

Age-related macular degeneration: Prevalence and risk factors – a cross-sectional study

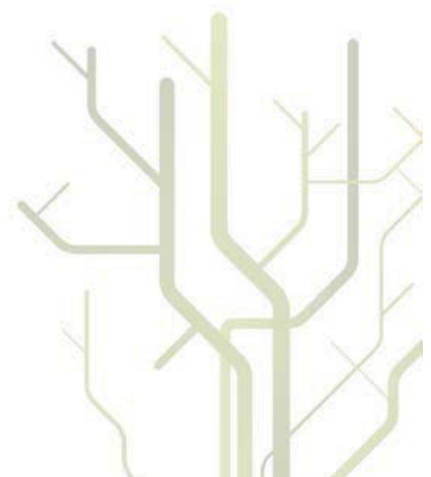
The Tromsø Study 2007/2008



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Tromsø, October 2012

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LIST OF PAPERS

This thesis is based on the work described in following papers:

- I. Bertelsen G, Erke MG, von Hanno T, Mathiesen EB, Peto T, Sjølie AK, Njølstad I. The Tromsø Eye Study: study design, methodology and results on visual acuity and refractive errors. *Acta Ophthalmol.* Epub 2012 Sep 11.
- II. Erke MG, Bertelsen G, Peto T, Sjølie AK, Lindekleiv H, Njølstad I. Prevalence of Age-Related Macular Degeneration in Elderly Caucasians: The Tromsø Eye Study. *Ophthalmology.* 2012 Sep;119(9):1737-43. Epub 2012 May 16.
- III. Erke MG, Bertelsen G, Peto T, Sjølie AK, Lindekleiv H, Njølstad I. Cardiovascular risk factors associated with age-related macular degeneration: The Tromsø Study. Submitted.
- IV. Erke MG, Bertelsen G, Peto T, Sjølie AK, Lindekleiv H, Njølstad I. Lactation, female hormones and age-related macular degeneration: The Tromsø Study. Submitted.

ABBREVIATIONS

| | |
|-------------------|--|
| AMD | Age-related macular degeneration |
| BMI | Body mass index |
| CI | Confidence interval |
| CVD | Cardiovascular disease |
| CZM | Carl Zeiss Meditec |
| GA | Geographic atrophy |
| HbA _{1c} | Glycosylated haemoglobin A _{1c} |
| HDL | High density lipoprotein |
| LDL | Low density lipoprotein |
| nvAMD | Neovascular AMD |
| OHT | Oral hormone treatment |
| OR | Odds ratio |
| SD | Standard deviation |
| VEGF | Vascular endothelial growth factor |

SUMMARY

Age-related macular degeneration (AMD) is an important cause of visual impairment and blindness worldwide. The number of people affected by the disease is expected to rise due to increasing longevity. Development of adequate eye care for these patients should be based on knowledge about the prevalence of AMD. Further, preventive measures are the best strategy for any disease. The aims of this thesis were to estimate the prevalence of AMD and examine risk factors associated with AMD.

We described prevalence rates of AMD among Caucasian elderly participants from the Tromsø Eye Study, a population-based study in Norway. The overall prevalence of late AMD was 3.5 % among the participants aged 65-87 years old. Neovascular AMD outnumbered geographic atrophy. Symmetry between eyes was relatively low. Prevalence increased strongly with age. No significant sex differences in prevalence rates of AMD were observed. Refractive error was lower in eyes with late AMD than in eyes without late AMD.

We then analysed relationships between traditional cardiovascular risk factors and AMD. Daily smoking was a strong predictor for the presence of late AMD. We found a significant interaction between age and sex for late AMD, suggesting that age may be a stronger risk factor for late AMD in women than in men. Higher systolic blood pressure, higher pulse pressure, infrequent physical exercise and overweight or obesity were in adjusted analyses associated with late AMD in females, but this was not observed in men.

Based on our observation of sex and AMD, we studied associations between female hormone related factors and AMD. We found a significant inverse relationship between duration of lactation and late

AMD. No significant relationships were found between late AMD and exogenous oestrogen exposure in the form of contraceptives or hormone therapy. Nor did we find an association between late AMD and onset, end or length of fertile years, bilateral oophorectomy or parity as surrogate measures.

1. INTRODUCTION

1.1 Background

Age-related macular degeneration (AMD) can lead to severe visual impairment and blindness. As the name implies, the disease affects elderly. Macula, the central retina in the back of the eye, is responsible for our sharp-sightedness. The macula undergoes destructive and irreversible changes throughout the course of the disease that endangers visual acuity. Early AMD consist of retinal or subretinal drusen (yellow-white spots) and/or retinal pigment abnormalities. Early AMD has been shown to increase the risk of developing late AMD. Late or end-stage AMD is divided into neovascular AMD (nvAMD), also called wet or exudative AMD, and geographic atrophy (GA). Confusingly, both early AMD and GA are called dry AMD even though the clinical difference is considerable. Examples of drusen and late AMD are presented below on photographs taken from Tromsø Eye Study (Figure 1-3).

Figure 1. Fundus photograph; numerous drusen of different sizes.

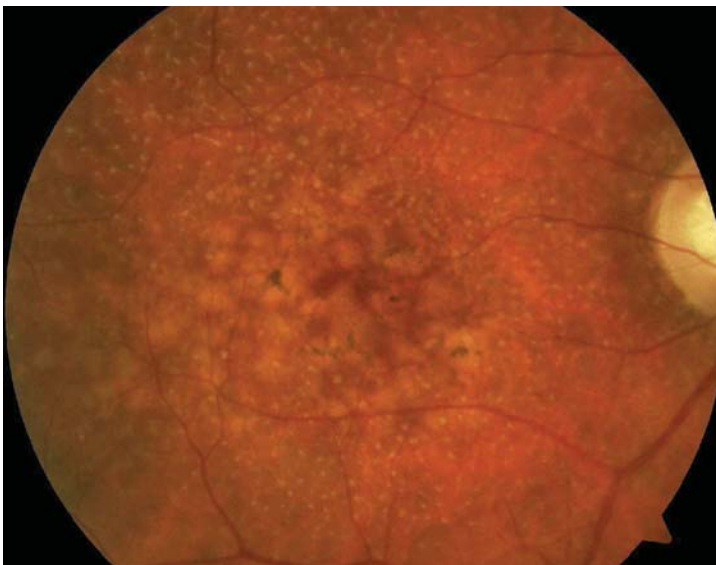
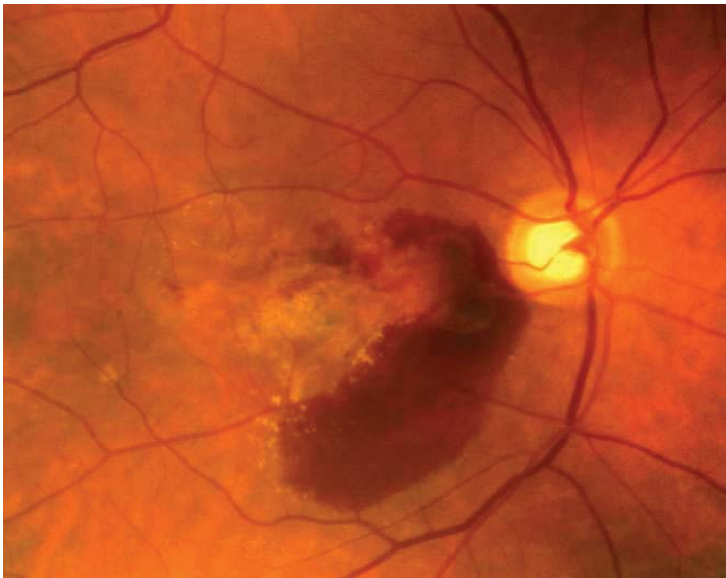


Figure 2. Fundus photograph; geographic atrophy.



Figure 3. Fundus photograph; neovascular age-related macular degeneration.



Patients with early AMD do not necessarily experience visual loss. When GA develops there is no visual function in the affected area due to permanent loss of photoreceptors and retinal pigment epithelium. Wet AMD is a result of neovascularisation within or beneath the retina with leakage of fluid and/or blood in the macula. Without treatment, the eye will rapidly deteriorate due to retinal destruction and eventually scarring.

Preventive measures have been to advise cessation of smoking and anti-oxidant supplementation for those at high risk of developing late stage disease. Currently, treatment is only available for wet AMD. It consists mainly of inhibitors of vascular endothelial growth factor (VEGF) injected into the eye at intervals of usually 1-3 months. Although not curative, it has since its debut in the mid-2000 revolutionised the treatment of wet AMD. This has also imposed a considerable economic and logistic burden on the health care system due to high numbers of patients needing repeated intravitreal injections. According to numbers reported by the Norwegian Ophthalmological Association more than 30 000 injections were given in Norway in 2010 [1].

1.2 Epidemiology of AMD

AMD has been identified as the leading cause of blindness in the developed part of the world and ranks as the third leading cause globally [2]. Previous population-based surveys on AMD which have used standardised classification protocols based on fundus photography have reported varying prevalence. The Beaver Dam Eye Study [3-5] from USA found late AMD in 7.7 % in their cohort aged 75-86 years old. The Blue Mountains Eye Study [6-8] found a lower prevalence of 5.7 %. In Europe results from two larger surveys have been published. The Rotterdam Study [9-11] reported a prevalence of 3.7 % in people aged 75-84 years old. The European Eye Study [12] is a multicentre survey including participants 65 years and older from 7 European countries. A few other surveys have been conducted in North Europe and in the Arctic population (Copenhagen [13, 14], Reykjavik [15-17], Greenland [18, 19]. High prevalence of late AMD was reported among Inuit on Greenland aged ≥ 60 years of 9.5 % [18]. The prevalence of AMD has previously been described in Norway

only in a small study from Oslo [20] and as part of the multinational European Eye Study [12].

Table 1. Prevalence of AMD among elderly, selected population-based studies.

| Study | Prevalence by age groups | | Differing age groups: | Prevalence, overall | |
|---|--------------------------|-------------|-----------------------|---------------------|----------------|
| | 65-74 years | 75-86 years | | Late AMD | Drusen >125 µm |
| Tromsø [21] | 1.4 | 7.7 | 65-87 years | 3.50 | 24 |
| Beaver Dam [3] | 1.4 | 7.1 | - | - | - |
| Blue Mountains [6] | 0.7 | 5.7 | - | - | - |
| Rotterdam [11] | 0.8 | 3.7 | 75-84 years | - | - |
| European Eye Study* [12] | - | - | ≥65 years | 3.46 | 16 |
| Oslo [20] | - | - | 61-90 years | 4.35 | - |
| Reykjavik/ AGES [16] | - | - | ≥66 years | 5.7 | 31 |
| Greenland [18] | - | - | ≥60 years | 9.5 | 15 |
| AMD: age-related macular degeneration Numbers are percentages if not otherwise labelled. *Only participants from the Norwegian sub-study included | | | | | |

1.3 Risk factors for AMD

Evidence so far suggests that AMD is a multi-factorial disease but the full aetiopathogenesis of AMD has not yet been unveiled. High age and smoking are consistently reported as strong risk factors for late AMD [22-27]. Further have family history, genetics and early AMD shown to be strong risk factors for developing late AMD [5, 9, 28-31]. Due to the similarities between drusen deposition and the development of atherosclerosis [32, 33], traditional cardiovascular risk factors have been suggested as risk factors also for AMD. Persons

with AMD are reported to have increased risk of stroke and coronary heart disease in some studies [34-36], but previous epidemiologic studies evaluating risk factors for cardiovascular disease and AMD have not yielded consistent relationships or strong associations [24]. The exception is the strong evidence for increasing age and smoking as factors common for both diseases [22, 24, 25]. There are some evidence for high blood pressure [37-39] and obesity [40, 41] as risk factors for AMD. Sex, dyslipidaemia, and diabetes have also been associated with AMD in some, but not all studies [22-25, 36, 38, 42-45]. Physical activity has shown a protective effect in a few studies [46, 47].

Some publications suggest sex differences in the epidemiology of AMD. A recent large meta-analysis found that women might have a slightly higher risk for neovascular AMD compared to men [22]. Reports have suggested female hormones may play a role in the epidemiology of AMD [24, 48]. Various surrogates have been used for exogenous and endogenous oestrogen exposure in both cross-sectional and longitudinal studies and the association with AMD has been inconsistent [24, 49, 50]. To our knowledge, studies have not addressed the effect of lactation on maternal AMD.

Lately, an increasing body of evidence has shown that genetic susceptibility seems to play a significant role in the development of AMD [24, 51]. Twin studies have estimated the genetic contribution on the genesis of AMD range between 46-71 % [52]. In other words, there is a considerable opportunity altering the prevalence of AMD through identification and management of modifiable risk factors.

2. OBJECTIVES

The aims of this thesis were:

- To describe the sex- and age-specific prevalence of AMD in elderly Caucasians, the symmetry of disease, vision and refraction in eyes with AMD.
- To examine associations between traditional cardiovascular risk factors and AMD.
- To examine associations between female hormone related factors and AMD in women.

3. MATERIAL AND METHODS

3.1 Tromsø, the Tromsø Study and the Tromsø Eye Study

Tromsø is a municipality in Troms County and the largest city of North Norway. It is situated at sea level at 69 degrees north with a Caucasian urban population of 70 000 inhabitants in the municipality (2011 Statistics Norway). Although located above the Arctic Circle, it has a sub-arctic climate due to the Gulf Stream, with middle temperature of 10-12 degrees Celsius in July and about zero in January. Tromsø has an extreme seasonal variation in daylight sun exposure. The polar night lasts for 2 months in the winter with no sun over the horizon, and the duration of the midnight sun period is 2 months in the summer.

The Tromsø Study is an investigator initiated population-based prospective study. The design includes repeated health surveys conducted between 1974 and 2008. The 6th survey consisted of two separate consecutive visits, an initial 1st visit where basic information was collected and a 2nd visit a few weeks later where special investigations were performed. Eye examination was one of the special investigations included in the 6th survey and laid the foundation for the Tromsø Eye Study, a sub-study of the 6th Tromsø Study. The present thesis is based on data from the Tromsø Eye Study conducted in 2007/2008. The methodology is described in paper I.

