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Retinopathy with and without diabetes: Risk factors and visual impairment.

The Tromsø Eye Study and a Norwegian screening study

Geir Bertelsen

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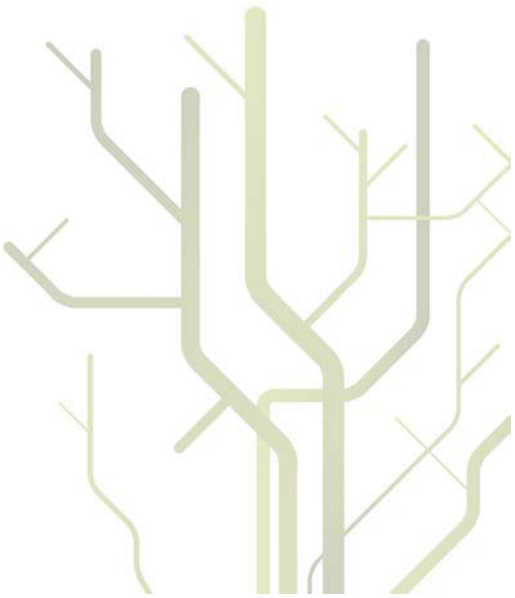

Retinopathy with and without diabetes: Risk factors and visual impairment.

The Tromsø Eye Study and a Norwegian screening study

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By choosing a clinical career in ophthalmology it became difficult to continue the cardiovascular research. The research at the Ophthalmology Department was limited without any possibilities for supervising a PhD-project and we had to find other alternatives. At the same time the sixth survey of the Tromsø Study was under planning. Inger Njølstad at the Department of Community Medicine, University of Tromsø, agreed to supervise a PhD-project in the Tromsø Study and has been important for all parts of the study from beginning until end. This thesis and the Tromsø Eye Study would not have happened without you.

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Norsk populærvitenskapelig sammendrag

Diabetes retinopati er en av mange komplikasjoner knyttet til diabetes. I den vestlige verden er dette den viktigste årsak til nedsatt syn og blindhet i arbeidsfør alder.

Vi gjennomførte øyeundersøkelser av deltagere i den sjette Tromsøundersøkelsen. Forekomsten av diabetes retinopati var 26,9% blant deltakere med diabetes, og varigheten av diabetes, blodsukker nivå, blodtrykk og mikroalbuminuri var risikofaktorer. Det var en lav andel med redusert syn.

Vi undersøkte også forekomsten av diabetes retinopati blant diabetikere rekruttert fra allmennpraktikere i Tromsø, Tønsberg og Stavanger og fant en forekomst på 28,2%. Denne studien viste også at omtrent en tredjedel av deltagerne ikke hadde vært undersøkt av øyelege i løpet at de siste to år slik de nasjonale retningslinjer anbefaler.

Videre undersøkte vi forekomsten av retinopati hos deltakere i Tromsøundersøkelsen uten diabetes og fant at det var forskjeller mellom menn og kvinner. Forekomsten hos menn var 15,9% og hos kvinner 14,0%. Risikofaktorer for kvinner var blodtrykk, alder og mikroalbuminuri og for menn blodtrykk og blodsukkernivå målt ved forsukret hemoglobin (HbA1c).

Summary

Diabetic retinopathy is a well-known complication of diabetes and a major cause of visual impairment and blindness in developed countries.

We explored visual impairment and diabetic retinopathy among participants with diabetes in the Tromsø Eye Study. The prevalence of visual impairment (corrected Snellen visual acuity < 20/40) was 4.1% in the better-seeing eye. We found no legally blind participants. The prevalence of diabetic retinopathy was 26.9% and macular edema 3.9%. In a multivariable logistic regression model, retinopathy was associated with longer diabetes duration, insulin use, non-fasting glucose and urinary albumin excretion. We found a very low microalbuminuria cut-off level for increased risk of diabetic retinopathy (urinary albumin-creatinine ratio > 1.16 mg/mmol).

