.1)	97.4 (674)		
- **Yes**	1.3 (14)	1.5 (36)	1.5 (52)	2.0 (62)	1.9 (32)	2.6 (18)	0.008	0.29
Age at first event (years)	52.92 (17.28)	54.21 (15.0)	53.08 (17.92)	52.77 (18.88)	52.29 (21.56)	62.41 (17.88)	0.40	0.052
Heart attack or AP in close family								
- **No**	50.0 (527)	51.7 (1189)	53.4 (1735)	51.4 (1495)	52.0 (800)	51.0 (330)	0.82	<0.001
- **Yes**	50.0 (527)	48.3 (1113)	46.6 (1512)	48.6 (1411)	48.0 (739)	49.0 (317)		
Menopause								
- **No**	74.5 (834)	70.0 (1700)	66.5 (2281)	58.5 (1810)	53.0 (873)	48.7 (338)	<0.001	0.004
- **Yes**	25.5 (286)	30.0 (728)	33.5 (1148)	41.5 (1282)	47.0 (773)	51.3 (356)		
Age at menopause (years)	47.14 (5.51)	47.35 (5.52)	47.84 (4.98)	48.02 (4.87)	47.89 (4.82)	48.85 (4.99)	<0.001	0.14

Table 4: Descriptive of disease characteristics according to menarcheal age groups. The descriptives are presented as percentages with numbers (% (N)) or means with standard deviation. The table also includes p-values and age adjusted p-values for all included variables.

3.3 Survival analysis (age-adjusted and adjusted for other covariates)

3.3.1 All-cause mortality

The age-adjusted survival analysis is presented in table 5. No significant association between AAM and death from all-causes before or after adjusting for confounding factors for any categories of menarche (mean AAM (13 years) was reference) (Table 6). Confounding factors included in the analysis were: age (years), body mass index (kg/m^2), physical activity, hypertension, smoking, diabetes and triglycerides (mmol/l) (all which were significantly associated with all-cause mortality). Underweight, low leisure time physical activity, hypertension, smoking and diabetes increased total mortality (Table 5).

After stratification by age (women younger than 60 years and older than 59 years at start of follow up) and adjusted for age, we found that women who were younger than 60 years at start of follow-up *and* had menarcheal age of 15 years had a higher all-cause mortality compared to those who were 13 years at menarche (HR: 1.38, 95% CI; 1.04 – 1.82, p=0.02). No association between menarcheal age and all-cause mortality was observed among women older than 59 years of age in Tromsø 4 (results not presented in tables). No significant linear trend was observed for either age group. When testing for a U-shaped relationship, no significant association was found. The results were essentially the same for current, ex- and never smokers.

Separate multivariate analyses contrasting women with low and high AAM (<13 years vs. 13 + years) indicated a 4.4% higher all-cause mortality among those with a high menarcheal age (13 + years) compared to those with a low menarcheal age (< 13 years). The result was non-significant.

	N (%)	Deaths †	Person years	HR*	CI (95 %)	P-value
AAM:						
- **< 12**	1120 (9.0)	112	21849	1.07	(0.87 – 1.32)	0.51
- **12**	2428 (19.6)	302	46702	0.99	(0.86 – 1.14)	0.90
- **13**	3429 (27.6)	515	65075	1		
- **14**	3092 (24.9)	656	57060	1.05	(0.93 – 1.18)	0.44
- **15**	1646 (13.3)	410	29682	1.00	(0.88 – 1.14)	0.98
- **>15**	694 (5.6)	208	12201	1.10	(0.93 – 1.29)	0.26
Age (years)	12409	2203	232570	1.13	(1.12 – 1.13)	<0.001
BMI (kg/m^2):						
- **Underweight**	268 (2.2)	57	4850	1.72	(1.31 – 2.24)	<0.001
- **Normal-weight**	7108 (57.4)	936	136016	1		
- **Over-weight**	3620 (29.2)	757	66906	0.83	(0.76 – 0.92)	<0.001
- **Obese**	1387 (11.2)	442	24409	0.99	(0.88 – 1.11)	0.84
Physical activity						
- **Sedate**	2363 (19.2)	761	40574	1		
- **Moderate**	6862 (55.8)	1216	129343	0.76	(0.69 – 0.83)	<0.001
- **Active**	3062 (24.9)	198	60354	0.64	(0.55 – 0.76)	<0.001
Hypertension						
- **No**	9891 (80.0)	935	193005			
- **Yes**	2490 (20.0)	1257	39159	1.34	(1.22 – 1.47)	<0.001
Smoke:						
- **Never**	4921 (40.6)	1038	90842	1		
- **Ex-smoker**	2784 (23.0)	455	52432	1.06	(0.95 – 1.18)	0.31
- **Current**	4411 (36.4)	678	83666	1.83	(1.65 – 2.03)	<0.001
Diabetes						
- **No**	12168 (98.3)	2055	229252			
- **Yes**	214 (1.7)	139	2844	2.05	(1.72 – 2.43)	<0.001
Triglycerides mmol/l	12376	2193	231980	1.08	(1.03 – 1.12)	<0.001

Table 5: Survival analysis (age adjusted) for all-cause mortality: with AAM (reference: 13 years of age), age (years), body mass index (kg/m^2) (reference: normal), physical activity (reference: sedate), hypertension (reference: no), smoking (reference: never smoker), diabetes (reference: no) and triglycerides (mmol/l).

*HR: age-adjusted

	N (%)	No. of Deaths †	Person-years	HR (age-adjust.)	CI (95 %)	P-value	HR (adjust.)*	CI (95%)	Adjusted p-value
AAM:									
- **< 12**	1120 (9.0)	112	21849	1.07	(0.87 – 1.32)	0.51	1.05	(0.85 – 1.29)	0.65
- **12**	2428 (19.6)	302	46702	0.99	(0.86 – 1.14)	0.90	0.96	(0.83 – 1.11)	0.55
- **13**	3429 (27.6)	515	65075	1			1		
- **14**	3092 (24.9)	656	57060	1.05	(0.93 – 1.18)	0.44	1.04	(0.92 – 1.17)	0.57
- **15**	1646 (13.3)	410	29682	1.00	(0.88 – 1.14)	0.98	1.02	(0.89 – 1.17)	0.77
- **>15**	694 (5.6)	208	12201	1.10	(0.93 – 1.29)	0.26	1.04	(0.89 – 1.23)	0.61
P-value for linear trend						0.55			0.48

Table 6: Survival analysis (adjusted) of the relationship between AAM and all-cause mortality; age adjusted and adjusted HR for all-cause mortality by menarcheal age groups. Mean menarcheal age (13 years) is used as reference.

*HR age-adjusted: Only adjusted for age

*HR (adjusted): Adjusted for the following confounding factors: Age, BMI, physical activity, hypertension, smoking, diabetes and triglycerides).

3.3.2 Cardiovascular mortality

3.3.2.1 Total CVD mortality

Table 7 presents results from the survival analysis of total cardiovascular mortality (combined stroke, IHD and other CVD causes). A total of 654 women died from CVD during the 16.7 years of follow-up for cardiovascular mortality. No statistically significantly linear association between menarcheal age and total CVD mortality was observed in age adjusted analysis (p=0.1). Results showed that menarcheal age groups <12, 12 and 15 years had a lower CVD mortality, while those in menarcheal age group 14 and >15 had a higher CVD mortality compared to the reference of 13 years. None of the point estimates were statistically significant. After adjusting for the following confounding factors; age, diabetes, physical activity, hypertension, HDL and smoking (all of which were individually significantly associated with CVD mortality after age-adjustment) there was an indication of an increasing trend in CVD mortality with increasing menarcheal age. This was confirmed by a significant p-value (p=0.03) for linear trend and a positive effect estimate. One year increase in AAM was associated with a 7 % increased mortality (HR: 1.07, 95% CI: 1.01 – 1.14, p=0.03).

After stratification by age (<60 and ≥ 60 years), no statistically significant association between AAM and total CVD mortality was observed in either of the age groups.

When comparing low menarcheal age (<13 years) and high menarcheal age (13 + years) there was significant higher CVD mortality among those with a high menarcheal age compared to those with low menarcheal age after adjusting for age, HDL, smoking, physical activity, hypertension and diabetes (HR; 1.40, 95% CI; 1.11 – 1.75, p=0.004).

3.3.2.2 Stroke mortality

Table 8 present results from survival analysis of AAM and stroke mortality. A total of 184 women died from stroke during the follow up of cardiovascular mortality. Age-adjusted survival analysis showed no linear association between AAM and stroke mortality in either direction. Compared to the reference-group of menarcheal age of 13 years, all age-groups (except those >15 years) had a lower stroke mortality. Those who were >15 year at menarche had a 43 % higher stroke mortality compared to the reference-group of 13 years. None of the results were statistically significant. After adjusting for the following confounding factors; age, diabetes, physical activity, alcohol and smoking (all which were significantly associated with increased stroke mortality when being adjusted for age), the same trend in stroke mortality by AAM-groups was observed. The linear trend remained non-significant.

Stratification by age (<60 and ≥ 60) showed no significant association with AAM and stroke mortality in either age- groups.

When comparing low and high menarcheal age, those with high menarcheal age (13+ years) had a 33 % higher stroke mortality compared to those with low menarcheal age (<13 years). The result was not significant (p=0.2).