3.2 Study population

The eligible population for the Tromsø Study consisted of residents in the municipality of Tromsø based on the official population registry. Both whole birth cohorts and random samples from the population have been invited to participate in the Tromsø Study. Different sampling methods have been used and are described elsewhere in

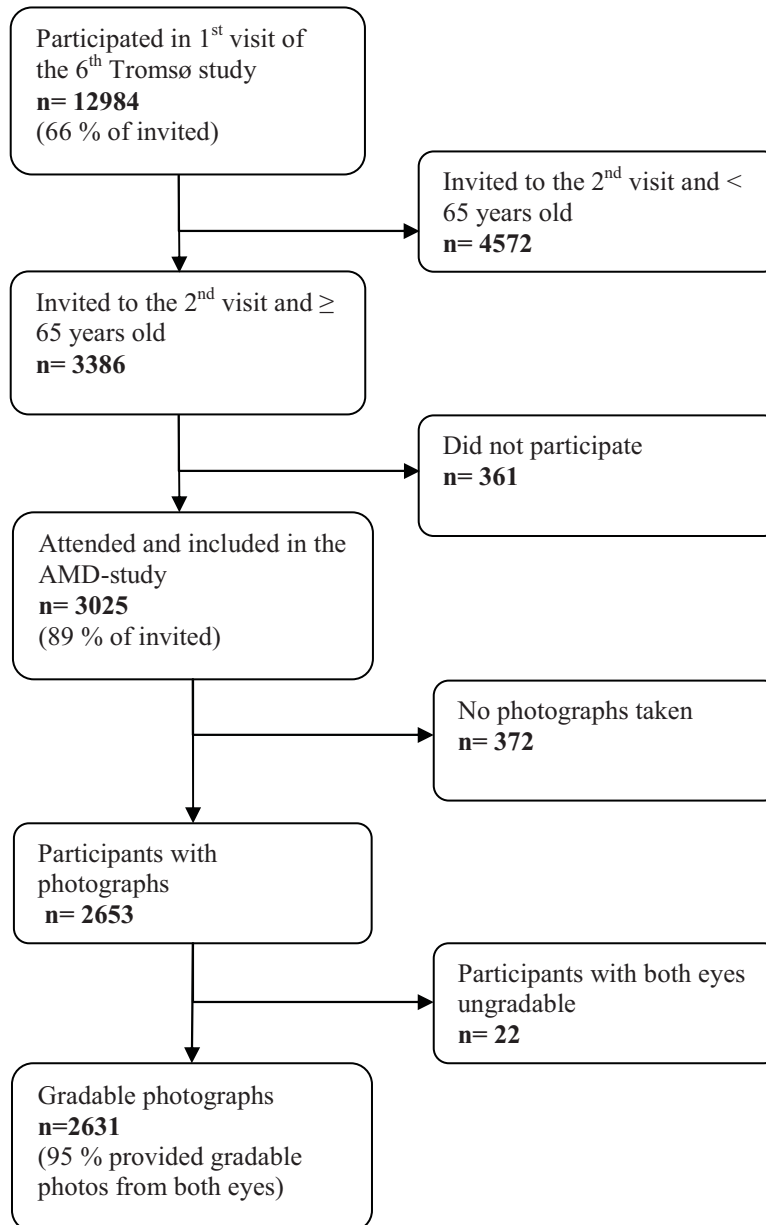
detail [53]. In the 6th survey all residents aged 40-42 years and 60-87 years (n=12578), were invited to the 1st visit. An additional 10 % random sample of individuals aged 30-39 years (n=1056), a 40 % random sample of individuals aged 43-59 years (n= 5787), and subjects who had attended the 2nd visit of the 4th survey, if not already included in the three groups above (n=341) were invited. The participation rate in the 1st visit was 66 %, with a total of 12984 subjects participating.

The eligible subjects for the 2nd visit were pre-selected and participation in the 1st visit was a prerequisite. The groups invited were; all subjects aged 50-62 years or aged 75-84 years (n=7657), a 20 % random sample aged 63-74 years (n=942) and subjects, if not already included in the two groups above, who had attended the 2nd visit of the 4th survey (n=2885). The participation rate in the 2nd visit was 92 %, with a total of 7307 subjects participating.

The participants in the 2nd visit were mainly Caucasians with 91 % reporting Norwegian ethnicity and 1.5 % reporting Sami ethnicity.

The study population which this thesis was based on included 3025 participants aged ≥ 65 years from the 2nd visit of the 6th Tromsø Study. In paper IV, only female participants were included (n=1743). A participation flowchart is presented in Figure 4.

Figure 1. Participation flowchart for the 6th Tromsø study and Tromsø Eye Study



3.3 Ethics

The 6th survey of the Tromsø Study and cross-sectional studies originating from it were approved by the Regional Committee for Medical and Health Research Ethics and the Data Inspectorate. The study followed the tenets of the Helsinki Declaration. All participants have given written informed consent.

3.4 Data acquisition

3.4.1 1st visit: General part

Questionnaires

The invitation to participation included a questionnaire (Appendix A) addressing life style habits and extent of smoking and alcohol use, socioeconomic status, physical activity, health and diseases, and use of medication. Women were also asked questions relevant to female hormones, pregnancy and childbirth. A more extensive questionnaire (Appendix B) was given participants at the 1st visit.

General examination and measurements

All participants underwent a standardised medical examination comprising measuring height, weight, waist and hip circumference, heart rate and blood pressure. A non-fasting blood sample was collected.

Cardiovascular risk factors

Based on the self-reported questionnaires and physical examinations, we classified variables as follow: Persons living with their spouse or other persons >18 years were classified as cohabiting. Education was defined as highest completed level equivalent to primary school only or to higher education. Alcohol use was categorized after frequency of intake to 1) never 2) monthly or 3) weekly. A binary variable was in addition constructed for an approximate intake of more or less than one unit of alcohol daily (consumption 2-3 times a week and usually 3 units or more each time). To be physically active was defined as at least one hour weekly exercise and becoming sweaty or short-winded, or two days weekly with at least 1 hour each without becoming sweaty and short-winded. Four other binary variables were also constructed; 1) minimum activity 30 minutes when exercising versus less 2) the exercise makes the person sweaty/short-winded versus not 3)

exercises minimum weekly versus less and 4) practice hard training/sports competitions versus not. The use of lipid-lowering drugs was dichotomized as never used versus uses/has used.

Waist-to-hip ratio was calculated as the waist circumference divided by the hip circumference. Blood pressure was recorded with a fully automatic device (Dinamap Vital Signs Monitor, Tampa, FL, USA). The average of the last two of three recordings was used for analysis. Pulse pressure was calculated as systolic minus diastolic blood pressure.

Blood samples were analyzed for glycosylated hemoglobin A_{1c} (HbA_{1c}) and serum lipids (total cholesterol, low density lipoprotein (LDL) cholesterol, high density lipoprotein (HDL) cholesterol and triglycerides) by standard enzymatic methods at the Department of Clinical Chemistry, University Hospital of North Norway. Body mass index (BMI) was calculated as weight in kilograms divided by the square of the height in meters. BMI was handled as both continuous and categorized as underweight <20 kg/m², normal 20-24.9 kg/m², overweight 25.0-29.9 kg/m², and obese ≥30 kg/m². Diabetes was defined as non-fasting serum glucose ≥11.1 mmol/L or HbA_{1c} >6.5 % or current use of insulin or anti-diabetic tablets. We defined cardiovascular disease as heart attack or stroke. The Tromsø Study runs a continuously updated and validated endpoint registry of cardiovascular events [54]. All first time cardiovascular events are recorded and confirmed by hospital records or the Cause of Death Registry of Norway. Data from this registry were linked to the study sample for identification and verification of subjects with cardiovascular disease. All other variables were used as they were recorded and stored in the Tromsø Study database (available at: <http://tromsundersokelsen.uit.no/tromso/>).

Female hormone related factors

Data on number of children given birth to, age at first childbirth, duration of breastfeeding for each child, age at menarche, age at menopause, number of fertile years, reason for menopause, use of contraceptives and/or oral hormone therapy (OHT) were obtained from questionnaires. The variable “number of children” was handled with ≥ 6 children as maximum. Length of breastfeeding was defined as months of breastfeeding in total divided by number of children, and additional 4 dichotomized variables were constructed; 1) ever breastfed versus never breastfed, 2) breastfed all children minimum 3 months versus not, 3) breastfed all children minimum 4 months versus not and 4) breastfed all children minimum 6 months versus not. The reason for menopause was dichotomized as 1) natural (stopped by itself) versus not (hysterectomy, both ovaries removed, other reasons) and 2) had both ovaries removed versus not (stopped by itself, hysterectomy and other reasons). The use of hormones was dichotomized to 1) ever used contraceptives versus never used 2) ever used OHT versus never used and 3) ever used contraceptives and/or OHT versus never used. The remaining risk factors were used as continuous variables.

3.4.2 2nd visit: Special investigations

Interview

Subjects participating in the Tromsø Eye Study were interviewed in Norwegian whether they had or ever have had AMD, diabetic retinopathy, cataract, glaucoma or any other eye disease or eye surgery. The Norwegian common terms were also used.

Eye examinations

Detailed information on the eye examinations is described in paper I. Visual acuity was measured by Nidek AR 660A auto refractor (Nidek

CO., LTD. Japan). Mydriasis was obtained by application of one drop Tropicamide 0.5 % (Chauvin Pharmaceuticals Ltd. Kingston upon Thames, Surrey, England) in both eyes after visual acuity measurements. Retinal photography was performed in both eyes with a Visucam PRONM (Carl Zeiss Meditec (CZM)) digital retinal camera 10-45 minutes after application of Tropicamide. Five field's 45 degree colour retinal photographs with resolution 2196x1958 pixels were taken using the camera pre-set internal fixation. A sixth image, 30 degree (resolution 1620x1444 pixels) was taken centred on the macula. Images were stored using Visupac 4.4.1/4.4.3 (CZM). Grading of retinal images was performed using high quality 24" LCD-monitors (Eizo ColorEdge CG241W/CG242W). The same monitor was used throughout the grading process in a room with subdued light.

3.5 Grading of photographs and definitions

The retinal photographs were graded by a single grader (MG Erke) trained at Moorfields Eye Hospital Reading Centre, London, UK. The grader was masked for all other variables. Both eyes were graded consecutively. The grading protocol for retinal photographs was based on The International Classification and Grading System for AMD [55, 56] with modifications. All photos on every participant were used in the grading in order to achieve the best possible grading. A Visupac Analysis Grid (CZM v. 4.4) was centred over foveola in the macular field image and used for determining lesion size and fields (Figure 4). The diameter of the outer circle corresponded to 6000 μm . Standard circles of 63 μm , 125 μm and 175 μm were used to estimate size of lesion, and only features within the grid as a whole were graded.

Figure 5. Normal fundus photograph with analysis grid.

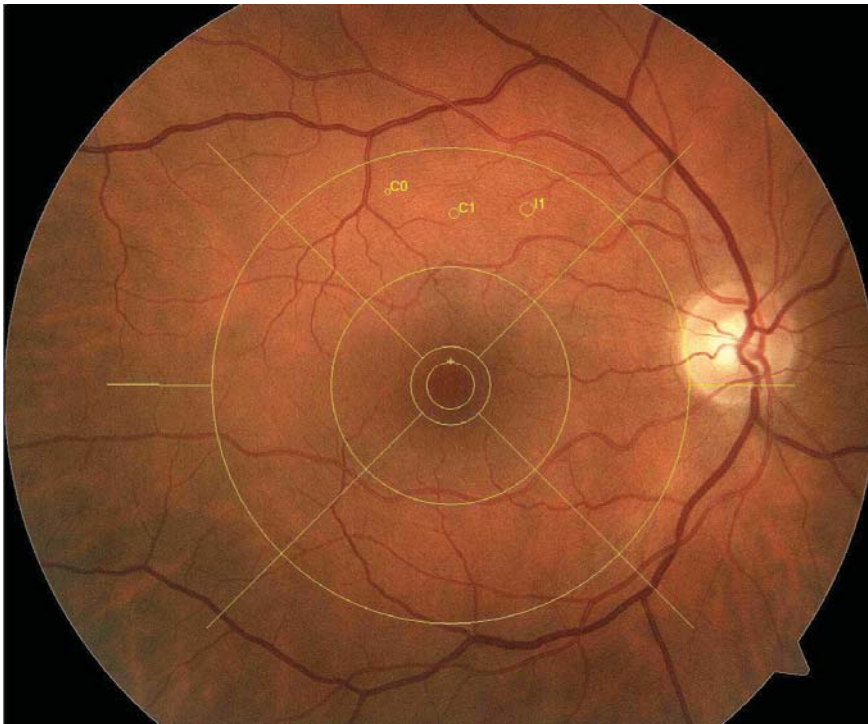


Image quality was classified in five categories: “good”, “fair”, “poor but gradable”, “ungradable because of poor quality” and “good quality but not properly centred on fovea”. All photographs were classified by predominant phenotype. Retinal pigment abnormalities were not graded. In case of uncertainty about the predominant phenotype, the image was adjudicated by the Reading Centre. All photos with end-stage AMD were reassessed by two retinal specialists (AK Sjølie and T Peto) and the final predominant phenotype was then created in a hierarchical manner for those with multiple grades. Intra and intergrader reliability was evaluated by regrading five percent of the images by MG Erke and the Reading Centre independently. Images were randomly selected from all categories by the Reading Centre. In addition, a set of photos provided by the Reading Centre was graded by MG Erke at the start and at the end of the grading period to assess temporal drift.

3.6 Data management and statistical methods

Common for all papers

Custom-made databases (Microsoft Access 2002) were developed for handling AMD grading. Stata/SE 10.0-12.0 (StataCorp LP, Texas, USA) was used for all statistical analysis. Independent t-test or Wilcoxon rank sum test, as appropriate, was used for comparison of means; Pearson chi square test or Fisher's exact test, as appropriate, was used for comparing proportions. P-values <0.05 were considered significant. We used multivariable logistic regression to describe associations and calculate odds ratios (ORs) with 95 % confidence intervals (CIs). Interactions were assessed by including the cross-product term in the multivariable model. Significant interaction terms were evaluated multiplicatively by -2 log likelihood test. The assumptions of logistic regression were tested.

Paper I- II

In paper I/II we evaluated the inter- and intra-grader variability by exact agreement and kappa (κ) statistics between original grading, second grading and external grading. Intra-grader variability was evaluated similarly for temporal drift in grading. Symmetry in phenotype between eyes was calculated by unweighted and linear weighted κ statistics. Prevalence of drusen and AMD was stratified by sex and age groups (5 or 7 year) and presented with 95 % CIs. Visual acuity was presented by eye in categories adjusted to the World Health Organization's and International Statistical Classification of Diseases and Related Health Problems 10th Revision's recommendations for low vision (Snellen < 6/18 or 0.3 and \geq to 3/60 or 0.05) and blindness (Snellen < 3/60 or 0.05).

The overall intra-grader exact agreement was 75 % and κ 0.66. Inter-grader exact agreement was 63 % and κ 0.48. Exact agreement and κ for temporal drift was 68 % and 0.54 respectively. κ results were considered moderate to substantial according to Landis and Koch [57].