3.3.2.1 IHD mortality

Results from survival analysis with IHD are presented in table 9. A total of 250 women died from IHD during the follow-up for CVD. Age adjusted survival analysis showed no significant relationship between AAM and IHD mortality. All menarcheal age groups, except those with AAM of 14 years, had a lower IHD mortality compared to the reference-group of 13 years. Those in menarcheal age group of 14 years had 2 % higher IHD mortality compared to the reference

group. All results were non-significant. After adjusting for the following identified confounders: age, diabetes, physical activity level, hypertension, HDL and smoking (all which were significantly associated with IHD mortality after age-adjustment), there was higher IHD mortality in both menarcheal age groups 14 and 15 years compared to the reference group of 13 years. All other menarcheal age groups had a lower IHD mortality. All results remained non-significant.

No significant association between AAM and IHD mortality was observed after stratification by age (<60 and ≥ 60 years in Tromsø 4).

In comparison of low and high menarcheal age, those with a high menarcheal age (13 years +) had 36 % higher IHD mortality compared to those with a low menarcheal age (<13 years). The result was non-significant (p=0.1).

	N	Deaths †	Person years	Death Rate (unadjusted)*	HR (age adj.)	CI (95 %)	HR (adj.)*	CI (95%)	P-value (adj.)*
AAM									
<12	1120	20	19330	1.03	0.76	0.48 – 1.21	0.72	0.45 – 1.15	0.17
12	2428	72	41412	1.74	0.81	0.61 – 1.07	0.75	0.56 – 1.00	0.05
13	3429	155	57789	2.68	1		1		
14	3092	212	50916	4.16	1.07	0.87 – 1.31	1.09	0.89 – 1.35	0.41
15	1646	124	26566	4.67	0.91	0.72 – 1.15	0.95	0.75 – 1.21	0.69
>15	694	71	10970	6.47	1.13	0.86 – 1.50	1.09	0.82 – 1.44	0.56
P-value for trend						0.100			0.03

Table 7: Survival analysis (age adjusted and adjusted) of the relationship between AAM and total CVD mortality:

*HR (adj.): adjusted for age, diabetes, physical activity, hypertension, HDL and smoking (all which were significantly associated with CVD mortality after adjusting for each-other).

* Death rate unadjusted is presented per 1000 person-years.

	N	Deaths †	Person years	Death Rate (unadjusted)*	HR (age adj.)	CI (95 %)	HR (adj.)*	CI (95%)	P-value (adj.)*
AAM									
<12	1120	6	19330	0.31	0.73	0.31 – 1.70	0.72	0.31 – 1.69	0.45
12	2428	21	41412	0.51	0.79	0.47 – 1.32	0.76	0.45 – 1.29	0.30
13	3429	46	57789	0.80	1		1		
14	3092	55	50916	1.08	0.95	0.64 – 1.41	0.99	0.66 – 1.47	0.94
15	1646	30	26566	1.13	0.77	0.48 – 1.22	0.76	0.47 – 1.24	0.27
>15	694	26	10970	2.37	1.43	0.88 – 2.32	1.40	0.86 – 2.28	0.17
P-value for trend						0.21			0.18

Table 8: Survival analysis (age adjusted and adjusted) of the relationship between AAM and stroke mortality:

*HR (adj.): adjusted for age, diabetes, physical activity, hypertension, alcohol and smoking (all which were significantly associated with stroke mortality after adjusting for each-other).

*Death rate unadjusted is presenter per 1000 person-years

	N	Deaths †	Person years	Death Rate (unadjusted)*	HR (age adj.)	CI (95%)	HR (adj.)*	CI (95%)	P-value (adj.)*
AAM									
<12	1120	9	19330	0.47	0.90	0.45 – 1.82	0.84	0.42 – 1.71	0.64
12	2428	27	41412	0.65	0.78	0.49 – 1.22	0.73	0.46 – 1.16	0.18
13	3429	61	57789	1.06	1		1		
14	3092	79	50916	1.55	1.02	0.73 – 1.42	1.09	0.77 – 1.53	0.63
15	1646	50	26566	1.88	0.93	0.64 – 1.35	1.02	0.69 – 1.50	0.93
>15	694	24	10970	2.19	0.96	0.60 – 1.55	0.91	0.57 – 1.47	0.71
P-value for trend						0.62			0.37

Table 9: Survival analysis (age adjusted and adjusted) of the relationship between AAM and IHD mortality:

*HR (adj.) is adjusted for age, diabetes, physical activity, hypertension, HDL and smoking (all which were significantly associated with IHD mortality after adjusting for each-other).

*Death rate (unadjusted) is presented per 1000 person-years

4.0 Discussion

4.1 Reproducibility

4.1.1 Sum up

The reproducibility study demonstrated a strong correlation and a good agreement in self-reported AAM between Tromsø 3 and in Tromsø 4. This correlation strengthened with increasing age.

4.1.2 Our results compared to previous studies

With a total of 6731 women who answered AAM in both Tromsø 3 and Tromsø 4, we had a good opportunity to investigate the reproducibility of self-reported AAM and draw a conclusion which is generalizable for similar populations. We also had the opportunity to make an important contribution to previous research of reproducibility of self-reported events that occurred earlier in life. The oldest woman that participated *and* reported menarcheal age in both Tromsø 3 and Tromsø 4 was 73 years in 1994. She was 66 years at the time of the Tromsø 3 survey, and is the oldest woman eligible for analyses for reproducibility. Since there are women in our dataset aged 25-73 years in Tromsø 4 that reported AAM in both Tromsø 3 and Tromsø 4, we also had the opportunity to investigate the correlation of reported menarcheal age between different age-groups. One might hypothesize that the recall of menarcheal age could decrease with increased age due to the length of time since the event occurred. This have been observed in a previous study which investigated the validity of self-reported AAM (39). There were few women with high attained age eligible for analyses. Only 1 % (N=65) of the 6731 women that answered menarcheal age in Tromsø 3 and Tromsø 4 were older than 65 years of age in Tromsø 4. Despite this, we included the older women in our reproducibility study and kept in mind that the limited

number of females for comparison might weaken the possibility for concluding for this age group.

If there is a low concordance between reported menarcheal age at two points in time there will be non-differential misclassification in the survival analyses. If the self-reported variable is not reliable, the use of self-reported AAM cannot be recommended for research purposes.

Previous studies support our findings of a high reproducibility of reported AAM (36, 38, 41). No other studies with such a large study population or such a strong correlation of self-reported AAM as we found here, was identified. This especially applies to the group with the highest attained age in Tromsø 4, where the correlation between reported AAM at two points in time was high (r = 0.91). It should be noted that the length of follow-up in the reproducibility study was only 7 years. Tromsø 3 was the first survey where AAM was reported and a follow-up of 7 years was the maximum length possible in this sample. As mentioned above, there were few participants in the oldest age group for comparison (65 participants). There are no data available for older women.

Previous studies have tried to explain why age of menarche is well remembered and hypothesize that either menarche is remembered as an awkward, embarrassing event, or it is experienced as a "gift", welcoming the girl to adulthood. Either way, the event in itself is an important milestone that seems to be well remembered among most females (49, 50). One previous article from Brazil that investigated how women related to the menarcheal event, showed that the mothers reaction to the occurrence of menarche had a large impact on how the girls experience menarche, either in a positive or negative direction (49). A review with combined results from 14 studies regarding experience of menarche, summed up the 5 following concepts as important for how girls

experience their first menstruation; how well they are prepared for the occurrence of menarche, the response from significant others, physical- and psychological experience of menarche and the socio-cultural perspective of menarche (51). The menarcheal event seems to be an important milestone to most girls, independent of culture and religion. However, the difference in how girls experience menarche is large, and while some remember it as an event that lead to awkward conversations and shame, other cultures celebrated the girls as they reached menarche. Both a negative and a positive association of the menarcheal occurrence would most likely be remembered and linked to an approximate place, time and age of event. This explains why both validity and reproducibility of these types of events normally are accurate and strong.

4.2 All-cause mortality

4.2.1 Sum up

There was no association between AAM and mortality from all-causes before or after adjusting for confounding factors. When adjusted for age only, there was a visual indication of a U - shaped relationship between AAM and all-cause mortality, where both those in the youngest and those in the oldest menarcheal age groups had a higher all-cause mortality compared to those with menarcheal age of 13 years. After adjusting for potential confounders this u-shaped association was still visually present but weakened. None of the results were significant, and no statistically significant U-shaped relationship was identified.

4.2.2. Our results compared to previous studies

Previous studies have concluded that there may be a significant inverse relationship between AAM and all-cause mortality. This is not in line with our results. The review by Charalampopoulos et al. (17), which included 9 studies that investigated the relationship between AAM and death from all-causes, cardiovascular death, stroke and death from IHD, found an

association between AAM and death from all-causes. They report that two of the included studies showed a U-shaped association between AAM and death from all-causes, which is consistent with the visual observations of estimates in the all-cause survival analysis. One study observed a U-shaped (or an inversed J-shaped) association between AAM and all-cause mortality as they found a higher all-cause mortality among those with a high menarcheal age (18 or 19 years) and among those with a low menarcheal age (< 14 years) compared to menarcheal age of 14 years (35). However, the U-shaped association in our findings did not remain after being tested statistically.