Figures for inter-grader agreement and κ in paper I and II are unequal. In paper I we compared with the second grading by the Reading Centre which was performed in Tromsø with the same screen as used throughout the original grading. In paper II and above, we used the first grading which was performed at the Reading Centre in London.

Paper III

In paper III we examined the associations between traditional cardiovascular risk factors and AMD using multivariable logistic regression. Late AMD cases were excluded from analyses of associations with drusen $>125 \mu\text{m}$. We performed a stepwise backward selection procedure in a multivariable logistic regression model including sex and all variables with p-values <0.25 from univariable analyses. The variable with highest p-value was removed for each step, except for sex. Next, variables were singly added to the reduced model and the model assessed by Hosmer-Lemeshow chi-square tests and $-2 \log$ likelihood tests. Interactions were assessed between smoking and pulse pressure; and between smoking and BMI, smoking and sex and between smoking and age; further between sex and age; sex and pulse pressure; and between sex and variables of physical activity.

Paper IV

In paper IV we examined the associations between female hormone related factors and AMD using multivariable logistic regression. Late AMD cases were excluded from analyses of associations with drusen $>125 \mu\text{m}$. Women with extreme values for duration of breastfeeding were excluded from analysis ($n=2$ for total months of breastfeeding >80 and $n=4$ for months of breastfeeding per child >22). Interactions were assessed between breastfeeding and smoking; breastfeeding and systolic blood pressure; and breastfeeding and BMI.

4. SUMMARY OF RESULTS

General for papers II-III

Among the 3025 participants, 372 subjects had no photos and 22 subjects had ungradable photos from both eyes. The remaining 2631 participants had photographs gradable for AMD. Participants not providing photos were older (73.8 vs. 72.3 years, $p < 0.0001$) than participants with gradable photographs.

Paper II

Participants without photographs had lower visual acuity (Snellen ≤ 0.32 , 6.4 % vs. 2.2 %, $p < 0.01$), and had higher frequency of self-reported glaucoma (13.2 % vs. 5.2 %, $p < 0.001$) and cataract (39.9 % vs. 21.3 %, $p < 0.001$) than participants with gradable photographs. No difference with respect to sex, self-reported AMD, diabetic retinopathy, and diabetes mellitus was observed.

The crude prevalence of late AMD was 3.5 % ($n = 92$), for subjects 75 years and older it was 7.1 % and for those 80 years or older it was 10.9 %. The prevalence of both drusen $>125 \mu\text{m}$ and late AMD increased significantly with age. For drusen $>125 \mu\text{m}$ OR per 5-year increase was 1.44 (95 % CI, 1.33–1.57), no significant sex difference was observed. For late AMD OR per 5-year increase was 2.32; 95 % CI, 1.92–2.82 and no sex difference was observed.

Sixty-five percent of participants had the same predominant phenotype in both eyes (κ 0.44). When subjects with bilateral normal phenotype, defined as no drusen or only hard drusen ($n = 920$), were excluded, overall agreement with respect to symmetry was 44 % (κ 0.16). Percentages of symmetry were 44 % for soft drusen $>125 \mu\text{m}$, 36 % for geographic atrophy, and 29 % for neovascular AMD. Among persons with unilateral late AMD, 78 % had drusen $>125 \mu\text{m}$ in the

other eye. The proportion of late AMD cases with bilateral involvement increased from 14 % in participants aged 65 to 69 years to 67 % in participants aged 80 to 87 years. There was no significant sex difference in overall symmetry.

Visual acuity ≤ 0.32 was present in 42.5 % of eyes with late AMD. Refractive error differed between eyes with and without late AMD: spherical equivalent +0.078 (SD 1.82) versus +0.99 (SD 2.03) diopters, respectively ($P < 0.0001$). This remained highly significant when adjusted for age, sex and self-reported cataract (OR 0.83; 95 % CI, 0.76–0.90).

Paper III

Subjects without photos gradable for AMD had higher frequency of diabetes (13.8 % vs. 9.6 %, $p = 0.008$) and cardiovascular disease (18.5 % vs. 13.4 %, $p = 0.006$), and were less physically active (24.0 % vs. 34.5 %, $p < 0.001$) than participants with gradable photographs. No difference between these two groups was observed with respect to education, blood pressure, BMI, daily smoking and serum lipids. Among those with gradable photos, men and women differed with respect to age, smoking habits, blood pressure, physical activity, serum cholesterol, and cardiovascular disease (all p -values < 0.01).

Both late AMD and drusen $> 125\mu\text{m}$ were significantly associated with cohabiting, physical activity and pulse pressure in unadjusted analysis. Further, late AMD was associated with current smoking, longer duration of smoking, systolic blood pressure and underweight, whilst the presence of drusen $> 125\mu\text{m}$ was associated with education at primary school level only, lower alcohol consumption and lower triglyceride level.

Underweight, current daily smoking, longer duration of smoking, systolic blood pressure and pulse pressure remained significant risk factors for late AMD after controlling for age and sex. Exercising more than 30 minutes related to less, showed a significant relationship with drusen >125 μm . This relationship remained significant with additional adjustments for daily smoking, BMI and systolic blood pressure (OR=0.75, 95 % CI 0.58-0.97).

No significant relationships were observed between late AMD and waist circumference, waist-to-hip ratio, cohabiting, education, alcohol consumption, diabetes mellitus or cardiovascular disease. Neither were HbA_{1c} nor serum lipids significantly associated with late AMD.

In the model with late AMD as the outcome and including daily smoking, pulse pressure, age and sex, we observed a significant interaction between sex and age ($p=0.029$). Inclusion of the interaction term altered the log likelihood ($p=0.028$). In sex-specific analysis, we found that age was a stronger risk factor for women than for men. Current daily smoking was a strong risk factor for both women and men, but the association for former smokers was not significant. We found a dose-response relationship with the number of years smoked. Physical inactivity, higher pulse pressure, higher systolic blood pressure and overweight were associated with late AMD among women only. The effect estimates for exercise frequency were acting in opposite directions, protective for women but associated with higher odds, although not significant, for late AMD in men. The association between late AMD in women and weekly exercise was attenuated to a non-significant level when controlled further for visual impairment in addition to age and daily smoking (OR 0.61, 95 % CI 0.28-1.30).

In sex-specific analysis, no associations were observed between any of the risk factors and the presence of drusen $>125 \mu\text{m}$ except for the association with age.

Paper IV

Included in paper IV were 1512 women with gradable photos from at least one eye. Of these, 1426 had data on past use of female hormones, 1411 on age of menarche, 1213 on menopause, 1470 subjects had data on childbirth, of which 1168 women given birth had data on breastfeeding. Women without gradable photos were older (73.8 years vs. 72.2 years, $p<0.0001$), had higher frequency of diabetes (14.0 % vs. 8.9 %, $p=0.014$) and self reported cardiovascular disease (24.6 % vs. 15.3 %, $p=0.001$), and were less physically active (20.4 % vs. 30.6 %, $p=0.003$). The groups did not differ with respect to smoking, serum cholesterol, blood pressure, BMI, education, age of menarche or menopause, age at first birth, number of children given birth to, extent of breastfeeding, past use of contraceptives or OHT. A total of 48 (3.2 %) participants had late AMD and of the remaining, 378 (25 %) participants had at least one large drusen $> 125 \mu\text{m}$. Of the participants without missing data, 732 (58 %) had never used any kind of female hormones, and of 1261 with data on childbearing and breastfeeding; 139 (11 %) had never breastfed of whom 93 (7.4 %) had never given birth.

No associations were observed between late AMD and past use of contraceptives, past use of OHT, parity, age at first childbirth, age of menarche, age of menopause, number of menstruating years or the reason for menopause, all controlled for age.

Women that had breastfed all their children for at least 6 months had significantly lower odds for late AMD in multivariable analysis adjusted for age, smoking, systolic blood pressure, BMI, total cholesterol, number of children given birth to and physical activity (OR 0.12, 95 % CI 0.027-0.53). Comparable, estimates for

breastfeeding all children minimum 4 or 3 months were also significant with OR 0.27, 95 % CI 0.11-0.68 and OR 0.41, 95 % 0.19-0.90 respectively. We observed the same relationship for duration of breastfeeding per child as a continuous variable (OR 0.86 per month, 95 % CI 0.76-0.97). These associations were strengthened when women who never had given birth were excluded from analyses. Additional adjustments for alcohol consumption and education did not alter the relationships. No interactions between breastfeeding and smoking status, systolic blood pressure or BMI were significant. The presence of large drusen >125 μm was not significantly associated with any of the female hormone related factors.

5. DISCUSSION

The main findings of this thesis are:

- The overall prevalence of late AMD was 3.5 %, and among those aged ≥ 80 years it was almost 11 %. Neovascular disease outnumbered geographic atrophy. Symmetry between eyes was relatively low. Refractive error was lower in eyes with late AMD than in eyes without late AMD.
- Age and smoking were strong predictors for the presence of AMD. We found a significant effect modification on age by sex with respect to late AMD in adjusted analysis. Sex-specific multivariable analysis showed that higher systolic blood pressure, higher pulse pressure, infrequent exercise and overweight or obesity were associated with late AMD in females, but this was not observed in men. Only age was associated with the presence of large drusen.
- Longer duration of lactation was associated with lower frequency of maternal late AMD controlled for confounders. Other reproductive or female hormone related factors were not significantly associated with AMD.

5.1 Methodological considerations

Internal validity

Inference from epidemiological research depends on the study's internal validity. Bias occurs as results of systematic errors in planning, conduct or interpretation of measurements. Main types of bias that can threaten the study's internal validity are selection bias, information bias and confounding. Selection bias is the event when "systematic error in the ascertainment of study subjects (...) results in a tendency toward distorting the measure expressing the association

between exposure and outcome” [58]. The same mechanism applies to survival bias. Information bias in epidemiologic studies is defined as “results from either imperfect definitions of study variables or flawed data collection procedures” [58]. This includes among other misclassification and recall bias. Another threat to the internal validity is confounding. A confounding variable is a variable associated with both the exposure and the outcome under study. This third variable can lead to inducing, weakening, strengthening or elimination of the association between the putative risk factor and the outcome [58]. Medical epidemiological research is challenging because of the complexity of the disease, with possibility for co-dependent factors and that influence of factors can be evident decades after exposure.

External validity

Inference from population-based studies upon the background population or other populations depends on the studies external validity, its generalizability. This study included a homogenous Caucasian population and results can be extrapolated to similar populations of Western European ancestry. However, it might not be appropriate to assume these results apply to populations of other ethnicities. The epidemiology of AMD has been shown to differ across racial/ethnic groups [59].

Strengths and limitations

Strengths of the present research include a population-based design, a large study sample and high participation rate. Further, the use of standardized protocols and co-operation with a professional reading centre in the grading of photographs facilitated valid results comparable with previous reports on the epidemiology of AMD.

Limitations include possible selection bias due to lower number of participants with gradable photographs in the oldest age group.

Further, it is possible that visual impaired people might be less likely to attend the study. The response rate for participants 80 years and older was 40 % for the first visit of the study. The prevalence rates may therefore be underestimated. The definition of early AMD differs between studies and this might limit direct comparison of prevalence of early AMD stages. Misclassification might have been introduced during the grading process in those who were undergoing VEGF inhibitor therapy for neovascular AMD. Further, we had no access to fluorescein angiography or stereo photography. Spectral domain optic coherence tomography was available. We graded samples of scans and decided the topic beyond the scope of this thesis and results will be presented later. Data on visual acuity were not available for 9 % of subjects with late AMD. This may have impacted our finding of lower refractive error among late AMD cases.

In paper III the linkage to an endpoint registry validated the data on cardiovascular disease in the study population. Limitations were the cross-sectional design which precludes causal inference, classification bias, selection bias and survival bias. Further limitations were insufficient power and hence no sub-groups analysis due to few late AMD cases and the lack of fasting blood samples and genetic profiling.

Limitations in paper IV include residual confounding, recall bias, lack of power and selection bias. The cross-sectional design precludes causal inference. As we examined several variables, it is possible that the relationship between lactation and late AMD in the present study is due to chance. However, the stronger relationship with longer duration of breastfeeding suggests that the relationship is relevant.

5.2 Prevalence of AMD

Our findings are consistent with results from previous cross-sectional studies examining the prevalence of late AMD, such as the Age, Gene/Environment Susceptibility Study [16] from Reykjavik, Iceland, the Beaver Dam Eye Study [3], USA and the Norwegian participants in the European Eye Study [12]. Greenland, on the other hand, reported a very high prevalence of late AMD of 9.5 % in 642 participants 60 years or older [18]. Lower rates of late AMD were observed in the Blue Mountains Eye Study [6] (65 to 74 years; 0.7 % and 74 to 86 years; 5.7 %) and the Rotterdam Study [11] (65 to 74 years; 0.8 % and 75 to 84 years; 3.7 %). Recently, the Beaver Dam Offspring Study presented prevalence estimates for AMD where no cases of late AMD was found in their cohort of 174 persons 65 years or older [60].

Different grading procedures, study equipment, and age distribution limit comparison of AMD between studies. The International classification [55] defined early AMD as hyper- or hypopigmentation of the retinal pigment epithelium associated with drusen, or soft drusen alone. The studies from Oslo, Greenland and Reykjavik included pigment abnormalities $\geq 63 \mu\text{m}$ present alone in the definition, but the Blue Mountain Eye, Beaver Dam or Rotterdam studies did not. A study from Norway found prevalence of drusen $\geq 63\mu\text{m}$ to be 43 % in persons aged ≥ 51 years [20]. Similarly, the Rotterdam Study [11] found a prevalence of 49 % (persons aged ≥ 55 years); and for drusen $\geq 125\mu\text{m}$ the prevalence was 8.8 %. The Beaver Dam Offspring Study [60] reported a prevalence of 9.2 % for drusen $\geq 125\mu\text{m}$ in persons aged ≥ 65 years while the Age, Gene/Environment Susceptibility study from Reykjavik reported 30.7 % [16]. The Inuit study from Greenland with participants from the high north showed high prevalence of drusen, as 45 % had intermediate drusen (63-125 μm) and 15 % had large drusen $\geq 125\mu\text{m}$ [18]. In our work, we found

high frequencies of both intermediate (35 %) and large drusen (24 %). As we see, the combined prevalence of drusen $>63 \mu\text{m}$ was similar in the latter two studies.

No overall sex differences in the prevalence of large drusen $>125\mu\text{m}$ or late AMD were observed. This is consistent with studies from Western populations [6, 11, 12] and contradicts the findings from Asian populations where higher prevalence of drusen and late AMD was found in men than in women [61, 62]. Our findings of an increasing prevalence of large drusen and late AMD with age were similar to previously published studies.