Wu et al. (22), (not included in the review) confirm an inverse association between AAM and all-cause mortality. Lakshman et al. (20), (included in the review) observed that those in the younger categories for age at menarche had higher body mass index, hypertension, elevated cholesterol and triglyceride levels, and higher glycated hemoglobin (that is strongly related to risk of diabetes). They report that those in the younger menarcheal age groups were more likely to have a history of heart attack in their close family and were more likely to use blood pressure lowering drugs (20). This is similar to our findings where hypertension, increased body mass index, increased triglycerides, increased total cholesterol and decreased HDL is significantly associated with decreasing AAM after adjusting for age.

Despite these corresponding results for risk factors for mortality with previous studies, we do not find an association between menarcheal age and all-cause mortality. It has been suggested that the women with a late menarcheal age alone, or in addition to a high menopausal age could have a lower mortality because these women are biologically younger than their actual age reflects (35). If the latter hypothesis was true in our study sample, we should have found a relationship between increased menarcheal age and decreased all-cause mortality, but none of the results

regarding all-cause mortality and AAM were significant. We have no obvious explanation to why our result contrasts from other studies. A potential explanation is that we have adjusted for numerous confounders which might not have been done in all previous studies.

4.3 Cardiovascular disease mortality

4.3.1 Sum up

Both age-adjusted analysis and adjusted analyses for stroke and IHD were non-significant and no linear association was observed in either direction. Adjusted analyses for total CVD mortality did, however, show a significant positive linear association between AAM and total CVD.

4.3.2 Our results compared to previous studies

The majority of previous studies have observed an inverse relationship between AAM and death from CVD. This is not in accordance with our results. In contrast, some previous studies did not find a significant association between menarcheal age and CVD mortality. This corresponds to our results regarding total CVD, IHD and stroke mortality according to menarcheal age categories. Charalampopoulos et al. (17), did not observe a significant association between AAM and CVD mortality in combined analysis. Palmer et al. (52), did not find a relationship between AAM and risk for myocardial infarction either, in their case-control study. They discuss that there is probably a presence of recall bias, as AAM occurred approximately 30-50 years earlier. They state that sorting this misclassification would however probably not have changed their end-result (52). In a combined dataset from three different case-control studies from Italy, they did not find an increased risk of myocardial infarction among those with young menarcheal age (<12 years) compared to those with older menarcheal ages (up to >15 years) (53). A review of "Reproductive history and cardiovascular disease risk in postmenopausal women" found that in the 4 included studies that investigated AAM, there was no effect of AAM on cardiovascular

disease among the postmenopausal women (53). There could be limited relevance for our study as they only searched the Medline database and only included postmenopausal women. However, the mean age at occurrence of CVD death in our dataset was 72 years and the majority of the women were in fact postmenopausal. One of the 4 studies included in the review, by Colditz et al. (54), reported that they did not find a significant association between menarcheal age and coronary heart disease, even when comparing menarcheal age <11 and >15 years. These studies correspond to our findings with regards to total CVD, IHD and stroke mortality according to menarcheal age categories, but not our results of a significant higher CVD mortality among those with a menarcheal age of 13 years or older compared to those younger at 13 years at menarche.

We did find a significant association between AAM and family history of heart attack or angina, after adjusting for age only, where increased menarcheal age decreased the odds of having heart attack or angina in close family. This is in line with the findings from Lakshman et al. (20), mentioned above.

Some previous studies show a positive relationship between menarcheal age and CVD mortality. This corresponds to our adjusted p-value for linear trend for total CVD mortality and in the comparison of those with menarcheal age of 13 years and older with those younger than 13 years of age. Cui et al. (55), found that those with a high menarcheal age (>17 years) have a higher risk for CVD compared to those with a low menarcheal age (<13 years). They suggest that this could be attributed to a protective effect from estrogen on CVD, and that menarcheal age is a marker for estrogen exposure (as presented when explaining the association between AAM, estrogen and breast cancer). The same hypothesis was presented by De Kleijn et al. (53), who states that it is widely believed that estrogen protects women from cardiovascular disease. These statements have been frequently investigated, as one previously believed that if estrogen has a

protective effect for CVD in premenopausal age, then estrogen therapy in postmenopausal age should decrease the risk for CVD in this age group. Previous studies show contradictive results regarding this and a recently conducted review by The Cochrane Library showed no protective effect of estrogen therapy on CVD in postmenopausal women (56).

Premenopausal estrogen exposure reduces the risk of cardiovascular disease through several mechanisms; both genomic, non-genomic and systemic which protects women in reproductive age against cardiovascular disease (57). Estrogen contributes in the regulation of important vascular functions like blood pressure, vasodilatation and -constriction of blood vessels. In addition it has important effects on some of the major determinants for the development of atherosclerosis, e.g. effect on the blood lipids, leading to an increased level of HDL and triglycerides and decreased LDL cholesterol, which again decreases the risk for atherosclerosis (57, 58). Among the women who died from CVD in our sample, 73.9 % were postmenopausal in Tromsø 4, and could, based on the latter explanation, have a higher risk for CVD because they were no longer exposed to high levels of estrogen.

Previous studies illustrating an inverse association between AAM and CVD mortality have tried to explain why such an association occurs. A proposed explanation is that lower menarcheal age seems to be associated with an increase in the risk factors related to metabolic syndrome and further cardiovascular disease (2, 27, 32, 33). Metabolic syndrome is the combination of a group of risk factors that further increases the risk for cardiovascular disease, stroke and diabetes. These risk factors are: a large waist circumference, elevated triglyceride levels, low HDL cholesterol, hypertension and high fasting blood sugar (related to diabetes) (59). In our study, even though no inverse association between categories of AAM and death from CVD was found, there was an

association between AAM and 4 of the 5 included risk factors mentioned above (when using high body mass index as an indicator of increased waist-line).

The inverse relationship between menarcheal age and body mass index has been suggested to be related to childhood body mass index and weight. High body mass index and high weight in childhood is presented as one of the determining factors for earlier AAM (60-62). This could be related to the role of the "fat-protein" leptin, which has been hypothesized to be the link between increased body mass index, fat distribution and earlier menarche. It is also well documented that elevated childhood body mass index is linked to higher body mass index in adulthood (26, 63, 64). It could, for later research, be interesting to include an additional question regarding the women's childhood body mass index. A previous study concludes that women remembered their childhood body mass index, or body size, with high accuracy, and that self-reported childhood body mass index or body size is satisfactory for research purposes (38).

4.4 Other findings and previous studies

Some previous studies have suggested that there is higher occurrence of risk-taking behavior like early sexual intercourse and more unprotected sex (before the age of 15-16) , earlier alcohol drinking, drunken experiences and smoking among girls with early menarcheal age (28, 29). This behavior could be linked to the experiences of early maturation, and the emotion of entering adulthood could be strengthened by exploring behavior associated to being an adult. How girls relate to the occurrence of menarche is affected by, among other; culture, their knowledge regarding the menarcheal event and the views regarding menarche of their parents, guardian or next of kin (51, 65). In our study no association between smoking, alcohol and AAM was observed after adjusting for age. Both variables (alcohol and smoking) are subject to under-reporting due to their commonly known negative effects. However, a previous review presented

that self-reported smoking appeared valid in most included studies and was therefore regarded accurate enough for research purposes (66).

Both unadjusted analysis of previous occurrence of heart attack, angina pectoris, and stroke, in addition to unadjusted survival analysis showed a significant higher risk for event among the oldest menarcheal age group. These associations were no longer present after age-adjustment. The reversed trend after age-adjustment is most likely linked to the secular trend of menarche. The older women in the study experienced a higher menarcheal age than the younger women and it is well documented that the risk for heart attack, AP and stroke increases with increasing age. This explains the reversed results after age-adjustment.

Previous studies support our findings regarding the decreasing trend for menarcheal age according to time. Chang et al. (4), investigated how AAM changed from one generation to another. They found that the distribution of AAM decreased by approximately one year from one generation to the next (from grandmother to granddaughters). The secular trend of AAM has been confirmed by several previous studies. A recent study from China found that menarcheal age decreased significantly from 1985 to 2010 among both urban and rural girls (6). There was a more rapid decline in AAM among rural girls, but this difference was reduced after year 2005 (the difference in 1985 and 2010 was 0.66 years and 0.24 years, respectively). They state that "correlation analysis showed that AAM was significantly and negatively associated with per capita GDP and consumption level, both in 1985 and 2010" (6, p. 4). This could explain why a decreasing menarcheal trend in relation to increasing living standards has been observed. Zhu et al. (6), also discuss that the improved living standards in rural areas could be the reason why the difference between menarcheal age in rural and urban areas have decreased. Two suggested explanations for the secular trend in age at menarche is; increased body weight and increased

energy intake. Both factors are strongly related to income and living standards. These changes in lifestyle have been observed in Tromsø (and Norway) as well as other high income countries around the world. This could partly explain why the secular trend is observed more rapidly in high income areas. Despite this, the secular trend in menarcheal age is suggested to be stabilizing in Europe, while it is still declining other parts of the world (5, 6). This stabilization might be attributed to the increased focus on healthy diets and physical activity related to the obesity epidemic the developed world is facing.