Published data on symmetry of phenotype between eyes are limited. An Australian study [63] of 230 participants aged ≥ 49 years found symmetrical phenotype in 57 % of cases with late AMD (for geographic atrophy 56 % and for neovascular AMD 40 %). However, they included only lesions involving the foveal centre. They found the proportion of bilateral drusen $>125\mu\text{m}$ was 76 %. A hospital-based study [64] of 1114 patients from the UK found symmetry of late AMD in 55 %, geographic atrophy in 40 % and neovascular AMD in 37.5 %. The symmetry rates in our study were consistently lower. Bilaterality of late AMD was 34 %, for geographic atrophy 36 % and for neovascular AMD 29 %. Symmetry was highest for soft drusen $>125\mu\text{m}$ (44 %). On the basis of different study samples and methods, comparison of rates is restricted. Nevertheless, the order of bilaterality is similar across studies with highest rates for large drusen followed by geographic atrophy and thereafter neovascular disease.

5.3 Risk factors for AMD

We observed a lower refractive error among late AMD cases. The Rotterdam Study [65] and the Beijing Eye Study [66] have reported

hyperopia as risk factor for AMD. In contrast we observed a 17 % reduction in odds for every dioptre increase in spherical equivalent.

It has been hypothesized that sun exposure is a risk factor for AMD [67-69]. The Arctic Circle marks the southern extremity of the polar night (24 hour sunless night) and polar day (24-hour sunlit day). Our findings of prevalence rates of late AMD similar to that in studies south of the Arctic Circle suggest that variation in daylight exposure might not be a crucial factor that contributes to the pathogenesis of AMD. The study conducted among the Inuit in Greenland [18] included a subset of participants from Sisimiut (66 degrees north). Although they found high frequency of late AMD we think other differences, for example diet, are more likely to explain the higher prevalence than varying sunlight exposure [70].

The strength and consistency of associations between cardiovascular risk factors and AMD vary in the literature. Besides age, smoking is a well-established risk factor for late AMD in both cross-sectional [71-73] and longitudinal studies [67]. In the current study we observed a strong association between current daily smoking and prevalent late AMD (OR 3.43 compared to never smokers controlled for sex and age) and for men 12 % higher odds of late AMD per 5 years of daily smoking. To date, smoking is the single most important modifiable risk factor for late AMD, and cessation of smoking should be emphasised also on the basis of preventing visual loss and blindness.

High systolic blood pressure has been shown to be associated with lower choroidal blood flow in patients with AMD and through this ischemic mechanism suggested as one of the etiologic factors for developing AMD [74, 75]. However, there is still lack of convincing evidence for a relationship with AMD [37, 40, 45, 67]. Results from

the current work support an association between AMD and systemic blood pressure and/or pulse pressure.

Mares et al found a protective effect of physical activity in their study [47]. Further, results from the Beaver Dam Eye Study [76] reported an inverse association between substantial exercise and the incidence of late AMD. Another report from the same study population stated a reduced incidence of neovascular AMD in people with an active lifestyle [46]. Physical activity is associated with decreased cardiovascular risk and mortality [77]. Several beneficial effects on the cardiovascular system have been discussed, such as decreased oxidative stress, inflammation and vascular tone [78], hence a healthy vascular status should be an advantage also in the eye. In our study, we found that women who exercised weekly compared to less have significant lower odds of late AMD. It should be noted that the relationship between AMD and physical activity did not reach statistical significance for duration, intensity or type of physical activity.

BMI outside the normal limit has been associated with AMD in a growing number of studies [41, 42, 79, 80]. Seddon et al. [41] showed an increased risk of progression to a more advanced stage of AMD with higher levels of BMI. Smith et al. [79] reported only significant findings with early AMD, whilst the pooled Rotterdam, Beaver Dam and Blue Mountain Studies [67, 72] failed to confirm a relationship. In our study, we found the association with higher BMI only to be significant for women, and overweight showed a stronger relationship than did obesity, although this could be due to selective mortality. We also observed higher odds of late AMD in lean subjects, but within this category were only few cases and hence these results should be interpreted with caution. A recent meta-analysis suggested that women may have an increased risk of neovascular AMD compared to

men [22]. Our findings may contribute to the understanding of a small female preponderance in AMD. Apart from a possible sex-dependent causal relationship between obesity and AMD, other factors may confound this relationship. However, factors associated with increased BMI such as diabetes, HbA_{1c}, and serum lipids were not associated with AMD in our study.

We found a significant interaction between age and sex for late AMD, indicating that the effect of age on late AMD is sex-dependent. In their recent review, Parker, Kalasky and Proctor postulated that the sex-specific plasticity of the aging cardiovascular system may contribute to the observed interactions between sex, aging, physical activity and disease risk [81]. For example, muscle sympathetic nerve activity has been shown to increase more in aging women than in men. This could in turn explain the increased risk of hypertension and cardiovascular disease progression in older women. The differences in development of atherosclerotic plaques have been described in several studies [82]. Adiposity measures seem to exert similar effect in both sexes [82]. The Framingham study reported higher hazard ratio for cardiovascular events associated with blood pressure in the higher normal range (<140/90 mmHg) in females than in males compared with subjects with optimal blood pressure (<120/80 mmHg) [83]. Diabetes is a more important risk factors for cardiovascular disease and death for women than in men [84]. Moreover, physical activity may have a more pronounced effect in women compared to men [85]. Differences in sex hormones might explain part of the sex disparity in the epidemiology of cardiovascular disease due to their influence on vascular processes [86]. Nevertheless, for AMD, results from epidemiological studies are inconsistent on whether or not a true sex difference exists [22, 72].

Previous cross-sectional studies have shown both protective effect of oestrogen exposure and no association at all [24]. Results from incidence data are also conflicting; the pooled incidence data from three continents showed no association between female reproductive factors or hormone use, and AMD [24, 67]. We did not find an association between late AMD and exogenous oestrogen exposure in the form of contraceptives or OHT. Nor did we find an association between late AMD and onset, end or length of fertile years, bilateral oophorectomy or parity as surrogate measures.

To our knowledge, no prior study has examined the association between breastfeeding and maternal AMD. Our results are in line with studies showing that breastfeeding confers protection against maternal diseases later in life, such as breast cancer and cardiovascular diseases [87, 88]. Although the pathophysiological explanation for the maternal benefits of lactation is not clear, we hypothesize that breastfeeding reduce the cardiovascular risk profile which in turn results in protection against AMD [89].

The importance of our new finding is that it shows that late AMD may be influenced by risk factor exposure during early adulthood. Further, the findings add to a growing body of literature showing maternal benefits of breastfeeding. From a public health point of view, promotion of longer lactation could have a significant impact on eye health in elderly women. However, this is a novel finding that needs confirmation in other studies.

5.4 Implications and further research

Increasing numbers of patients with AMD is anticipated due to ageing populations. Estimates of AMD prevalence are hence important for adequate community planning of eye health services and rehabilitation. Standardisation of definitions and grading procedures is

advocated to facilitate comparison between studies and provide accurate and precise rates.

Detection of modifiable risk factors is most likely a cost-effective goal as the cost associated with this disease is high. This thesis confirms age and smoking as important risk factors. Cessation of smoking should be emphasised as a preventive measure for visual loss. The sex disparity in the cardiovascular risk factors and lactation as a protective factor for late AMD implicates that further research should also include sex-specific analysis. This should preferably be carried out in larger or pooled studies due to the low prevalence of late AMD with sub-analysis on GA and nvAMD.

Risk factors for AMD in populations living in the high north are scarcely described in the literature. Further studies on this cohort will provide valuable data on AMD in a unique population and such data can provide additional aspects to the epidemiology of AMD and its interaction with environmental factors

6. CONCLUSIONS

- I. The Tromsø Eye Study utilised methodology with standardised protocols, large sample size, high attendance rates and it provides a valuable collection of data.

- II. The prevalence of AMD among elderly in this study was similar to results from other Caucasian populations. Late AMD was present in 10.9 % of subjects aged 80 years and older. No sex differences in prevalence of large drusen or late AMD were observed. Age was a strong risk factor for large drusen and late AMD. The symmetry between eyes was highest for large drusen followed by geographic atrophy and thereafter neovascular disease. Lower refractive error was observed in eyes with late AMD than in eyes without late AMD.

- III. Smoking was a strong risk factor for late AMD in both sexes as consistently reported worldwide. Late AMD significantly associated with higher BMI, higher pulse pressure and infrequent physical exercise in women but not in men. No significant association between serum lipids, education, alcohol consumption, diabetes, cardiovascular disease and late AMD was observed.

- IV. Longer duration of breastfeeding was associated with lower risk of maternal late AMD. We did not find an association between use of contraceptives or OHT and late AMD. Nor did we find an association between late AMD and onset, end or length of fertile years, bilateral oophorectomy or parity.

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Paper I

Paper II

Paper III

Paper IV

Appendix A



The Tromsø Study

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

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HEALTH AND DISEASES

1 How do you in general consider your own health to be?

- Very good
- Good
- Neither good nor bad
- Bad
- Very bad

2 How is your health compared to others in your age?

- Much better
- A little better
- About the same
- A little worse
- Much worse

3 Do you have, or have you had?

Yes No

Age first time

- | | | | |
|--|--------------------------|--------------------------|----------------------|
| A heart attack | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Angina pectoris (<i>heart cramp</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Cerebral stroke/brain hemorrhage.. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Atrial fibrillation | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| High blood pressure | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Osteoporosis | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Asthma | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Chronic bronchitis/Emphysema/COPD ... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Diabetes | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Psychological problems (<i>for which you have sought help</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Hypothyroidism | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Kidney disease, <i>not including urinary tract infection (UTI)</i> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Migraine | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |

4 Do you have persistent or constantly recurring pain that has lasted for 3 months or more?

- Yes
- No

5 How often have you suffered from sleeplessness during the last 12 months?

- Never, or just a few times
- 1-3 times a month
- Approximately once a week
- More that once a week

6 Below you find a list of various problems.

Have you experienced any of this during the last week (including today)? (Tick once for each complaint)

- | | | | | | |
|---|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| | | No | Little | Pretty | Very |
| | + | complaint | complaint | much | much |
| Sudden fear without reason | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Felt afraid or anxious | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Faintness or dizziness | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Felt tense or upset | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Tend to blame yourself | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Sleeping problems | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Depressed, sad | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Feeling of being useless, worthless | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Feeling that everything is a struggle | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Feeling of hopelessness with regard to the future | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

USE OF HEALTH SERVICES

7 Have you during the last 12 months visited:

If YES; how many times?

- | | | | |
|--|--------------------------|--------------------------|----------------------|
| | Yes | No | No. of times |
| General practitioner (GP) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Psychiatrist/psychologist | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Medical specialist outside hospital (<i>other than general practitioner/psychiatrist</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Physiotherapist | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Chiropractor | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Alternative practitioner (<i>homeopath, acupuncturist, foot zone therapist, herbal medicine practitioner, laying on hands practitioner, healer, clairvoyant, etc.</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Dentist/dental service | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |

8 Have you during the last 12 months been to a hospital?

- | | | | |
|---|--------------------------|--------------------------|----------------------|
| | Yes | No | No. of times |
| Admitted to a hospital | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Had consultation in a hospital without admission; | | | |
| At psychiatric out-patient clinic | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| At another out-patient clinic | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |

9 Have you undergone any surgery during the last 3 years?

- Yes
- No

USE OF MEDICINES

- 10 Do you currently use, or have you used some of the following medicines? (Tick once for each line)

| | Never used | | | Age first time |
|-------------------------------|--------------------------|--------------------------|--------------------------|----------------------|
| | Now | Earlier | | |
| Blood pressure lowering drugs | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Cholesterol lowering drugs | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Drugs for heart disease | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Diuretics | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Drugs for osteoporosis | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Insulin | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Tablets for diabetes | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| The drugs for hypothyroidism | | | | |
| Thyroxine/levaxin | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |

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

| | Not used in the last 4 weeks | Less than every week | Every week, but not daily | Daily |
|------------------------------|------------------------------|--------------------------|---------------------------|--------------------------|
| Painkillers on prescription | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Painkillers non-prescription | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Sleeping pills | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Tranquillizers | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Antidepressants | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

- 12 State the name of all medicines -both those on prescription and non-prescription drugs- you have used regularly during the last 4 weeks. Do not include vitamins, minerals, herbs, natural remedies, other nutritional supplements, etc.

If there is not enough space for all medicines, continue on a separate sheet.

When attending you will be asked whether you have used antibiotics or painkillers the last 24 hours. If you have, you will be asked to provide the name of the drug, strength, dose and time of use.