4.5 Limitations and strengths

4.5.1 Limitations

This study has some limitations. There is no available information regarding the women's physical appearance (weight and height) or physical activity level before menarche occurred. Characteristics and physical appearance in childhood follow individuals to adulthood, e.g. high childhood body mass index is closely linked to high body mass index in adulthood. In addition, these factors (e.g. physical activity and childhood weight) influence at what age menarche occur. It would have been interesting to know more about the women’s physical appearance during childhood, and to investigate if this was associated to AAM and adult physical characteristics (like blood pressure, blood lipids etc.) in our population. It is also possible that childhood characteristics could affect the risk for premature mortality due to increased length of exposure to risk factors, and mortality according to childhood characteristics could have been tested.

There is a possibility of information bias due to subjective self-reporting in the original scheme. This especially concerns behavioral factors like smoking and alcohol consumption which could be “victim” to under-reporting due to their well-known negative effects. Also AAM, which is a

private matter, could be influenced by information-bias; if actual recalled menarcheal age occurred very early or very late compared to the social-circle of the woman, there is a possibility that she would rather report a menarcheal age similar to the known mean. If women do not report menarcheal age similar to the actual AAM, it would affect our conclusion. It is difficult to completely control for this potential bias other than by carrying out a prospective follow-up from pre-menarcheal childhood to adulthood to secure that the information regarding menarcheal age is valid, but this would be very costly. Previous investigations of the validity of self-reported menarche have concluded that women recall their menarcheal age specific enough to be used for research purposes (38, 39). In our study, previously reported AAM was very similar to reported AAM after 7 years of follow-up. This indicates, based on previous research that it is unlikely that reported AAM differ widely from actual AAM. Recall-bias regarding AAM is therefore not considered to be a problem in this study. One should however be aware that a high reproducibility does not confirm a high validity.

Another potential limitation is misclassification of CVD. There could be misclassification in both directions; deaths due to other causes could be misclassified as CVD deaths or deaths due to CVD could be misclassifies as deaths due to other causes. One can never be certain that all CVD causes are classified correctly or that none are "lost" due to misclassification if autopsies are not performed. Autopsies are seldom performed in Norway without special request. A larger study population would have given more strength to our findings, but we do not believe that this would have changed our final results.

4.5.2 Strength

This study has several strengths. It includes a large study-sample of 12 409 women, where 6731 women participated and answered the question regarding AAM in both Tromsø 3 and Tromsø 4.

This made it possible to include a reproducibility study to the analyses and strengthen the results from previous studies reporting a high correlation between self-reported AAM at different points in time. The response rate in the Tromsø study is high (74.9%), and after excluding those who did not report AAM, 65% of the women who were invited are included in our analyses. The results are believed to be representative for women in Tromsø, Norway and other areas with similar living conditions. Another strength is that physical examinations were performed by trained health care professionals. In addition the participants were provided with guidance when answering the questionnaire and the risk of bias due to misunderstanding questions or wrongfully reporting numbers from the physical examination is minimal.

4.6 External validity/generalizability

The results in this study are based on a large sample of the female population in Tromsø. As living-conditions in Tromsø are similar to those of other high-income areas there is reason to believe that the 12 409 women in Tromsø 4 are representative for the general female population and that our results have external validity. Also the reproducibility between self-reported menarcheal age in Tromsø 3 and Tromsø 4, which was investigated among 6731 women, is considered to be generalizable for populations living within the same conditions as the women from Tromsø. It is however an important factor that the follow-up only was 7 years, and that the length of follow-up was the maximum possible without including any more of the Tromsø surveys.

4.7 Implications

Implications from this study, even though we found no association between AAM and all-cause mortality and only weak evidence for a positive relationship with CVD mortality, is not to pursue a change in menarcheal age. We would rather aim to increase the knowledge regarding female

reproductive health and how reproductive factors could potentially affect health later in life. One should not deliberately influence menarcheal age. Conditions or behavior that is known to delay AAM is anorexia nervosa or excessive training and neither of these is preferable compared to early AAM as both conditions impose a major increased risk for morbidity and mortality compared to earlier AAM. Increased knowledge is in itself a contribution to the ongoing battle against lifestyle-diseases. When there is an indication that AAM could affect both CVD mortality and changeable risk factors like hypertension, higher blood lipid levels, higher body mass index etc. there should be an increased focus on preventive measures among women in the high risk-group. The contribution from the reproducibility study strengthens the results from previous studies, confirming that self-reported AAM is satisfactory for research purposes.

5.0 Conclusion

There is no significant association between categories of menarcheal age groups and all-cause mortality among the female population in Tromsø. There is, however, an indication of a positive relationship between total CVD mortality and menarcheal age (presented by the p-value for linear trend). As far as we were able to investigate, there is no systematic difference in, and a high correlation between self-reported AAM in Tromsø 3 and reported menarcheal age in Tromsø 4 (7 years later). This association strengthened by age. The highest correlation coefficient was found among the oldest age group available for comparison. The need for further studies should be emphasized. The results of no association between AAM and mortality (especially all-cause) do not fit with previous studies on the subject. Almost all previous studies observed an inverse association between earlier AAM and either all-cause or CVD mortality. It would also be interesting to investigate the reproducibility of menarcheal age with a longer period of follow-up.

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Appendix 1

Invitation and questionnaire 1 -Tromsø 4

Du er innbudt til den store helseundersøkelsen i Tromsø kommune 1994 - 95

Vi når fram til alle

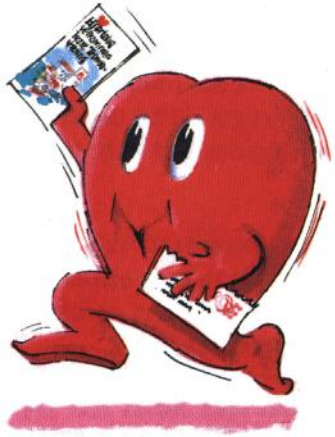
Vi begynner i de ytre distriktene i kommunen. Her vil undersøkelsen pågå i skolehus og andre lokaler - se opplysningene i innbydelsen som følger dette brevet.
Fra slutten av oktober 1994 til sommeren 1995 vil undersøkelsen foregå i Mellomveien 50 (Elisabeth-senteret; den gamle kvinneklinikken). Vi ser helst at du møter på stedet som er oppført i innbydelsesbrevet.

Hvorfor har du fått tilbudet ?

Fordi vi tilbyr undersøkelsen til alle som er født i 1969 eller tidligere.

Hva er formålet ?

Undersøkelsen er i første rekke rettet mot hjerte-karsykdom, men er også viktig for å få ny viten om andre alvorlige kroniske sykdommer (bl.a. kreft).
Denne gangen vil en i tillegg se spesielt på smertetilstander i muskler og skjelett, blant annet fibromyalgi. Derfor vil noen høsten 1995 bli invitert til en spesialundersøkelse.
Store hjerte-karundersøkelser ble gjort i Tromsø i 1974, 1979-80 og 1986-87. Det var stort frammøte, og det ble funnet en rekke tilfeller av hjerte-karsykdom - som nå får behandling.
Undersøkelsene har også gitt oss viktig kunnskap for å bekjempe disse sykdommene. Den kunnskap vi har fått gjennom de tidligere undersøkelsene, har gjort Universitetet i Tromsø til et av de fremste forskningsmiljøer i verden på hjerte-karsykdommer. Også denne gangen tar vi sikte på å finne personer som har hjerte-karsykdom uten å vite det. Vi vil også gjerne nå dem som har særlig høy risiko, slik at de kan få tilbud om forebygging og andre tiltak som kan hindre at sykdom utvikler seg. Hjerte-karsykdom er fortsatt et av våre største helseproblemer.



Ikke bare for din egen skyld.....

Undersøkelsen har ikke bare betydning for deg personlig. Det er også viktig at resultatene blir brukt i medisinsk forskning, bl.a. ved at vi sammenholder dem med framtidig forekomst av sykdom. Dermed lærer vi mer om hvordan hjerte-karsykdom, kreft og andre folkesykdommer oppstår og hvordan de kan forebygges. Ved å møte fram er du med i kampen mot disse sykdommene.

Undersøkelsen omfatter

- **Måling av høyde og vekt**
- **Måling av blodtrykk**
- **Blodprøve.** I denne måler vi innholdet av fettstoffer (bl.a. kolesterol), kalk og et leverenzym. Resultatet av disse målingene sendes din lege om du ønsker det. Resultatet av andre prøver blir bare brukt til medisinsk forskning. Prøven blir frosset ned, slik at det senere kan måles andre stoffer om det blir nødvendig for utforskning av sykdom. Før slike målinger blir gjort, blir studien forelagt den forskningsetiske komité for Nord-Norge.
- **EKG** er en undersøkelse som registrerer hjertets aktivitet. Den gjøres på en forenklet måte, og registreringene blir bare brukt til forskning.

- **Spørreskjema**
- **Spesialundersøkelse.** Alle født mellom 1920-1939, og et utvalg av de øvrige, blir tilbudt en mer omfattende undersøkelse gratis. Hva undersøkelsen omfatter varierer noe, men gir en bedre beskrivelse av hjertet, hovedpulsårens funksjon, åreforkalkning, og tendens til beinskjørhet. Du får time til undersøkelsen ved frammøte.