FAMILY AND FRIENDS

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

| | Yes | No | Number |
|----------------------------------|--------------------------|--------------------------|----------------------|
| Spouse/partner | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Other people older than 18 years | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| People younger than 18 years | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |

- 14 Tick for the relatives who have or have had

| | Parents | Children | Siblings |
|-----------------------------------|--------------------------|--------------------------|--------------------------|
| A heart attack | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| A heart attack before age of 60 | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Angina pectoris (heart cramp) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Cerebral stroke/brain haemorrhage | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Osteoporosis | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Gastric/duodenal ulcers | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Asthma | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Diabetes | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Dementia | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Psychological problems | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Substance abuse | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

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

Yes No

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

Yes No

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

- Never, or just a few times a year
 1-2 times a month
 Approximately once a week
 More than once a week

WORK, SOCIAL SECURITY AND INCOME

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

- Primary/secondary school, modern secondary school
 Technical school, vocational school, 1-2 years senior high school
 High school diploma
 College/university less than 4 years
 College/university 4 years or more

- 19 What is your main activity? (Tick once)

- Full time work Housekeeping
 Part time work Retired/benefit recipient
 Unemployed Student/military service

20 Do you receive any of the following benefits?

- Old-age, early retirement or survivor pension
- Sickness benefit (on sick leave)
- Rehabilitation benefit
- Full disability pension
- Partial disability pension
- Unemployment benefits
- Transition benefit for single parents
- Social welfare benefits

21 What was the household's total taxable income last year? Include income from work, pensions, benefits and similar

- Less than 125 000 NOK
- 125 000-200 000 NOK
- 201 000-300 000 NOK
- 301 000-400 000 NOK
- 401 000-550 000 NOK
- 551 000-700 000 NOK
- 701 000 -850 000 NOK
- More than 850 000 NOK

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

- Yes
- No

PHYSICAL ACTIVITY

23 If you have paid or unpaid work, which statement describes your work best?

- Mostly sedentary work
(e.g. office work, mounting)
- Work that requires a lot of walking
(e.g. shop assistant, light industrial work, teaching)
- Work that requires a lot of walking and lifting
(e.g. postman, nursing, construction)
- Heavy manual labour

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

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

25 How often do you exercise? (With exercise we mean for example walking, skiing, swimming or training/sports)

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

26 How hard do you exercise on average?

- Easy- do not become short-winded or sweaty
- You become short-winded and sweaty
- Hard- you become exhausted

27 For how long time do you exercise every time on average?

- Less than 15 minutes
- 15-29 minutes
- 30-60 minutes
- More than 1 hour

ALCOHOL AND TOBACCO

28 How often do you drink alcohol?

- Never
- Monthly or less frequently
- 2-4 times a month
- 2-3 times a week
- 4 or more times a week

29 How many units of alcohol (a beer, a glass of wine or a drink) do you usually drink when you drink alcohol?

- 1-2
- 3-4
- 5-6
- 7-9
- 10 or more

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

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

31 Do you smoke sometimes, but not daily?

- Yes
- No

32 Do you/did you smoke daily?

- Yes, now
- Yes, previously
- Never

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

Number of years

34 If you currently smoke, or have smoked previously: How many cigarettes do you or did you usually smoke per day?

Number of cigarettes

35 How old were you when you began daily smoking?

Age in years

36 How many years in all have you smoked daily?

Number of years

37 Do you use or have you used snuff or chewing tobacco?

- No, never
- Yes, previously
- Yes, sometimes
- Yes, daily

DIET

38 Do you usually eat breakfast every day?

Yes No

39 How many units of fruit or vegetables do you eat on average per day? (units means for example a fruit, a cup of juice, potatoes, vegetables)

Number of units +

40 How many times a week do you eat warm dinner?

Number

41 How often do you usually eat these foods?

(Tick once for each line)

| | 0-1 times/ mth | 2-3 times/ mth | 1-3 times/ week | 4-6 times/ week | 1-2 times/ day |
|--|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| Potatoes | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Pasta/rice | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Meat (<i>not processed</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Processed meat (<i>sausages, hamburger, etc.</i>) ... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Fruits, vegetables, berries | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Lean fish | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Fatty fish | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <i>(e.g. salmon, trout, mackerel, herring, halibut, redfish)</i> | | | | | |

42 How much do you usually drink the following?

(Tick once for each line)

| | Rarely/ never | 1-6 glasses /week | 1 glass /day | 2-3 glasses /day | 4 or more glasses /day |
|--------------------------------------|--------------------------|--------------------------|--------------------------|--------------------------|------------------------------|
| Milk, curdled milk, yoghurt | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Juice | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Soft drinks with sugar | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

43 How many cups of coffee and tea do you drink daily? (Put 0 for the types you do not drink daily)

| | Number of cups |
|---|---|
| Filtered coffee | <input type="text"/> <input type="text"/> |
| Boiled coffee (<i>coarsely ground coffee for brewing</i>) | <input type="text"/> <input type="text"/> |
| Other types of coffee | <input type="text"/> <input type="text"/> |
| Tea | <input type="text"/> <input type="text"/> |

44 How often do you usually eat cod liver and roe? (i.e. "mølje")

Rarely/never 1-3 times/year 4-6 times/year
 7-12 times/year More than 12 times/year

45 Do you use the following nutritional supplements?

| | Daily | Sometimes | No |
|--|--------------------------|--------------------------|--------------------------|
| + Cod liver oil or fish oil capsules | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Omega 3 capsules (<i>fish oil, seal oil</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Calcium tablets | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

QUESTIONS FOR WOMEN

46 Are you pregnant at the moment?

Yes No Uncertain

47 How many children have you given birth to?

Number +

48 If you have given birth, fill in for each child: birth year, birth weight and months of breastfeeding (Fill in the best you can)

| Child | Birth year | Birth weight in grams | Months of breastfeeding |
|-------|---|---|---|
| 1 | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> |
| 2 | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> |
| 3 | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> |
| 4 | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> |
| 5 | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> |
| 6 | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> |

49 Have you during pregnancy had high blood pressure?

Yes No

50 If yes, during which pregnancy?

The first Second or later

51 Have you during pregnancy had proteinuria?

Yes No

52 If yes, during which pregnancy?

The first Second or later

53 Were any of your children delivered prematurely (a month or more before the due date) because of preeclampsia?

Yes No

54 If yes, which child?

1st child 2nd child 3rd child 4th child 5th child 6th child

55 How old were you when you started menstruating?

Age +

56 Do you currently use any prescribed drug influencing the menstruation?

Oral contraceptives, hormonal intrauterine or similar

Yes No

Hormone treatment for menopausal problems

Yes No

When attending you will get supplementary questions about menstruation and any use of hormones. Write down on a sheet of paper the names of all the hormones you have used and bring it with you. You will also be asked whether your menstruation have ceased and possibly when and why.



The Tromsø Study

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

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HEALTH AND DISEASES

1 How do you in general consider your own health to be?

- Very good
- Good
- Neither good nor bad
- Bad
- Very bad

2 How is your health compared to others in your age?

- Much better
- A little better
- About the same
- A little worse
- Much worse

3 Do you have, or have you had?

Yes No

Age first time

- | | | | |
|--|--------------------------|--------------------------|----------------------|
| A heart attack | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Angina pectoris (<i>heart cramp</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Cerebral stroke/brain hemorrhage.. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Atrial fibrillation | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| High blood pressure | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Osteoporosis | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Asthma | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Chronic bronchitis/Emphysema/COPD ... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Diabetes | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Psychological problems (<i>for which you have sought help</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Hypothyroidism | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Kidney disease, <i>not including urinary tract infection (UTI)</i> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Migraine | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |

4 Do you have persistent or constantly recurring pain that has lasted for 3 months or more?

- Yes
- No

5 How often have you suffered from sleeplessness during the last 12 months?

- Never, or just a few times
- 1-3 times a month
- Approximately once a week
- More that once a week

6 Below you find a list of various problems.

Have you experienced any of this during the last week (including today)? (Tick once for each complaint)

| | | | | |
|---|-----------|-----------|--------|------|
| + | No | Little | Pretty | Very |
| | complaint | complaint | much | much |

- | | | | | |
|---|--------------------------|--------------------------|--------------------------|--------------------------|
| Sudden fear without reason | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Felt afraid or anxious | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Faintness or dizziness | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Felt tense or upset | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Tend to blame yourself | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Sleeping problems | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Depressed, sad | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Feeling of being useless, worthless | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Feeling that everything is a struggle | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Feeling of hopelessness with regard to the future | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

USE OF HEALTH SERVICES

7 Have you during the last 12 months visited:

If YES; how many times?

Yes No No. of times

- | | | | |
|---|--------------------------|--------------------------|----------------------|
| General practitioner (GP) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Psychiatrist/psychologist | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Medical specialist outside hospital (<i>other than general practitioner/psychiatrist</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Physiotherapist | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Chiropractor | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Alternative practitioner (<i>homeopath, acupuncturist, foot zone therapist, herbal medicine practitioner, laying on hands practitioner, healer, clairvoyant, etc.</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Dentist/dental service | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |

8 Have you during the last 12 months been to a hospital?

Yes No No. of times

- | | | | |
|---|--------------------------|--------------------------|----------------------|
| Admitted to a hospital | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Had consultation in a hospital without admission; | | | |
| At psychiatric out-patient clinic | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| At another out-patient clinic | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |

9 Have you undergone any surgery during the last 3 years?

- Yes
- No

+

USE OF MEDICINES

- 10 Do you currently use, or have you used some of the following medicines? (Tick once for each line)

| | Never used | Now | Earlier | Age first time |
|-------------------------------|--------------------------|--------------------------|--------------------------|----------------------|
| Blood pressure lowering drugs | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Cholesterol lowering drugs | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Drugs for heart disease | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Diuretics | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Drugs for osteoporosis | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Insulin | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Tablets for diabetes | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| The drugs for hypothyroidism | | | | |
| Thyroxine/levaxin | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |

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

| | Not used in the last 4 weeks | Less than every week | Every week, but not daily | Daily |
|------------------------------|------------------------------|--------------------------|---------------------------|--------------------------|
| Painkillers on prescription | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Painkillers non-prescription | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Sleeping pills | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Tranquillizers | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Antidepressants | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

- 12 State the name of all medicines -both those on prescription and non-prescription drugs- you have used regularly during the last 4 weeks. Do not include vitamins, minerals, herbs, natural remedies, other nutritional supplements, etc.

If there is not enough space for all medicines, continue on a separate sheet.

When attending you will be asked whether you have used antibiotics or painkillers the last 24 hours. If you have, you will be asked to provide the name of the drug, strength, dose and time of use.

FAMILY AND FRIENDS

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

| | Yes | No | Number |
|----------------------------------|--------------------------|--------------------------|----------------------|
| Spouse/partner | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Other people older than 18 years | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| People younger than 18 years | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |

- 14 Tick for the relatives who have or have had

| | Parents | Children | Siblings |
|-----------------------------------|--------------------------|--------------------------|--------------------------|
| A heart attack | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| A heart attack before age of 60 | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Angina pectoris (heart cramp) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Cerebral stroke/brain haemorrhage | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Osteoporosis | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Gastric/duodenal ulcers | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Asthma | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Diabetes | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Dementia | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Psychological problems | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Substance abuse | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

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

Yes No

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

Yes No

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

- Never, or just a few times a year
 1-2 times a month
 Approximately once a week
 More than once a week

WORK, SOCIAL SECURITY AND INCOME

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

- Primary/secondary school, modern secondary school
 Technical school, vocational school, 1-2 years senior high school
 High school diploma
 College/university less than 4 years
 College/university 4 years or more

- 19 What is your main activity? (Tick once)

- Full time work Housekeeping
 Part time work Retired/benefit recipient
 Unemployed Student/military service

20 Do you receive any of the following benefits?

- Old-age, early retirement or survivor pension
- Sickness benefit (on sick leave)
- Rehabilitation benefit
- Full disability pension
- Partial disability pension
- Unemployment benefits
- Transition benefit for single parents
- Social welfare benefits

21 What was the household's total taxable income last year? Include income from work, pensions, benefits and similar

- Less than 125 000 NOK
- 125 000-200 000 NOK
- 201 000-300 000 NOK
- 301 000-400 000 NOK
- 401 000-550 000 NOK
- 551 000-700 000 NOK
- 701 000 -850 000 NOK
- More than 850 000 NOK

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

- Yes
- No

PHYSICAL ACTIVITY

23 If you have paid or unpaid work, which statement describes your work best?

- Mostly sedentary work
(e.g. office work, mounting)
- Work that requires a lot of walking
(e.g. shop assistant, light industrial work, teaching)
- Work that requires a lot of walking and lifting
(e.g. postman, nursing, construction)
- Heavy manual labour

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

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

25 How often do you exercise? (With exercise we mean for example walking, skiing, swimming or training/sports)

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

26 How hard do you exercise on average?

- Easy- do not become short-winded or sweaty
- You become short-winded and sweaty
- Hard- you become exhausted

27 For how long time do you exercise every time on average?

- Less than 15 minutes
- 15-29 minutes
- 30-60 minutes
- More than 1 hour

ALCOHOL AND TOBACCO

28 How often do you drink alcohol?

- Never
- Monthly or less frequently
- 2-4 times a month
- 2-3 times a week
- 4 or more times a week

29 How many units of alcohol (a beer, a glass of wine or a drink) do you usually drink when you drink alcohol?

- 1-2
- 3-4
- 5-6
- 7-9
- 10 or more

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

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

31 Do you smoke sometimes, but not daily?

- Yes
- No

32 Do you/did you smoke daily?

- Yes, now
- Yes, previously
- Never

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

Number of years

34 If you currently smoke, or have smoked previously: How many cigarettes do you or did you usually smoke per day?

Number of cigarettes

35 How old were you when you began daily smoking?

Age in years

36 How many years in all have you smoked daily?

Number of years

37 Do you use or have you used snuff or chewing tobacco?

- No, never
- Yes, previously
- Yes, sometimes
- Yes, daily

DIET

38 Do you usually eat breakfast every day?

Yes No

39 How many units of fruit or vegetables do you eat on average per day? (units means for example a fruit, a cup of juice, potatoes, vegetables)

Number of units +

40 How many times a week do you eat warm dinner?

Number

41 How often do you usually eat these foods?

(Tick once for each line)

| | 0-1 times/ mth | 2-3 times/ mth | 1-3 times/ week | 4-6 times/ week | 1-2 times/ day |
|--|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| Potatoes | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Pasta/rice | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Meat (<i>not processed</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Processed meat (<i>sausages, hamburger, etc.</i>) ... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Fruits, vegetables, berries | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Lean fish | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Fatty fish | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| <i>(e.g. salmon, trout, mackerel, herring, halibut, redfish)</i> | | | | | |

42 How much do you usually drink the following?

(Tick once for each line)

| | Rarely/ never | 1-6 glasses /week | 1 glass /day | 2-3 glasses /day | 4 or more glasses /day |
|--------------------------------------|--------------------------|--------------------------|--------------------------|--------------------------|------------------------------|
| Milk, curdled milk, yoghurt | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Juice | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Soft drinks with sugar | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

43 How many cups of coffee and tea do you drink daily? (Put 0 for the types you do not drink daily)

| | Number of cups |
|---|---|
| Filtered coffee | <input type="text"/> <input type="text"/> |
| Boiled coffee (<i>coarsely ground coffee for brewing</i>) | <input type="text"/> <input type="text"/> |
| Other types of coffee | <input type="text"/> <input type="text"/> |
| Tea | <input type="text"/> <input type="text"/> |

44 How often do you usually eat cod liver and roe? (i.e. "mølje")

Rarely/never 1-3 times/year 4-6 times/year
 7-12 times/year More than 12 times/year

45 Do you use the following nutritional supplements?

| | Daily | Sometimes | No |
|--|--------------------------|--------------------------|--------------------------|
| + Cod liver oil or fish oil capsules | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Omega 3 capsules (<i>fish oil, seal oil</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Calcium tablets | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

QUESTIONS FOR WOMEN

46 Are you pregnant at the moment?

Yes No Uncertain

47 How many children have you given birth to?

Number +

48 If you have given birth, fill in for each child: birth year, birth weight and months of breastfeeding (Fill in the best you can)

| Child | Birth year | Birth weight in grams | Months of breastfeeding |
|-------|---|---|---|
| 1 | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> |
| 2 | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> |
| 3 | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> |
| 4 | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> |
| 5 | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> |
| 6 | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> <input type="text"/> | <input type="text"/> <input type="text"/> |

49 Have you during pregnancy had high blood pressure?

Yes No

50 If yes, during which pregnancy?

The first Second or later

51 Have you during pregnancy had proteinuria?

Yes No

52 If yes, during which pregnancy?

The first Second or later

53 Were any of your children delivered prematurely (a month or more before the due date) because of preeclampsia?

Yes No

54 If yes, which child?

1st child 2nd child 3rd child 4th child 5th child 6th child

55 How old were you when you started menstruating?

Age +

56 Do you currently use any prescribed drug influencing the menstruation?

Oral contraceptives, hormonal intrauterine or similar

Yes No

Hormone treatment for menopausal problems

Yes No

When attending you will get supplementary questions about menstruation and any use of hormones. Write down on a sheet of paper the names of all the hormones you have used and bring it with you. You will also be asked whether your menstruation have ceased and possibly when and why.

Appendix B



Tromsø

- part of The Tromsø Study



FILL OUT THE FORM IN THIS WAY:

The form would be read by machine, it is therefore important that you tick appropriately:

Correct

Wrong

Wrong

If you tick the wrong box, correct by filling the box like this

Write the numbers clearly *1 2 3 4 5 6 7 8 9 0*

| | |
|---|---|
| 7 | 4 |
|---|---|

 Correct

| | |
|---|---|
| 7 | 4 |
|---|---|

 Wrong

Use only black or blue pen, do not use pencil or felt tip pen

1. DESCRIPTION OF YOUR HEALTH STATUS

By placing a tick in one box in each group below, please indicate which statements best describe your own health state today:

1.6 To allow you to show us how good or bad your state of health is we have made a scale (almost like a thermometer) where the best state of health you can imagine is marked 100 and the worst 0. We ask you to show your state of health by drawing a line from the box below to the point on the scale that best fits your state of health.

1.01 Mobility

- I have no problems in walking about
- I have some problems in walking about
- I am confined to bed

1.02 Self-care

- I have no problems with self-care
- I have some problems washing or dressing myself
- I am unable to wash or dress myself

1.03 Usual activities (e.g. work, study, housework, family or leisure activities)

- I have no problems with performing my usual activities
- I have some problems with performing my usual activities
- I am unable to perform my usual activities

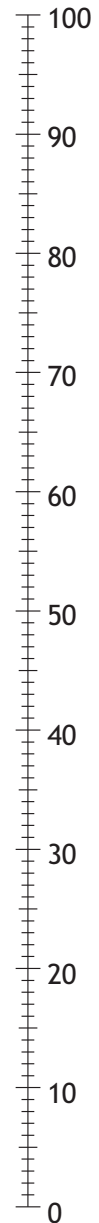
1.04 Pain and discomfort

- I have no pain or discomfort
- I have moderate pain or discomfort
- I have extreme pain or discomfort

1.05 Anxiety and depression

- I am not anxious or depressed
- I am moderately anxious or depressed
- I am extremely anxious or depressed

Best imaginable health state



Your own health state today

Worst imaginable health state

2. CHILDHOOD/YOUTH AND AFFILIATION

2.01 **Where did you live at the age of 1 year?**

- In Tromsø (*with present municipal borders*)
- In Troms, but not Tromsø
- In Finnmark
- In Nordland
- Another place in Norway
- Abroad

2.02 **How was your family's financial situation during your childhood?**

- Very good
- Good
- Difficult
- Very difficult

2.03 **What is the importance of religion in your life?**

- Very important
- Somewhat important
- Not important

2.07 **What was/is the highest completed education for your parents and your spouse/partner?**
(Tick once for each column)

| | Mother | Father | Spouse/ partner |
|---|--------------------------|--------------------------|--------------------------|
| 7-10 years primary/secondary school, modern secondary school | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Technical school, vocational school, 1-2 years senior high school | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| High school diploma | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| College or university (less than 4 years) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| College or university (4 years or more) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

2.04 **What do you consider yourself as? (Tick for one or more alternatives)**

- Norwegian
- Sami
- Kven/Finnish
- Another

2.05 **How many siblings and children do you have/have you had?**

Number of siblings

Number of children

2.06 **Is your mother alive?**

- Yes No

If NO: her age when she died

Is your father alive?

- Yes No

If NO: his age when he died

3. WELL BEING AND LIVING CONDITIONS

3.01 Below are three statements about satisfaction with life as a whole. Then there are two statements about views on your own health. Show how you agree or disagree with each of the statements by ticking in the box for the number you think fits best for you. (tick once for each statement)

| | Completely disagree | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Completely agree |
|---|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|------------------|
| In most ways my life is close to my ideal | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| My life conditions are excellent | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| I am satisfied with my life | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| I have a positive view of my future health | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| By living healthy, I can prevent serious diseases | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |

3.02 Below are four statements concerning your current job conditions, or if you are not working now, the last job you had. (Tick once for each statement)

| | Completely disagree | 1 | 2 | 3 | 4 | 5 | 6 | 7 | Completely agree |
|--|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|------------------|
| My work is tiring, physically or mentally | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| I have sufficient influence on when and how my work should be done | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| I am being bullied or harassed at work | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| I am being treated fairly at work | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |

3.03 I consider my occupation to have the following social status in the society (if you are not currently employed, think about your latest occupation)

- Very high status
- Fairly high status
- Medium status
- Fairly low status
- Very low status

3.04 Have you over a long period experienced any of the following? (Tick one or more for each line)

| | No | Yes, as a child | Yes, as adult | Yes, last year |
|--|--------------------------|--------------------------|--------------------------|--------------------------|
| Been tormented, or threatened with violence | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Been beaten, kicked at or victim of other types of violence | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Someone in your close family have used alcohol or drugs in such a way that it has caused you worry | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

If you have experienced anything of the above, how much are you affected by that now?

- Not affected Affected to some extent Affected to a large extent

4. ILLNESS AND WORRIES

4.01 **Have you during the last month experienced any illness or injury?**

Yes No

If YES: have you during the same period?
(Tick once for each line)

| | Yes | No |
|---|--------------------------|--------------------------|
| Been to a general practitioner | <input type="checkbox"/> | <input type="checkbox"/> |
| Been to a medical specialist | <input type="checkbox"/> | <input type="checkbox"/> |
| Been to emergency department | <input type="checkbox"/> | <input type="checkbox"/> |
| Been admitted to a hospital | <input type="checkbox"/> | <input type="checkbox"/> |
| Been to an alternative practitioner (chiropractor, homeopath or similar) | <input type="checkbox"/> | <input type="checkbox"/> |

4.02 **Have you noticed sudden changes in your pulse or heart rhythm in the last year?**

Yes No

4.03 **Do you become breathless in the following situations? (tick once for each question)**

| | Yes | No |
|--|--------------------------|--------------------------|
| When you walk rapidly on level ground or up a moderate slope | <input type="checkbox"/> | <input type="checkbox"/> |
| When you walk calmly on level ground | <input type="checkbox"/> | <input type="checkbox"/> |
| While you are washing or dressing | <input type="checkbox"/> | <input type="checkbox"/> |
| At rest | <input type="checkbox"/> | <input type="checkbox"/> |

4.04 **Do you cough about daily for some periods of the year?**

Yes No

If YES: Is the cough usually productive?

Yes No

Have you had this kind of cough for as long as 3 months in each of the last two years?

Yes No

4.05 **How often do you suffer from sleeplessness? (tick once)**

Never, or just a few times a year
 1-3 times a month
 Approximately once a week
 More than once a week

If you suffer from sleeplessness monthly or more often, what time of the year does it affect you most? (Put one or more ticks)

No particular time
 Polar night time
 Midnight sun time
 Spring and autumn

4.06 **Have you had difficulty sleeping during the past couple of weeks?**

Not at all
 No more than usual
 Rather more than usual
 Much more than usual

4.07 **Have you during the last two weeks felt unhappy and depressed?**

Not at all
 No more than usual
 Rather more than usual
 Much more than usual

4.08 **Have you during the last two weeks felt unable to cope with your difficulties?**

Not at all
 No more than usual
 Rather more than usual
 Much more than usual

4.09 **Below, please answer a few questions about your memory: (tick once for each question)**

| | Yes | No |
|--|--------------------------|--------------------------|
| Do you think that your memory has declined? | <input type="checkbox"/> | <input type="checkbox"/> |
| Do you often forget where you have placed your things? | <input type="checkbox"/> | <input type="checkbox"/> |
| Do you have difficulties finding common words in a conversation? | <input type="checkbox"/> | <input type="checkbox"/> |
| Have you problems performing daily tasks you used to master? | <input type="checkbox"/> | <input type="checkbox"/> |
| Have you been examined for memory problems? | <input type="checkbox"/> | <input type="checkbox"/> |

If YES to at least one of the first four questions above: Is this a problem in your daily life?

Yes No

4.10 Have you during the last last year suffered from pain and/or stiffness in muscles or joints in your neck/shoulders lasting for at least 3 consecutive months? (tick once for each line)

| | No complaint | Little complaint | Severe complaint |
|---------------------------|--------------------------|--------------------------|--------------------------|
| Neck, shoulders | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Arms, hands..... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Upper part of the back... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| The lumbar region..... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Hips, leg, feet..... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Other places..... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

4.11 Have you suffered from pain and/or stiffness in muscles or joints during the last 4 weeks? (tick once for each line)

| | No complaint | Little complaint | Severe complaint |
|----------------------------|--------------------------|--------------------------|--------------------------|
| Neck, shoulders | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Arms, hands | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Upper part of the back ... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| The lumbar region | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Hips, leg, feet | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Other places | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

4.12 Have you ever had:

| | Yes | No | Age last time |
|--------------------------------------|--------------------------|--------------------------|----------------------|
| Fracture in the wrist/forearm? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Hip fracture? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |

4.13 Have you been diagnosed with arthrosis by a physician?

Yes No

4.14 Do you have or have you ever had some of the following:

| | Never | Some | Much |
|-----------------------|--------------------------|--------------------------|--------------------------|
| Nickel allergy | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Pollen allergy | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Other allergies | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

4.15 Have you ever experienced infertility for more than 1 year?

Yes No

If Yes: was it due to:

| | Yes | No | Do not know |
|---|--------------------------|--------------------------|--------------------------|
| A condition concerning you?..... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| A condition concerning your partner?..... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

4.16 To which degree have you had the following complaints during the last 12 months?

| | Never | Some | Much |
|---|--------------------------|--------------------------|--------------------------|
| Nausea | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Heartburn/regurgitation.... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Diarrhoea..... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Constipation..... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Alternating diarrhoea and constipation..... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Bloated stomach..... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Abdominal pain..... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

4.17 If you have had abdominal pain or discomfort during the last year:

| | Yes | No |
|--|--------------------------|--------------------------|
| Was it located in your upper stomach? | <input type="checkbox"/> | <input type="checkbox"/> |
| Were you bothered as often as once a week or more during the last 3 months?... | <input type="checkbox"/> | <input type="checkbox"/> |
| Do you feel symptoms relief after bowel movement?..... | <input type="checkbox"/> | <input type="checkbox"/> |
| Are the symptoms related to more frequent or rare bowel movements than normally? | <input type="checkbox"/> | <input type="checkbox"/> |
| Are the symptoms related to more loose or hard stool than normally?..... | <input type="checkbox"/> | <input type="checkbox"/> |
| Do the symptoms appear after a meal? ... | <input type="checkbox"/> | <input type="checkbox"/> |

4.18 Have you ever had:

| | Yes | No | Age last time |
|----------------------|--------------------------|--------------------------|----------------------|
| Gastric ulcer | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Duodenal ulcer | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |
| Ulcer surgery | <input type="checkbox"/> | <input type="checkbox"/> | <input type="text"/> |

4.19 For women: Have you ever had a miscarriage?

Yes No Do not know

If Yes: number of times

4.20 For men: Have your partner ever had a miscarriage?

Yes No Do not know

If Yes: number of times

4.21 Is your diet gluten-free?

Yes No Do not know

4.22 Have you been diagnosed with Dermatitis Herpetiformis (DH)?

Yes No Do not know

4.23 Have you been diagnosed with coeliac disease, based on a biopsy from your intestine taken in a gastroscopy examination?

Yes No Do not know

4.24 Do you have your natural teeth?

Yes No

4.25 How many amalgam tooth fillings do you have/have you had?

0 1-5 6-10 10+

4.26 Have you been suffering from headache the last year?

Yes No

If No: go to section 5, food habits

4.27 What kind of headache are you suffering from?

Migraine Other headache

4.28 How many days per month do you suffer from headache?

Less than one day
 1-6 days
 7-14 days
 More than 14 days

4.29 Is the headache attacks usually:
(tick once for each line)

| | Yes | No |
|--|--------------------------|--------------------------|
| Pounding/pulsatory pain | <input type="checkbox"/> | <input type="checkbox"/> |
| Pressing/tightening pain | <input type="checkbox"/> | <input type="checkbox"/> |
| Unilateral pain (<i>right or left</i>) | <input type="checkbox"/> | <input type="checkbox"/> |

4.30 What is the normal intensity of your headache attacks?

Mild (*do not hinder normal activity*)
 Moderate (*decrease normal activity*)
 Strong (*block normal activity*)

4.31 What is the normal duration of the headache attacks?

Less than 4 hours
 4 hours - 1 day
 1-3 days
 More than 3 days

4.32 If you suffer from headache, when during the year does it affect you most? (tick one or more)

No particular time
 Polar night time
 Midnight sun time
 Spring and/or Autumn

4.33 Before or during the headache, do you have a temporary:

| | Yes | No |
|---|--------------------------|--------------------------|
| Visual disturbances? (<i>flickering, blurred vision, flashes of light</i>)..... | <input type="checkbox"/> | <input type="checkbox"/> |
| Unilateral numbness in your face or hand? | <input type="checkbox"/> | <input type="checkbox"/> |
| Aggravated pain by moderate physical activity? | <input type="checkbox"/> | <input type="checkbox"/> |
| Nausea and/or vomiting? | <input type="checkbox"/> | <input type="checkbox"/> |

4.34 Describe how many days you have been away from work or school during the last month due to headache?

Number of days.....