Spørreskjema

Dette finner du på baksiden av det brevet du har fått. Vennligst fyll ut skjemaet på forhånd og ta det med til undersøkelsen. Dersom enkelte spørsmål er vanskelige å fylle ut, kan du få hjelp når du møter fram.

Om samtykke

Opplysningene om deg blir behandlet strengt fortrolig. De oppbevares og brukes etter regler gitt av Datatilsynet og den forskningsetiske komité for Nord-Norge. For at opplysningene skal brukes i medisinsk forskning, må du samtykke til det. Samtykke er også nødvendig for at din lege skal få resultat av de målinger som gjøres (og som du selv får tilsendt resultat av) og svar du gir på spørreskjemaet som ligger ved dette brevet. Vi ber derfor at du ved frammøte samtykker i:

- at melding om dine resultat sendes til din faste lege, og inngår i din journal hos legen.
- at blodprøven kan brukes til analyser som ledd i medisinsk forskning. Hensikten med slike analyser er å forstå årsak til sykdom.
- at dine resultater kan brukes til medisinsk forskning, ved å sammenholde opplysningene med andre helse- og sykdomsregister (f.eks. kreftregister og dødsårsaksregister) og opplysninger fra de tidligere helseundersøkelsene i Tromsø. Før opplysningene analyseres, blir navn og person-nummer fjernet. Selv om du gir samtykke, kan du senere reservere deg mot bruk av dine resultat.

Etterundersøkelse

Noen av dem som blir undersøkt, blir senere innkalt til egen lege for nærmere kontroll. Trenger du behandling, får du tilbud om det.

Hva koster undersøkelsen ?

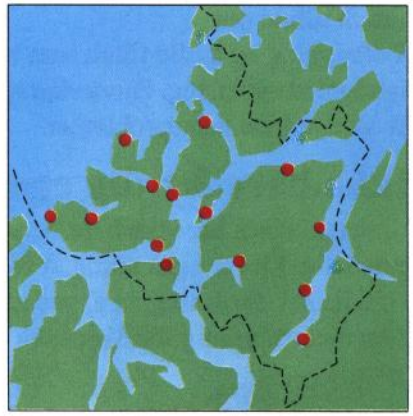
Det er nødvendig med en egenandel ved undersøkelsen. Den er beskjeden i forhold til de totale kostnadene. Beløpets størrelse vil du finne i brevet du nå har mottatt. Spesialundersøkelsen er gratis. Trenger du ny undersøkelse hos egen lege eller ved Regionsykehuset, betaler du vanlig egenandel.

Antrekk

Av hensyn til blodtrykkmålingen ber vi om at du tar på plagg uten ermer eller med korte ermer som ikke strammer. Det er ikke nødvendig å ta av seg på overkroppen.

Steder som får besøk av helseundersøkelsen

- Kaldfjord
- Tromvik
- Lakselvbukt
- Sjursnes
- Breivikeidet
- Fagernes
- Skittenelv
- Ersfjordbotn
- Straumsbukta
- Brensholmen
- Vikran
- Trondjord
- Sjøtun
- Tromsø sentrum



Vel møtt!

Hjertelig hilsen

- Kommunehelsetjenesten
- Fagområdet medisin, Universitetet i Tromsø

Statens helseundersøkelser

Repro & Skive A/S 380 96 955

Hjertelig velkommen, kjære Tromsøværing

Innbydelse til

HELSEUNDERSØKELSEN

Fødselsdato	Personnr.	Kommune	Kretsnr.

Velkommen til helseundersøkelsen i Tromsø!

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

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

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

Vennlig hilsen
Kommunehelsetjenesten
Fagområdet medisin, Universitetet i Tromsø
Statens helseundersøkelser

EGEN HELSE

Hvordan er helsen din nå? *Sett bare ett kryss.*

Dårlig	12	1
Ikke helt god		2
God		3
Svært god		4

Har du, eller har du hatt:

	JA	NEI	Alder første gang
Hjerteinfarkt 13			år
Angina pectoris (hjertekrampe) 16			år
Hjerneslag/hjerneblødning 19			år
Astma 22			år
Diabetes (sukkersyke) 25			år

Bruker du medisin mot høyt blodtrykk?

Nå	28	1
Før, men ikke nå		2
Aldri brukt		3

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? 29 — JA / NEI

Har du de siste to ukene følt deg:

	Nei	Litt	En god del	Svært mye
Nervøs og urolig? 30				
Plaget av angst? 31				
Trygg og rolig? 32				
Irritabel? 33				
Glad og optimistisk? 34				
Nedfor/deprimert? 35				
Ensom? 36				
	1	2	3	4

RØYKING

Røykte noen av de voksne hjemme da du vokste opp? 37 — JA / NEI

Bor du, eller har du bodd, sammen med noen dagligrøykere etter at du fylte 20 år? 38 — JA / NEI

Hvis "JA", hvor mange år tilsammen? 39 — Antall år

Hvor lenge er du vanligvis daglig tilstede i røykfylt rom? 41 — Antall timer

Sett 0 hvis du ikke oppholder deg i røykfylt rom.

Røyker du selv:

	JA	NEI
Sigaretter daglig? 43		
Sigarer/sigarillos daglig? 44		
Pipe daglig? 45		

Hvis du har røykt daglig tidligere, hvor lenge er det siden du sluttet? 46 — Antall år

Hvis du røyker daglig nå eller har røykt tidligere:

Hvor mange sigaretter røyker eller røykte du vanligvis daglig? 48 — Antall sigaretter

Hvor gammel var du da du begynte å røyke daglig? 52 — Alder år

Hvor mange år tilsammen har du røykt daglig? 54 — Antall år

MOSJON

Hvordan har din fysiske aktivitet i fritiden vært det siste året? *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)* 56				
Hard fysisk aktivitet *(svett/andpusten)* 57				
	1	2	3	4

KAFFE

Hvor mange kopper kaffe drikker du daglig?
Sett 0 hvis du ikke drikker kaffe daglig.

Kokekaffe	58	Antall kopper
Annen kaffe	60	Antall kopper

ALKOHOL

Er du total avholdsmann/-kvinne? 62 — JA / NEI

Hvor mange ganger i måneden drikker du vanligvis alkohol? *Regn ikke med lettøl.*
Sett 0 hvis mindre enn 1 gang i mnd. 63 — Antall ganger

Hvor mange glass øl, vin eller brennevin drikker du vanligvis i løpet av to uker? 65
Regn ikke med lettøl.
Sett 0 hvis du ikke drikker alkohol.

Øl	Vin	Brennevin
glass	glass	glass

FETT

Hva slags margarin eller smør bruker du vanligvis på brødet? *Sett ett kryss.*

Bruker ikke smør/margarin	71	1
Meierismør		2
Hard margarin		3
Bløt (soft) margarin		4
Smør/margarin blanding		5
Lettmargarin		6

UTDANNING/ARBEID

Hvilken utdanning er den høyeste du har fullført?

Grunnskole, 7-10 år, framhaldsskole, folkehøgskole	72	1
Realskole, middelskole, yrkesskole, 1-2-årig videregående skole		2
Artium, øk.gymnas, allmennfaglig retning i videregående skole		3
Høgskole/universitet, mindre enn 4 år		4
Høgskole/universitet, 4 år eller mer		5

Hva slags arbeidssituasjon har du nå?

Lønnet arbeid	73	
Heltids husarbeid	74	
Utdanning, militærtjeneste	75	
Arbeidsledig, permittert	76	

Hvor mange timer lønnet arbeid har du i uka? 77 — Antall timer

Mottar du nå noen av følgende ytelser?

Syketrygd (sykmeldt)	79	
Attføring	80	
Uførepensjon	81	
Alderspensjon	82	
Sosialstøtte	83	
Arbeidsløshetstrygd	84	

SYKDOM I FAMILIEN

Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)? 85 — JA / NEI / VET IKKE

Appendix 2

Questionnaire 2 -Tromsø 4

(< 70 years)

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 ..... 17 ❑

Dag Mnd År

Dato for utfylling av skjema: ..... 18 ...../...../.....

OPPVEKST

I hvilken kommune bodde du da du fylte 1 år?

..... 24 - 28

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

Hvordan var de økonomiske forhold i familien under din oppvekst?

- Meget gode ..... 29 ❑
- Gode ..... ❑
- Vanskelige ..... ❑
- Meget vanskelige ..... ❑

Hvor mange av de første 3 årene av ditt liv
- bodde du i by? ..... 30 _____ år
- hadde dere katt eller hund i hjemmet? ..... 31 _____ år

Hvor mange av de første 15 årene av ditt liv
- bodde du i by? ..... 32 _____ år
- hadde dere katt eller hund i hjemmet? ..... 34 _____ år

BOLIG

Hvem bor du sammen med?

Sett ett kryss for hvert spørsmål og angi antall.		Ja	Nei	Antall
Ektefelle/samboer	36	❑	❑	
Andre personer over 18 år	37	❑	❑	_____
Personer under 18 år	40	❑	❑	_____

Hvor mange av barna har plass i barnehage? ..... 43 _____

Hvilken type bolig bor du i?
- Enebolig/villa ..... 45 ❑ 1
- Gårdsbruk ..... ❑ 2
- Blokk/terrasseleilighet ..... ❑ 3
- Rekkehus/2-4 mannsbolig ..... ❑ 4
- Annen bolig ..... ❑ 5

Hvor stor er din boenhet? ..... 46 _____ m^2

I omtrent hvilket år ble boligen bygget? ..... 49 _____

		Ja	Nei
Er boligen isolert etter 1970?	53	❑	❑
Bor du i underetasje/kjeller?	54	❑	❑
Hvis "Ja", er gulvbelegget lagt på betong?	55	❑	❑

Hvordan er boligen hovedsakelig oppvarmet?
- Elektrisk oppvarming ..... 56 ❑
- Vedfyring ..... ❑
- Sentralvarmeanlegg oppvarmet med:
  - Parafin ..... ❑
  - Elektrisitet ..... ❑

		Ja	Nei
Er det heldekkende tepper i stua?	60	❑	❑
Er det katt i boligen?	61	❑	❑
Er det hund i boligen?	62	❑	❑

ARBEID

Hvis du er i lønnet eller ulønnet arbeid, hvordan vil du beskrive ditt arbeid?
- For det meste stillesittende arbeid? ..... 63 ❑ 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 ..... 64 ❑ 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?	65	❑	❑

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

Sett ett kryss for hvert spørsmål.		Ja	Nei
Sjåfør	66	❑	❑
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 69	❑	❑	_____
Brudd ved håndledd/underarm 72	❑	❑	_____
Nakkesleng (whiplash) 75	❑	❑	_____
Skade som førte til sykehusinnleggelse 78	❑	❑	_____
Sår på magesekken 81	❑	❑	_____
Sår på tolvfingertarmen 84	❑	❑	_____
Magesår-operasjon 87	❑	❑	_____
Operasjon på halsen 90	❑	❑	_____

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

	Ja	Nei
Kreftsykdom 93	❑	❑
Epilepsi (fallesyke)	❑	❑
Migrene	❑	❑
Kronisk bronkitt	❑	❑
Psoriasis	❑	❑
Benskjørhet (osteoporose) 98	❑	❑
Fibromyalgi/fibrositt/kronisk smertesyndrom	❑	❑
Psykiske plager som du har søkt hjelp for	❑	❑
Stoffskiftesykdom (skjoldbruskkjertel)	❑	❑
Sykdom i leveren	❑	❑
Nyrestein 103	❑	❑
Blindtarmsoperasjon	❑	❑
Allergi og overfølsomhet		
Atopisk eksem (f.eks. barneeksem)	❑	❑
Håndeksem	❑	❑
Høysnue	❑	❑
Matvareallergi 108	❑	❑
Annen overfølsomhet (ikke allergi)	❑	❑

Hvor mange ganger har du hatt forkjølelse, influensa, "ræksjuka" og lignende siste halvår? ..110 ____ ganger

	Ja	Nei
Har du hatt dette siste 14 dager? 112	❑	❑

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 113	❑	❑	❑	❑	❑	❑
Hjerteinfarkt før 60 års alder 119	❑	❑	❑	❑	❑	❑
Kreftsykdom 125	❑	❑	❑	❑	❑	❑
Astma 131	❑	❑	❑	❑	❑	❑
Mage/tolvfingertarm-sår 137	❑	❑	❑	❑	❑	❑
Benskjørhet (osteoporose) 143	❑	❑	❑	❑	❑	❑
Psykiske plager 149	❑	❑	❑	❑	❑	❑
Allergi 155	❑	❑	❑	❑	❑	❑
Diabetes (sukkersyke) 161	❑	❑	❑	❑	❑	❑
– alder da de fikk diabetes 167	____	____	____	____	____	____

SYMPTOMER

	Ja	Nei
Hoster du omtrent daglig i perioder av året? 177	❑	❑
Hvis "Ja":		
Er hosten vanligvis ledsaget av oppspytt? 178	❑	❑
Har du hatt slik hoste så lenge som i en 3 måneders periode i begge de to siste år? 179	❑	❑
Har du hatt episoder med piping i brystet? 180	❑	❑
Hvis "Ja", har dette oppstått:		
Sett ett kryss for hvert spørsmål.		
Om natten 181	❑	❑
Ved luftveisinfeksjoner	❑	❑
Ved fysiske anstrengelser	❑	❑
Ved sterk kulde	❑	❑
Har du merket anfall med plutselig endring i pulsen eller hjerterytmen siste år? 185	❑	❑

Hvor ofte er du plaget av søvnløshet?

Aldri, eller noen få ganger i året 186	❑ 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 187	❑ 1
Særlig i mørketiden	❑ 2
Særlig i midnattsoltiden	❑ 3
Særlig vår og høst	❑ 4

	Ja	Nei
Har du det siste året vært plaget av søvnløshet slik at det har gått ut over arbeidsevnen? 188	❑	❑

Hvor ofte er du plaget av hodepine?

Sjelden eller aldri 189	❑ 1
En eller flere ganger i måneden	❑ 2
En eller flere ganger i uken	❑ 3
Daglig	❑ 4

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

Ikke i det hele tatt 190	❑ 1
Bare i liten grad	❑ 2
En del	❑ 3
Ganske mye	❑ 4

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 191	_____
Hos psykolog eller psykiater	_____
Hos annen legespesialist utenfor sykehus	_____
På poliklinikk 197	_____
Innlagt i sykehus	_____
Hos bedriftslege	_____
Hos fysioterapeut 203	_____
Hos kiropraktor	_____
Hos akupunktør	_____
Hos tannlege 209	_____
Hos naturmedisiner (homøopat, soneterapeut o.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 ....215 _____ mnd.
- Sovemedisin .... _____ mnd.
- Beroligende midler .... _____ mnd.
- Medisin mot depresjon ....221 _____ mnd.
- Allergimedisin .... _____ mnd.
- Astmamedisin .... _____ mnd.

Kosttilskudd
- Jerntabletter ....227 _____ mnd.
- Kalktabletter eller benmel .... _____ mnd.
- Vitamin D-tilskudd .... _____ mnd.
- Andre vitamintilskudd ....233 _____ 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 237	❑	❑
Febersenkende medisin	❑	❑
Migrenemedisin	❑	❑
Eksemsalve	❑	❑
Hjertemedisin (ikke blodtrykksmedisin)	❑	❑
Kolesterolsenkende medisin 242	❑	❑
Sovemedisin	❑	❑
Beroligende medisin	❑	❑
Medisin mot depresjon	❑	❑
Annen nervemedisin	❑	❑
Syrenøytraliserende midler 247	❑	❑
Magesårsmedisin	❑	❑
Insulin	❑	❑
Tabletter mot diabetes (sukkersyke)	❑	❑
Tabletter mot lavt stoffskifte (thyroxin)	❑	❑
Kortisontabletter 252	❑	❑
Annen medisin	❑	❑
Kosttilskudd		
Jerntabletter	❑	❑
Kalktabletter eller benmel	❑	❑
Vitamin D-tilskudd	❑	❑
Andre vitamintilskudd 257	❑	❑
Tran eller fiskeoljekapsler	❑	❑

VENNER

Hvor mange gode venner har du som du kan snakke fortrolig med og gi deg hjelp når du trenger det? ....259 ____ 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? ....261 ____

	Ja	Nei
Føler du at du har nok gode venner? 263	❑	❑

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 ....264 ❑ 1
- 1-2 ganger i måneden .... ❑ 2
- Omtrent en gang i uken .... ❑ 3
- Mer enn en gang i uken .... ❑ 4

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 ....265 _____ skiver

Hva slags fett blir vanligvis brukt til **matlaging** (ikke på brødet) i din husholdning?
- Meierismør ....266 ❑
- Hard margarin .... ❑
- Bløt (Soft) margarin .... ❑
- Smør/margarin blanding .... ❑
- Oljer ....270 ❑

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:	❑ 271	❑	❑	❑	❑ 275

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) 276	❑	❑	❑	❑	❑	❑
Lettmelk (søt eller sur) (glass)	❑	❑	❑	❑	❑	❑
Skummet melk (søt eller sur) (glass)	❑	❑	❑	❑	❑	❑
Te (kopper)	❑	❑	❑	❑	❑	❑
Appelsinjuice (glass)	❑	❑	❑	❑	❑	❑
Poteter 281	❑	❑	❑	❑	❑	❑
Brødskiver totalt (inkl. knekkebrød)	❑	❑	❑	❑	❑	❑
Brødskiver med						
– fiskepålegg (f.eks. makrell i tomat)	❑	❑	❑	❑	❑	❑
– magert kjøttpålegg (f.eks. skinke)	❑	❑	❑	❑	❑	❑
– fetere kjøttpålegg (f.eks. salami)	❑	❑	❑	❑	❑	❑
– gulost 286	❑	❑	❑	❑	❑	❑
– brunost	❑	❑	❑	❑	❑	❑
– kaviar	❑	❑	❑	❑	❑	❑
– syltetøy og annet søtt pålegg	❑ 1	❑ 2	❑ 3	❑ 4	❑ 5	❑ 6