5. FOOD HABITS

5.01 How often do you usually eat the following? (tick once for each line)

| | 0-1 times per month | 2-3 times per month | 1-3 times per week | More than 3 times per week |
|---|--------------------------|--------------------------|--------------------------|-------------------------------|
| Fresh water fish (<i>not farmed</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Salt water fish (<i>not farmed</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Farmed fish (<i>salmon, trout, char</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Tuna fish (<i>fresh or canned</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Fish bread spread | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Mussels, shells | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| The brown content in crabs | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Whale or seal meat | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Pluck (liver/kidney/heart) from reindeer or elk/moose.. | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Pluck (liver/kidney/heart) from ptarmigan/grouse | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

5.02 How many times during the year do/did you usually eat the following? (number of times)

| | In adulthood | In childhood |
|---|--------------|--------------|
| Mølje (cod or pollack meat, liver, and roe) (Number of times per year) | | |
| Sea gull's egg (Number of eggs per year) | | |
| Reindeer meat (Number of times per year) | | |
| Local mushroom and wild berries (<i>blueberries/lingonberries/cloudberries</i>) (Number of times per year) | | |

5.03 How many times per month do you eat canned (tinned) foods (from metal boxes)?

Number

5.04 Do you take vitamins and/or mineral supplements?

Yes, daily Sometimes Never

5.05 How often do you eat?

| | Never | 1-3 times per month | 1-3 times per week | 4-6 times per week | 1-2 times per day | 3 times per day or more |
|--------------------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|----------------------------|
| Dark chocolate | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Light chocolate/milk chocolate | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Chocolate cake | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Other sweets | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

5.06 If you eat chocolate, how much do you usually eat each time?

Compared with the size of a Kvikk-Lunsj sjokolade (*a chocolate brand in the market*) and describe how much do you eat in relation to it.

$\frac{1}{4}$ $\frac{1}{2}$ 1 1 $\frac{1}{2}$ 2 More than 2

5.07 How often do you drink cocoa/hot chocolate?

| | Never | 1-3 times per month | 1-3 times per week | 4-6 times per week | 1-2 times per day | 3 times per day or more |
|--|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|----------------------------|
| | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

6. ALCOHOL

6.01 How often have you in the last year:

| | Never | Less than monthly | Monthly | Weekly | Daily or almost daily |
|---|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| Not been able to stop drinking alcohol when you have started? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Failed to do what was normally expected of you because of drinking? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Needed a drink in the morning to get yourself going after a heavy drinking session? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Had feeling of guilt or remorse after drinking? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Not been unable to remember what happened the night before because of your drinking?..... | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

| | Never | Yes, but not in the last year | Yes, during the last year |
|---|--------------------------|-------------------------------|---------------------------|
| 6.02 Have you or someone else been injured because of your drinking? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Has a relative, friend, physician, or other health care workers been concerned about your drinking or suggested you to cut down? | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

7. WEIGHT

| | |
|--|---|
| <p>7.01 Have you involuntary lost weight during the <u>last 6 months</u>? <input type="checkbox"/> Yes <input type="checkbox"/> No If Yes: how many kilograms? <input style="width: 40px;" type="text"/></p> <p>7.02 Estimate your body weight when you were 25 years old: Number of kilograms <input style="width: 40px;" type="text"/></p> | <p>7.03 Are you satisfied with your present body weight? <input type="checkbox"/> Yes <input type="checkbox"/> No</p> <p>7.04 What weight would you be satisfied with (your "ideal" weight)? Number of kilograms <input style="width: 40px;" type="text"/></p> |
|--|---|

8. SOLVENTS

| | |
|---|--|
| <p>8.01 How many hours per week, do you do the following <u>leisure- or professional activities</u>: Automobile repair/paint, ceramic work, painting/varnishing/solvents, hair dressing, glazier, electrician. (Put 0 if you do not engage in such leisure or professional activities) Number of hours per week on average <input style="width: 40px;" type="text"/></p> | <p>8.02 Do you use hair color preparations <input type="checkbox"/> Yes <input type="checkbox"/> No If Yes: How many times per year?.. <input style="width: 40px;" type="text"/></p> |
|---|--|

9. USE OF HEALTH SERVICES

9.01 **Have you ever experienced that diseases have been insufficiently examined or treated, and this had a serious consequence?**

- Yes, this has happened to me
 Yes, this has happened to a close relative
(*child, parents, spouse*)
 No

If Yes, was it caused by?
(tick once or more):

- general practitioner
 emergency medical doctor
 private practising specialist
 hospital doctor
 other health personnel
 alternative practitioner
 more than one person due to deficient routines and interaction

9.02 **Have you ever felt persuaded to accept an examination or treatment that you did not want?**

- Yes No

If Yes, do you think this has had unfortunate consequences for your health?

- Yes No

9.03 **Have you ever complained about a treatment you have received?**

- Have never had a reason for complaining
 Have considered complaining, but did not do
 Have complained verbally
 Have complained in writing

9.04 **How long have you had your current general practitioner/other physician?**

- Less than 6 months
 6 to 12 months
 12 to 24 months
 More than 2 years

9.05 **At the last visit to your GP, did you have a hard time to understand what the doctor(s) told you?** Answer on a scale from 0 to 10, where 0 = they were difficult to understand and 10 = they were always easy to understand

- 0 1 2 3 4 5 6 7 8 9 10

9.06 **How would you rate the treatment or counselling, you got at your last visit to your GP?** Answer on a scale from 0 to 10, where 0 = worst treatment or counselling, and 10 = best treatment or counselling

- 0 1 2 3 4 5 6 7 8 9 10

9.07 **During the last 12 months, how much of a problem, if any, was it to get a referral to special examinations (as x-ray, etc.) or to a specialist health care (private practising specialist or at hospital)?**

- Not relevant
 No problem
 Some problem
 Major problem

9.08 **During the last 12 months, how much of a problem, if any, was it to get a referral to physiotherapist, chiropractor, etc.?**

- Not relevant
 No problem
 Some problem
 Major problem

9.09 **Altogether, how much of a problem, if any, was it to get a referral to specialist health care?**

- Not relevant
 Very difficult
 Some difficulties
 Easy
 Very easy



9.10 During the last 12 months, have you been examined or treated by the specialist health care?

Yes No

If Yes, did you have a difficult time to understand what the doctor(s) told you? Answer on a scale from 0 to 10, where 0 = they were difficult to understand and 10 = they were always easy to understand

0 1 2 3 4 5 6 7 8 9 10

9.11 How would you rate the treatment or counselling you got at your last visit to a specialist? Answer on a scale from 0 to 10, where 0 = worst treatment or counselling, and 10 = best treatment or counselling

0 1 2 3 4 5 6 7 8 9 10



9.12 Have you ever, previous to the year 2002, had an operation at a hospital or a specialist clinic?

Yes No

9.13 Have you, during the last 12 months, used herbal or natural medicine?

Yes No

9.14 Have you, during the last 12 months, used meditation, yoga, qi gong or thai chi as self-treatment?

Yes No



10. USE OF ANTIBIOTICS

10.01 **Have you used antibiotics during the last 12 months?** (all penicillin-like medicine in the form of tablets, syrups or injections)

Yes No Do not remember

If YES: What did you get the treatment for?

Have you taken many antibiotic treatments, tick for each treatment.

| | Treatment 1 | Treatment 2 | Treatment 3 | Treatment 4 | Treatment 5 | Treatment 6 |
|---|---|---|---|---|---|---|
| • Urinary tract infection (<i>bladder infection, cystitis</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| • Respiratory tract infection (<i>ear, sinus, throat or lung infection, bronchitis</i>) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| • Other | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Treatment duration: number of days | <input style="width: 30px;" type="text"/> | <input style="width: 30px;" type="text"/> | <input style="width: 30px;" type="text"/> | <input style="width: 30px;" type="text"/> | <input style="width: 30px;" type="text"/> | <input style="width: 30px;" type="text"/> |

How did you acquire the antibiotics for treatment?

Have you acquired many treatments, tick for each one.

| | | | | | | |
|--|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|
| With prescription from a physician/dentist | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Without contacting a physician/without prescription: | | | | | | |
| • Purchase from a pharmacy abroad | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| • Purchase over the internet | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| • Remnants from earlier treatment at home | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| • From family/friends | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| • Other ways | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

10.02 **Do you presently have antibiotics at home?**

Yes No

If YES: is this after an agreement with your physician for treatment of chronic or frequently recurring disease?

Yes No

If No: how did you acquire this antibiotic? (Multiple ticks are possible)

- Purchased from a pharmacy abroad
- Purchased over the internet
- Remnants from earlier treatment
- From family/friends
- Other ways

10.03 **Would you consider using antibiotics without consulting your physician?**

Yes No

If YES: which conditions would you treat in such situation? (multiple ticks are possible)

- Common cold
- Cough
- Bronchitis
- Sore throat
- Sinusitis
- Fever
- Influenza
- Ear infection
- Diarrhoea
- Urinary tract infection
- Other infections

11. YOUR CIRCADIAN RHYTHM

We will ask you some questions about your sleeping habits

11.01 Have you worked in a shift work schedule during the last 3 months?

Yes No

11.02 Number of days per week which you cannot freely choose when you sleep (e.g. work days)?

0 1 2 3 4 5 6 7

Then I go to bed at

I get ready to fall asleep at

Number of minutes I need to fall asleep

I wake up at

With help of: Alarm clock External stimulus (*noise, family members etc.*) By myself

Number of minutes I need to get up

11.03 Number of days per week which you can freely choose when you sleep (e.g. free days or holidays)

0 1 2 3 4 5 6 7

Then I go to bed at

I get ready to fall asleep at

Number of minutes I need to fall asleep

I wake up at

With help of: Alarm clock External stimulus (*noise, family members etc.*) By myself

Number of minutes I need to get up

12. SKIN AND DERMATOLOGY

12.01 How often do you usually take a shower or a bath? (tick once)

- 2 or more times daily
- 1 time daily
- 4-6 times per week
- 2-3 times per week
- Once a week
- Less than once a week

12.02 How often do you usually wash your hands with soap daily? (tick once)

- 0 times
- 1-5 times
- 6-10 times
- 11-20 times
- More than 20 times

12.03 Have you ever taken any antibiotics (penicillin and penicillin-like medicines) because of a skin disease, for example infected eczema, acne, non-healing leg ulcers, recurrent abscess?

- Yes No

If Yes: How many times in average per year did you take antibiotics during the period you were most affected (tick once)

- 1-2 3-4 More than 4 times

12.04 Have you or have you ever had the following skin disorders? (tick once for each line)

- | | Yes | No |
|---|--------------------------|--------------------------|
| Psoriasis | <input type="checkbox"/> | <input type="checkbox"/> |
| Atopic eczema (children's eczema)... | <input type="checkbox"/> | <input type="checkbox"/> |
| Recurrent hand eczema | <input type="checkbox"/> | <input type="checkbox"/> |
| Recurrent pimples/spots for several months | <input type="checkbox"/> | <input type="checkbox"/> |
| Leg or foot ulcer that did not heal for 3-4 weeks | <input type="checkbox"/> | <input type="checkbox"/> |

If YES on the question concerning leg and/or foot ulcer, do you have any leg ulcer today?

- Yes No

12.05 Have you often or always any of the following complaints? (tick once for each line)

- | | Yes | No |
|---|--------------------------|--------------------------|
| Swelling in the ankles or legs, particularly in the evenings | <input type="checkbox"/> | <input type="checkbox"/> |
| Varicose veins | <input type="checkbox"/> | <input type="checkbox"/> |
| Eczema (red, itchy rash) on your legs | <input type="checkbox"/> | <input type="checkbox"/> |
| Leg pain that is getting worse when you are walking and is relieved when you are standing still | <input type="checkbox"/> | <input type="checkbox"/> |

12.06 Have you ever had the following diagnoses by a physician? (tick once for each line)

- | | Yes | No |
|---------------------|--------------------------|--------------------------|
| Psoriasis | <input type="checkbox"/> | <input type="checkbox"/> |
| Atopic eczema | <input type="checkbox"/> | <input type="checkbox"/> |
| Rosacea | <input type="checkbox"/> | <input type="checkbox"/> |

12.07 Have you recurring large acne/abscesses that are tender/painful and often form scars in the following places? (tick once for each line)

- | | Yes | No |
|--------------------------------|--------------------------|--------------------------|
| Armpits | <input type="checkbox"/> | <input type="checkbox"/> |
| Under the breasts | <input type="checkbox"/> | <input type="checkbox"/> |
| Stomach groove/the navel | <input type="checkbox"/> | <input type="checkbox"/> |
| Around the genitalia | <input type="checkbox"/> | <input type="checkbox"/> |
| Around the anus | <input type="checkbox"/> | <input type="checkbox"/> |
| The groin | <input type="checkbox"/> | <input type="checkbox"/> |

If Yes: Have you ever visited a physician because of abscesses?

- Yes No

If Yes, did you get any of the following treatments? (tick once for each line)

- | | Yes | No |
|---|--------------------------|--------------------------|
| Antibiotic ointment | <input type="checkbox"/> | <input type="checkbox"/> |
| Antibiotic tablets | <input type="checkbox"/> | <input type="checkbox"/> |
| Surgical drainage | <input type="checkbox"/> | <input type="checkbox"/> |
| A larger surgical intervention including skin removal | <input type="checkbox"/> | <input type="checkbox"/> |
| Surgical laser treatment | <input type="checkbox"/> | <input type="checkbox"/> |

Follow-up questions



INFORMATION TO FOLLOW-UP QUESTIONS

The following pages with questions should not be answered by everybody. If you have answered yes to one or more of questions below, we ask you to move on to the follow-up questions on the topic or topics you have answered yes to. The first four topics are from the first questionnaire and the last question is from this form.

We have for the sake of simplicity highlighted topics with different colours so that you will find the questions that applies to you.

If you answered YES to that you have: long-term or recurrent pain that has lasted for 3 months or more, please answer the questions on page 19 and 20. The margin is marked with green.

If you answered YES to that you have undergone any surgery during the last 3 years, please answer the questions on page 21 and 22. The margin is marked with purple.

If you answered YES to that you're working outdoors at least 25% of the time, or in facilities with low temperature, such as warehouse/industrial halls, please answer the questions on page 23. The margin is marked with red.

If you answered YES to that you have used non-prescription pain relievers, please answer questions on page 24. The margin is marked with orange.

If you answered YES to that you have or have ever had skin problems (such as psoriasis, atopic eczema, non-healing leg or foot ulcers, recurrent hand eczema, acne or abscesses), please answer the questions on page 25. The margin is marked with yellow.

If you have answered **NO** to these five questions, you are finished with your answers. The questionnaire is to be returned in the reply envelope you were given at the survey site. The postage is already paid.

Should you wish to give us written feedback on either the questionnaire or The Tromsø Study in general, you are welcome to that on page 26.

Do you have any questions, please contact us by phone or by e-mail. You can find the contact information on the back of the form. **THANK YOU** for taking the time to the survey and to answer our questions.

13. FOLLOW-UP QUESTIONS ON PAIN

You answered in the first questionnaire that you have protracted or constantly recurrent pain that has lasted for 3 months or more. Here, we ask you to describe the pain a little closer.