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

	Aldri	Færre enn 1	1	2-3	4-5	Omtrent daglig
Yoghurt 290	❑	❑	❑	❑	❑	❑
Kokt eller stekt egg	❑	❑	❑	❑	❑	❑
Frokostblanding/havregryn o.l.	❑	❑	❑	❑	❑	❑
Middag med						
– rent kjøtt	❑	❑	❑	❑	❑	❑
– pølser/kjøttpudding/-kaker	❑	❑	❑	❑	❑	❑
– feit fisk (f.eks. laks/uer) 295	❑	❑	❑	❑	❑	❑
– mager fisk (f.eks. torsk)	❑	❑	❑	❑	❑	❑
– fiskeboller/-pudding/-kaker	❑	❑	❑	❑	❑	❑
– grønnsaker	❑	❑	❑	❑	❑	❑
Majones, remulade o.l.	❑	❑	❑	❑	❑	❑
Gulrøtter 300	❑	❑	❑	❑	❑	❑
Blomkål/kål/brokkoli	❑	❑	❑	❑	❑	❑
Epler/pærer	❑	❑	❑	❑	❑	❑
Appelsiner, mandariner o.l.	❑	❑	❑	❑	❑	❑
Sukkerholdige leskedrikker	❑	❑	❑	❑	❑	❑
Sukkerfrie («Light») leskedrikker	❑	❑	❑	❑	❑	❑
Sjokolade	❑	❑	❑	❑	❑	❑
Vafler, kaker o.l. 307	❑ 1	❑ 2	❑ 3	❑ 4	❑ 5	❑ 6

ALKOHOL

Hvor ofte pleier du å drikke	øl?	vin?	brennevin?
Aldri, eller noen få ganger i året	❑ 308	❑	❑ 1
1-2 ganger i måneden	❑	❑	❑ 2
Omtrent 1 gang i uken	❑	❑	❑ 3
2-3 ganger i uken	❑	❑	❑ 4
Omtrent hver dag	❑	❑	❑ 5 310

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 ..... 311 ❑ 1
- Noen få ganger ..... ❑ 2
- 1 - 2 ganger per måned ..... ❑ 3
- 1 - 2 ganger i uken ..... ❑ 4
- 3 eller flere ganger i uken ..... ❑ 5

I omtrent hvor mange år har ditt alkoholforbruk vært slik du har svart i spørsmålene over? ..... 312 _____ år

SLANKING

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

- – før 20 år ..... 314 _____ ganger
- – senere ..... 316 _____ ganger

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

- – før 20 år ..... 318 _____ kg
- – senere ..... 320 _____ kg

Hvilken vekt ville du være tilfreds med (din "trivselsvekt")? ..... 322 _____ kg

UFRIVILLIG URINLEKKASJE

Hvor ofte har du ufrivillig urinlekkasje?

- Aldri ..... 325 ❑ 1
- Ikke mer enn en gang i måneden ..... ❑ 2
- To eller flere ganger i måneden ..... ❑ 3
- Ukentlig eller oftere ..... ❑ 4

Dine kommentarer:

BESVARES BARE AV KVINNER

MENSTRUASJON

Hvor gammel var du da du fikk menstruasjon første gang? ..... 326 _____ år

Hvis du ikke lenger har menstruasjon, hvor gammel var du da den sluttet? ..... 328 _____ år

Når du ser bort fra svangerskap og barselsperiode, har du noen gang vært blødningsfri i minst 6 måneder? 330	Ja ❑	Nei ❑

Hvis "Ja", hvor mange ganger? ..... 331 _____ ganger

Hvis du fremdeles har menstruasjon eller er gravid:

Hvilken dato startet din siste menstruasjon? ..... 333 dag/ mnd/ år ___/___/___

Bruker du vanligvis smertestillende legemidler for å dempe menstruasjonsplager? 339	Ja ❑	Nei ❑

SVANGERSKAP

Hvor mange barn har du født? ..... 340 _____ barn

Er du gravid nå? 342	Ja ❑	Nei ❑	Usikker ❑

Har du i forbindelse med svangerskap hatt for høyt blodtrykk og/eller eggehvite (protein) i urinen? 343	Ja ❑	Nei ❑

Hvis "Ja", i hvilket svangerskap?

	Svangerskap Første	Senere
For høyt blodtrykk 344	❑	❑
Eggehvite i urinen 346	❑	❑

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	348 _____	_____
2	_____	_____
3	356 _____	_____
4	_____	_____
5	364 _____	_____
6	_____	_____

PREVENSJON OG ØSTROGEN

Bruker du, eller har du brukt:	Nå	Før	Aldri
P-pille (også minipille) 372	❑	❑	❑
Hormonspiral	❑	❑	❑
Østrogen (tabletter eller plaster) 374	❑	❑	❑
Østrogen (krem eller stikkpiller)	❑ 1	❑ 2	❑ 3

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

376 .....

Hvis du bruker eller har brukt p-pille:

Alder da du begynte med P-piller? ..... 380 _____ år

Hvor mange år har du tilsammen brukt P-piller? ..... 382 _____ år

Dersom du har født, hvor mange år brukte du P-piller før første fødsel? ..... 384 _____ år

Hvis du har sluttet å bruke P-piller:

Alder da du sluttet? ..... 386 _____ år

Takk for hjelpen! Husk å postlegge skjemaet idag!

Helseundersøkelsen i Tromsø

Appendix 3

Questionnaire 2 -Tromsø 4

(≥ 70 years)

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 ..... 17 ❑

Dato for utfylling av skjema: ..... 18 Dag ...../ Mnd ...../ År .....

OPPVEKST

I hvilken kommune bodde du da du fylte 1 år?

..... 24 -28

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

Hvordan var de økonomiske forhold i familien under din oppvekst?

- Meget gode ..... 29 ❑ 1
- Gode ..... ❑ 2
- Vanskelige ..... ❑ 3
- Meget vanskelige ..... ❑ 4

Hvor gamle ble dine foreldre?

- Mor ble ..... 30 _____ år
- Far ble ..... 32 _____ år

BOLIG

Hvem bor du sammen med?

Sett ett kryss for hvert spørsmål og angi antall.	Ja	Nei	Antall
Ektefelle/samboer 34	❑	❑	
Andre personer over 18 år 35	❑	❑	_____
Personer under 18 år 38	❑	❑	_____

Hvilken type bolig bor du i?

- Enebolig/villa ..... 41 ❑ 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? ..... 42 _____ år

	Ja	Nei
Er boligen tilpasset til dine behov? 44	❑	❑
Hvis "Nei", er det problemer med:		
Plassen i boligen 45	❑	❑
Ujevn, for høy eller for lav temperatur 46	❑	❑
Trapper 47	❑	❑
Toalett 48	❑	❑
Bad/dusj 49	❑	❑
Vedlikehold 50	❑	❑
Annet (spesifiser) 51	❑	❑
Ønsker du å flytte til en eldrebolig? 52	❑	❑

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? ..... 53 ❑ 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 54	❑	❑
Bonde/gårdbruker 55	❑	❑
Fisker 56	❑	❑

Hvor gammel var du da du ble pensjonert? ..... 57 _____ år

Hva slags pensjon har du?

- Minstepensjon ..... 59 ❑
- Tilleggspensjon ..... 60 ❑

Hvordan er din økonomi nå?

- Meget god ..... 61 ❑ 1
- God ..... ❑ 2
- Vanskelig ..... ❑ 3
- Meget vanskelig ..... ❑ 4

HELSE OG SYKDOM

Er helsen din blitt forandret det siste året?

- Ja, dårligere ..... 62 ❑ 1
- Nei, uforandret ..... ❑ 2
- Ja, bedre ..... ❑ 3

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

- Mye dårligere ..... 63 ❑ 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 64	❑	❑	_____
Brudd ved håndledd/underarm 67	❑	❑	_____
Nakkesleng (whiplash) 70	❑	❑	_____
Skade som førte til sykehusinnleggelse 73	❑	❑	_____
Sår på magesekken 76	❑	❑	_____
Sår på tolvfingertarmen 79	❑	❑	_____
Magesår-operasjon 82	❑	❑	_____
Operasjon på halsen 85	❑	❑	_____

Har du eller har du hatt:

Sett ett kryss for hvert spørsmål.	Ja	Nei
Kreftsykdom 88	❑	❑
Epilepsi (fallesyke)	❑	❑
Migrene	❑	❑
Parkinsons sykdom	❑	❑
Kronisk bronkitt	❑	❑
Psoriasis 93	❑	❑
Benskjørhet (osteoporose)	❑	❑
Fibromyalgi/fibrositt/kronisk smertesyndrom	❑	❑
Psykiske plager som du har søkt hjelp for	❑	❑
Stoffskiftesykdom (skjoldbruskkjertel)	❑	❑
Sykdom i leveren 98	❑	❑
Gjentatt, ufrivillig urinlekkasje	❑	❑
Grønn stær	❑	❑
Grå stær	❑	❑
Slitasjegikt (artrose)	❑	❑
Leddgikt 103	❑	❑
Nyrestein	❑	❑
Blindtarmsoperasjon	❑	❑
Allergi og overfølsomhet		
Atopisk eksem (f.eks. barneeksem)	❑	❑
Håndeksem	❑	❑
Høysnue 108	❑	❑
Matvareallergi	❑	❑
Annen overfølsomhet (ikke allergi)	❑	❑

Hvor mange ganger har du hatt forkjølelse, influensa, "ræksjuka" og lignende siste halvår? 111 ____ ganger

	Ja	Nei
Har du hatt dette de siste 14 dager? 113	❑	❑

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 114	❑	❑	❑	❑	❑	❑
Hjerteinfarkt før 60 års alder 120	❑	❑	❑	❑	❑	❑
Kreftsykdom 126	❑	❑	❑	❑	❑	❑
Høyt blodtrykk 132	❑	❑	❑	❑	❑	❑
Astma 138	❑	❑	❑	❑	❑	❑
Benskjørhet (osteoporose) 144	❑	❑	❑	❑	❑	❑
Slitasjegikt (artrose) 150	❑	❑	❑	❑	❑	❑
Psykiske plager 156	❑	❑	❑	❑	❑	❑
Alderdomssløvhet 162	❑	❑	❑	❑	❑	❑
Diabetes (sukkersyke) 168	❑	❑	❑	❑	❑	❑
– alder da de fikk diabetes 174	__	__	__	__	__	

SYMPTOMER

	Ja	Nei
Hoster du omtrent daglig i perioder av året? 184	❑	❑
Hvis "Ja":		
Er hosten vanligvis ledsaget av oppspytt? 185	❑	❑
Har du hatt slik hoste så lenge som i en 3 måneders periode i begge de to siste år? 186	❑	❑
Har du hatt episoder med piping i brystet? 187	❑	❑
Hvis "Ja", har dette oppstått:		
Sett ett kryss for hvert spørsmål.		
Om natten 188	❑	❑
Ved luftveisinfeksjoner	❑	❑
Ved fysiske anstrengelser	❑	❑
Ved sterk kulde 191	❑	❑
Har du merket anfall med plutselig endring i pulsen eller hjerterytmen siste år? 192	❑	❑
Har du gått ned i vekt siste året? 193	❑	❑
Hvis "Ja":		
Hvor mange kilo? 194	_____ kg	

Hvor ofte er du plaget av søvnløshet?

- Aldri, eller noen få ganger i året ..... 196 ❑ 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 ..... 197 ❑ 1
- Særlig i mørketiden ..... ❑ 2
- Særlig i midnattsoltiden ..... ❑ 3
- Særlig vår og høst ..... ❑ 4

	Ja	Nei
Pleier du å ta en lur på dagen? 198	❑	❑
Føler du at du vanligvis får nok søvn?	❑	❑

Er du plaget av:	Nei	Litt	I stor grad
Svimmelhet 200	❑	❑	❑
Dårlig hukommelse	❑	❑	❑
Kraftløshet	❑	❑	❑
Forstoppelse 203	❑	❑	❑

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

- Ikke i det hele tatt ..... 204 ❑
- 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 205	❑	❑	❑
Gå i trapper	❑	❑	❑
Gå utendørs	❑	❑	❑
Gå ca. 500 meter	❑	❑	❑
Gå på toalettet	❑	❑	❑
Vaske deg på kroppen 210	❑	❑	❑
Bade eller dusje	❑	❑	❑
Kle på og av deg	❑	❑	❑
Legge deg og stå opp	❑	❑	❑
Spise selv	❑	❑	❑
Lage varm mat 215	❑	❑	❑
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)? 220	❑	❑	❑
Kan du lese (evt. med briller)? 221	❑	❑	❑

Er du avhengig av noen av disse hjelpemidlene?

	Ja	Nei
Stokk 222	❑	❑
Krykke	❑	❑
Gåstol (rullator)	❑	❑
Rullestol	❑	❑
Høreapparat	❑	❑
Trygghetsalarm 227	❑	❑

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 228	_____
Hos psykolog eller psykiater	_____
Hos annen legespesialist utenfor sykehus	_____
På poliklinikk 234	_____
Innlagt i sykehus	_____
Hos fysioterapeut	_____
Hos kiropraktor 240	_____
Hos akupunktør	_____
Hos tannlege	_____
Hos fotterapeut 246	_____
Hos naturmedisiner (homøopat, soneterapeut o.l.)	_____
Hos håndspålegger, synsk eller "leser"	_____

Har du hjemmehjelp?	Ja	Nei
Privat 252	❑	❑
Kommunal	❑	❑

Har du hjemmesykepleie? ..... ❑ ❑

Er du fornøyd med helse- og hjemmetjenesten i kommunen?	Ja	Nei	Vet ikke
Prinsippet med fast lege 255	❑	❑	❑
Hjemmesykepleien	❑	❑	❑
Hjemmehjelpen	❑	❑	❑

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

- Trygg ..... 258 ❑ 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 ..... 259 _____ mnd.
- Sovemedisin ..... _____ mnd.
- Beroligende midler ..... _____ mnd.
- Medisin mot depresjon ..... 265 _____ mnd.
- Allergimedisin ..... _____ mnd.
- Astmamedisin ..... _____ mnd.
- Hjertemedisin (ikke blodtrykksmedisin) ..... 271 _____ mnd.
- Insulin ..... _____ mnd.
- Tabletter mot diabetes (sukkersyke) ..... _____ mnd.
- Tabletter mot lavt stoffskifte (thyroxin) ..... 277 _____ mnd.
- Kortisontabletter ..... _____ mnd.
- Midler mot forstoppelse ..... _____ mnd.

Kosttilskudd

- Jerntabletter ..... 283 _____ mnd.
- Vitamin D-tilskudd ..... _____ mnd.
- Andre vitamintilskudd ..... _____ mnd.
- Kalktabletter eller benmel ..... 289 _____ mnd.
- Tran eller fiskeoljekapsler ..... _____ mnd.

FAMILIE OG VENNER

Har du nær familie som kan gi deg hjelp og støtte når du trenger det? 293	Ja	Nei
	❑	❑

Hvis "Ja": Hvem kan gi deg hjelp?

- Ektefelle/samboer ..... 294 ❑
- Barn ..... ❑
- Andre ..... ❑

Hvor mange gode venner har du som du kan snakke fortrolig med og gi deg hjelp når du trenger det? ..297 ____ **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? 299	❑	❑

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 ..... 300 ❑ 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 ..... 301 ❑ 1
- 1-2 ganger i måneden ..... ❑ 2
- Omtrent en gang i uken ..... ❑ 3
- Mer enn en gang i uken ..... ❑ 4

KOSTVANER

Hvor mange måltider spiser du vanligvis daglig (middag og brødmåltid)? ..... 302 _____ Antall

Hvor mange ganger i uken spiser du varm middag? ..... 304 _____

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:	❑ 306	❑	❑	❑	❑ 310

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

- Meierismør ..... 311 ❑
- Hard margarin ..... ❑
- Bløt (Soft) margarin ..... ❑
- Smør/margarin blanding ..... ❑
- Oljer ..... 315 ❑

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) 316	❑	❑	❑	❑
Appelsinjuice (glass)	❑	❑	❑	❑
Poteter	❑	❑	❑	❑
Brødskiver totalt (inkl. knekkebrød) ...	❑	❑	❑	❑
Brødskiver med				
– fiskepålegg (f.eks. makrell i tomat)	❑	❑	❑	❑
– gulost	❑	❑	❑	❑
– kaviar 322	❑ 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 323	❑	❑	❑	❑
Kokt eller stekt egg	❑	❑	❑	❑
Frokostblanding/havregryn o.l.	❑	❑	❑	❑
Middag med				
– rent kjøtt	❑	❑	❑	❑
– feit fisk (f.eks. laks/uer)	❑	❑	❑	❑
– mager fisk (f.eks. torsk) 328	❑	❑	❑	❑
– grønnsaker (rå eller kokte)	❑	❑	❑	❑
Gulrøtter (rå eller kokte)	❑	❑	❑	❑
Blomkål/kål/brokkoli	❑	❑	❑	❑
Epler/pærer	❑	❑	❑	❑
Appelsiner, mandariner o.l. 333	❑ 1	❑ 2	❑ 3	❑ 4

TRIVSEL

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

- Godt ..... 334 ❑ 1
- Ganske bra ..... ❑ 2
- Opp og ned ..... ❑ 3
- Dårlig ..... ❑ 4

Hvordan ser du på livet fremover?

- Lyst ..... 335 ❑ 1
- Ikke så verst ..... ❑ 2
- Nokså bekymret ..... ❑ 3
- Mørkt ..... ❑ 4

BESVARES BARE AV KVINNER

MENSTRUASJON

Hvor gammel var du da du fikk menstruasjon første gang? ..... 336 _____ år

Hvor gammel var du da menstruasjonen sluttet? ..... 338 _____ år

SVANGERSKAP

Hvor mange barn har du født? ..... 340 _____ 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	342 _____	_____
2	346 _____	_____
3	_____	_____
4	_____	_____
5	358 _____	_____
6	_____	_____

Har du i forbindelse med svangerskap hatt for høyt blodtrykk og/eller eggehvite (protein) i urinen? ..... 366 Ja ❑ Nei ❑

Hvis "Ja", i hvilket svangerskap?

	Svangerskap Første	Senere
For høyt blodtrykk 367	❑	❑
Eggehvite i urinen 369	❑	❑

ØSTROGEN-MEDISIN

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

	Nå	Før	Aldri
Tabletter eller plaster 371	❑	❑	❑
Krem eller stikkpiller 372	❑	❑	❑

Hvis du bruker østrogen, hvilket merke bruker du nå?

..... 373

Dine kommentarer:

Takk for hjelpen! Husk å postlegge skjemaet idag!
Helseundersøkelsen i Tromsø