13.01 **How long have you had this pain?**

Number of years months

13.02 **How often do you have this pain?**

- Every day Once a month or more
 Once a week or more Less than once a month

13.03 **Where does it hurt?** (Tick for all locations where you have protracted or constantly recurrent pain)

- | | |
|---|---|
| <input type="checkbox"/> Head/face | <input type="checkbox"/> Thigh/knee/leg |
| <input type="checkbox"/> Jaw/temporo-mandibular joint | <input type="checkbox"/> Ankle/foot |
| <input type="checkbox"/> Neck | <input type="checkbox"/> Chest/breast |
| <input type="checkbox"/> Back | <input type="checkbox"/> Stomach |
| <input type="checkbox"/> Shoulder | <input type="checkbox"/> Genitalia /reproductive organs |
| <input type="checkbox"/> Arm/elbow | <input type="checkbox"/> Skin |
| <input type="checkbox"/> Hand | <input type="checkbox"/> Other location |
| <input type="checkbox"/> Hip | |

13.04 **What do you believe is the cause of the pain?** (Tick for all known causes)

- | | |
|--|--|
| <input type="checkbox"/> Accident /acute injury | <input type="checkbox"/> Fibromyalgia |
| <input type="checkbox"/> Long-term stress | <input type="checkbox"/> Angina pectoris |
| <input type="checkbox"/> Surgical intervention/operation | <input type="checkbox"/> Poor blood circulation |
| <input type="checkbox"/> Herniated disk (<i>prolapse</i>) /lumbago | <input type="checkbox"/> Cancer |
| <input type="checkbox"/> Whiplash | <input type="checkbox"/> Nerve damage/neuropathy |
| <input type="checkbox"/> Migraine/headache | <input type="checkbox"/> Infection |
| <input type="checkbox"/> Osteoarthritis | <input type="checkbox"/> Herpes zoster |
| <input type="checkbox"/> Rheumatoid arthritis | <input type="checkbox"/> Another cause (<i>describe below</i>) |
| <input type="checkbox"/> Bechterews syndrome | <input type="checkbox"/> Don't know |

Describe the other cause:

.....

13.05 **Which kind of treatment have you received for the pain?** (Tick for all types of pain treatments you have received)

- | | |
|---|--|
| <input type="checkbox"/> No treatment | <input type="checkbox"/> Psycho-educative/relaxation training/psychotherapy |
| <input type="checkbox"/> Analgesic medications/painkillers | <input type="checkbox"/> Acupuncture |
| <input type="checkbox"/> Physiotherapy/chiropractic treatment | <input type="checkbox"/> Complimentary and alternative medicine (<i>homeopathy, healing, aromatherapy, etc.</i>) |
| <input type="checkbox"/> Treatment at a pain clinic | <input type="checkbox"/> Other treatment |
| <input type="checkbox"/> Surgery | |

13.06 On a scale of 0 to 10, where 0 corresponds to no pain and 10 corresponds to the worst possible pain you can imagine:

How strong would you say that the pain usually is?

| | | | | | | | | | | | | |
|---------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|-----------------------|
| No pain | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Worst imaginable pain |
| | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |

How strong is the pain when it is in its strongest Intense?

| | | | | | | | | | | | | |
|---------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|-----------------------|
| No pain | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Worst imaginable pain |
| | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |

To what degree does the pain interfere with your sleep?

| | | | | | | | | | | | | |
|-----------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|---------------------|
| No effect | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Impossible to sleep |
| | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |

To what degree does the pain interfere with performing common activities at home and at work?

| | | | | | | | | | | | | |
|-----------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|---------------------|
| No effect | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Can not do anything |
| | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |

14. FOLLOW-UP QUESTIONS ON SURGERY

In the first questionnaire you answered that you have undergone an operation during the last 3 years.

14.01 How many times have you undergone surgery during the last 3 years?

Number

Below, please describe the operation. If you have undergone several operations during the last 3 years, these questions concern the last surgery you underwent.

14.02 **Where in your body did you have surgery?**
(If you were operated simultaneously in several places in the body, tick more than once)

Surgery in the head/neck/back

- Head/face
- Neck/throat
- Back

Surgery in the chest

- Heart
- Lungs
- Breasts
- Another surgery in the chest region

Surgery in the stomach/pelvis

- Stomach/intestines
- Inguinal hernia
- Urinary tract/reproductive organs
- Gall bladder/biliary tract
- Another surgery in the stomach/pelvis

Surgery in the hip/legs

- Hip/thigh
- Knee/leg
- Ankle/foot
- Amputation

Surgery in the shoulder and arm

- Shoulder/overarm
- Elbow/underarm
- Hand
- Amputation

14.03 **Reason for the surgery:**

- Acute illness/trauma
- Planned non-cosmetic operation
- Planned cosmetic operation

14.04 **Where did you have the surgery?**

- The hospital in Tromsø
- The hospital in Harstad
- Other public hospital
- Private clinic

14.05 **How long time is it since you had surgery?**

Number of years Months

14.06 **Do you have reduced sensitivity in an area near the surgical scar?**

- Yes No

14.07 **Are you hypersensitive to touch, heat or cold in an area near the surgical scar?**

- Yes No

14.08 **Does slight touch from clothes, showering or similar cause discomfort/pain?**

- Yes No

14.09 **If you had pain at the site of surgery before you had surgery, do you have the same type of pain now?**

- Yes No



14.10

The pain at the site of surgery: Answer on a scale from 0 to 10, where 0=no pain and 10=worst pain you can imagine

| | | | | | | | | | | | | | |
|---|---------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|-----------------------|
| | No pain | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Worst imaginable pain |
| How strong pain did you have at the site of surgery <u>before</u> you had surgery | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |

| | | | | | | | | | | | | | |
|---|---------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|-----------------------|
| | No pain | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Worst imaginable pain |
| How strong pain do you normally have at the site of surgery now | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |

| | | | | | | | | | | | | | |
|---|---------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|-----------------------|
| | No pain | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Worst imaginable pain |
| How strong pain do you normally have at the site of surgery when it is most intense | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |



15. FOLLOW-UP QUESTIONS ABOUT WORK IN COLD ENVIRONMENT

In the first questionnaire you answered yes to that you work in cold environments. Here are some follow-up questions that we hope you will answer.

15.01 Do you feel cold at work?

- Yes, often
- Yes, sometimes
- No, never

15.02 For how long have you been exposed to cold air below 0°C during the last winter?

Leisure/hobbies (hours/week)

Work (hours/week)

Outdoors, with suitable clothing (hours/week)

Outdoors, without suitable clothing (hours/week)

Indoors, with no heating (hours/week)

In cold, with wet clothing (hours/week)

Contact with cold objects/tools (hours/week)

15.03 What ambient temperature prevents you from:

Under °C

Working outdoors

Training outdoors

Performing other activities outdoors

15.04 Have you during the last 12 months had a frostbite with blisters, sores or skin injury?

Yes No

If Yes, how many times?.....

15.05 Have you had itching and/or rash in relation to cold exposure?

Yes No

15.06 Have you during the last 12 months had an accident where cold has been involved, and which required medical treatment?

| | Yes | No |
|-----------------------|--------------------------|--------------------------|
| At work | <input type="checkbox"/> | <input type="checkbox"/> |
| In leisure time | <input type="checkbox"/> | <input type="checkbox"/> |

15.07 Do you experience any of the following symptoms while you are in a cold environment? If so, at what temperature do the symptoms occur?

| | Yes | No | Under °C |
|---|--------------------------|--------------------------|---|
| Breathing problems | <input type="checkbox"/> | <input type="checkbox"/> | <input style="width: 40px;" type="text"/> |
| Wheezy breathing | <input type="checkbox"/> | <input type="checkbox"/> | <input style="width: 40px;" type="text"/> |
| Mucus secretion from lungs | <input type="checkbox"/> | <input type="checkbox"/> | <input style="width: 40px;" type="text"/> |
| Chest pain | <input type="checkbox"/> | <input type="checkbox"/> | <input style="width: 40px;" type="text"/> |
| Disturbance in heart rhythm | <input type="checkbox"/> | <input type="checkbox"/> | <input style="width: 40px;" type="text"/> |
| Impaired blood circulation in hands/feet | <input type="checkbox"/> | <input type="checkbox"/> | <input style="width: 40px;" type="text"/> |
| Visual disturbance (short term/transient) | <input type="checkbox"/> | <input type="checkbox"/> | <input style="width: 40px;" type="text"/> |
| Migraine (short term/transient) | <input type="checkbox"/> | <input type="checkbox"/> | <input style="width: 40px;" type="text"/> |
| Fingers turning white (short term/transient) | <input type="checkbox"/> | <input type="checkbox"/> | <input style="width: 40px;" type="text"/> |
| Fingers turning blue-red (short term/transient) | <input type="checkbox"/> | <input type="checkbox"/> | <input style="width: 40px;" type="text"/> |

15.08 How does cold environments and cold-related symptoms influence your performance?

| | Decrease | No effect | Improve |
|--|--------------------------|--------------------------|--------------------------|
| Concentration | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Memory | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Finger sensitivity (feeling) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Finger dexterity (motor) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Control of movement (for example tremor) | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Heavy physical work | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |
| Long-lasting physical work | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> |

16. USE OF NON-PRESCRIPTION PAINKILLERS

In the first questionnaire you answered that you had used non-prescription painkillers (analgesics) in the last 4 weeks. Here are some follow-up questions we hope you will answer.

16.01 What types of non-prescription painkillers have you used?

Paracetamol: (*Pamol, Panodil, Paracet, Paracetamol, Pinex*)

- Not used
- Less than every week
- Every week, but not daily
- daily

How much do you usually take daily when you use these medicines?
(number of tablets, suppositories)

Acetylsalicylates: (*Aspirin, Dispril, Globoid*)

- Not used
- Less than every week
- Every week, but not daily
- Daily

How much do you usually take daily when you use these medicines?
(number of tablets)

Ibuprofen: (*Ibumetin, Ibuprofen, Ibuprox, Ibox*)

- Not used
- Less than every week
- Every week, but not daily
- Daily

How much do you usually take daily when you use these medicines?
(number of tablets, suppositories)

Naproxen: (*Ledox, Naproxen*)

- Not used
- Less than every week
- Every week, but not daily
- Daily

How much do you usually take daily when you use these medicines?
(number of tablets)

Phenazone with caffeine: (*Antineuralgica, Fanalgin, Fenazon-koffein, Fenazon-koffein sterke*)

- Not used
- Less than every week
- Every week, but not daily
- daily

How much do you usually take daily when you use these medicines?
(number of tablets)

16.02 For which complaints do you use non-prescription painkillers? (multiple ticks are possible)

- Headache
- Menstrual discomfort
- Migraine
- Back pain
- Muscle/joint pain
- Tooth pain
- Other

16.03 Do you think you have experienced side effects of some of the medicines? (tick once for each line)

| | Yes | No |
|-------------------------------|--------------------------|--------------------------|
| Paracetamol | <input type="checkbox"/> | <input type="checkbox"/> |
| Acetylsalicylates | <input type="checkbox"/> | <input type="checkbox"/> |
| Ibuprofen | <input type="checkbox"/> | <input type="checkbox"/> |
| Naproxen | <input type="checkbox"/> | <input type="checkbox"/> |
| Phenazone with caffeine | <input type="checkbox"/> | <input type="checkbox"/> |

16.04 Where do you usually purchase painkillers?

- Pharmacy
- Grocery
- Petrol stations
- Abroad
- Internet

16.05 Do you combine the treatment with the use of painkillers on prescription?

- Yes No

17. FOLLOW-UP QUESTIONS ABOUT SKIN DISEASES

On page 15 in this questionnaire you answered that you have or have had a skin disease. Here are some follow-up questions we hope you will answer.

Answer on a scale from 0 to 10, where 0 corresponds to no symptoms and 10 correspond to worst imaginable complaints. If you answered YES to that you have or have had:

| | | No complaint | 0 | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | Worst imaginable complaints |
|--|---|--|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|--------------------------|-----------------------------------|
| 17.01 Psoriasis | · How much are you affected by your psoriasis today? | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| | · How much are you affected by your psoriasis when it is most severe? | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| 17.02 Atopic eczema | · How much are you affected by your atopic eczema today? | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| | · How much are you affected by your atopic eczema when it is most severe? | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| 17.03 Hand eczema | · How much are you affected by your hand eczema today? | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| | · How much are you affected by your hand eczema when it is most severe? | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| 17.04 Acne | · How much are you affected by your acne today? | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| | · How much are you affected by your acne when it is most severe? | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| 17.05 Abscesses | · How much are you affected by your abscesses today? | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| | · How much are you affected by your abscesses when it is most severe? .. | | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | <input type="checkbox"/> | |
| 17.06 Here is a list of factors that might trigger or exacerbate abscesses, tick for what you think apply to you: | | Yes | No | | | | | | | | | | | |
| | Stress/psychological strain | <input type="checkbox"/> | <input type="checkbox"/> | | | | | | | | | | | |
| | Narrow/tight clothing | <input type="checkbox"/> | <input type="checkbox"/> | | | | | | | | | | | |
| | Menstrual periods | <input type="checkbox"/> | <input type="checkbox"/> | | | | | | | | | | | |
| | Pregnancy | <input type="checkbox"/> | <input type="checkbox"/> | | | | | | | | | | | |
| | Other | <input type="checkbox"/> | <input type="checkbox"/> | | | | | | | | | | | |
| 17.07 How many episodes of abscesses do you usually have per year? (tick once) | | | | | | | | | | | | | | |
| | <input type="checkbox"/> 0-1 | <input type="checkbox"/> 4-6 | | | | | | | | | | | | |
| | <input type="checkbox"/> 2-3 | <input type="checkbox"/> More than 6 | | | | | | | | | | | | |
| 17.08 How old were you when you got abscesses for the first time? | | | | | | | | | | | | | | |
| | <input type="checkbox"/> 0-12 years | <input type="checkbox"/> 26-35 years | | | | | | | | | | | | |
| | <input type="checkbox"/> 13-19 years | <input type="checkbox"/> 36-50 years | | | | | | | | | | | | |
| | <input type="checkbox"/> 20-25 years | <input type="checkbox"/> Older than 50 years | | | | | | | | | | | | |
| 17.09 If you no longer have abscesses, how old were you when it disappeared? | | | | | | | | | | | | | | |
| | <input type="checkbox"/> 0-12 years | <input type="checkbox"/> 26-35 years | | | | | | | | | | | | |
| | <input type="checkbox"/> 13-19 years | <input type="checkbox"/> 36-50 years | | | | | | | | | | | | |
| | <input type="checkbox"/> 20-25 years | <input type="checkbox"/> Older than 50 years | | | | | | | | | | | | |

Thank you for your help





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