Visual impairment and diabetic retinopathy were also explored in diabetes patients recruited from general practitioners in a multi-centre study conducted in Tromsø, Tønsberg and Stavanger. In this study the prevalence of visual impairment (corrected Snellen visual acuity < 20/40) was 5.4% and one participant was legally blind. The prevalence of diabetic retinopathy was 28.2%. This study also showed that about one third of the diabetes patients did not attend at least biannual eye examination as recommended by the national guidelines.

Retinopathy lesions, such as microaneurysms and retinal haemorrhages, are also common in subjects without diabetes. We explored retinopathy in subjects without diabetes in the Tromsø Eye Study, and the overall prevalence of retinopathy was 14.8%. Men had a higher prevalence of retinopathy compared to women (15.9% vs. 14.0%, p=0.04). In men retinopathy was associated with hypertension and HbA1c. In women retinopathy was associated with age, hypertension and urinary albumin excretion. In women, the microalbuminuria cut-off level for increased risk of retinopathy was very low (urinary albumin-creatinine ratio > 0.43 mg/mmol).

Visual impairment was also explored in a general population using data from both diabetic and non-diabetic participants in the Tromsø Eye Study and the overall prevalence of visual acuity < 20/60 was 1.2%.

List of 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. 2012; [Epub ahead of print].

II. Bertelsen G, Peto T, Lindekleiv H, Schirmer H, Solbu MD, Toft I, Sjølie AK, Njølstad I. **Tromsø Eye Study: prevalence and risk factors of diabetic retinopathy.** Acta Ophthalmol. 2012; [Epub ahead of print].

III. Bertelsen G, Peto T, Lindekleiv H, Schirmer H, Solbu MD, Toft I, Sjølie AK, Njølstad I. **Sex differences in risk factors for retinopathy in non-diabetic men and women. The Tromsø Eye Study.** [Submitted].

IV. Kilstad HN, Sjølie AK, Gøransson L, Hapnes R, Henschien HJ, Alsbirk KE, Fossen K, Bertelsen G, Holstad G, Bergrem H. **Prevalence of diabetic retinopathy in Norway: report from a screening study.** Acta Ophthalmol 2012; 90:609-12.

Abbreviations

ACR: Urinary Albumin/Creatinine Ratio

AGE: Advanced Glycation End-products

BMI: Body Mass Index

DCCT: Diabetes Control and Complications Trial

EDIC: Epidemiology of Diabetes Interventions and Complications

ETDRS: Early Treatment Diabetic Retinopathy Study

eGFR: Estimated Glomerular Filtration Rate

GP: General Practitioner

HbA1c: Glycosylated Haemoglobin

HPLC: High Performance Liquid Chromatography

ICPC-2: International Classification of Primary Care, Second edition

IRMA: Intra Retinal Microvascular Abnormalities

PKC: Protein Kinase C

UKPDS: UK Prospective Diabetes Study

WESDR: Wisconsin Epidemiologic Study of Diabetic Retinopathy

WHO: World Health Organization

Introduction

Diabetes

Diabetes Mellitus is a chronic metabolic disorder characterized by hyperglycaemia and disturbances in carbohydrate, fat and protein metabolism caused by defects in insulin secretion, action or both [1]. The global prevalence among adults is increasing and has been estimated to 6.4% in 2010 and 7.7% in 2030 [2]. The prevalence increases with age and a Norwegian study using data from 9 population based studies conducted from 1996 to 2001 reported an overall prevalence of 3.4% in adults 30 years and older. In subjects aged 80 years and older the prevalence was 12.4% in women and 11.5% in men [3].

Type 1 diabetes is characterised by an autoimmune destruction of insulin producing beta-cells usually leading to absolute insulin deficiency and accounts for 5-10% of the diabetes cases [4].

Type 2 diabetes is characterised by insulin resistance and usually a relative insulin deficiency, and accounts for 90-95% of diabetes cases [4]. The aetiology is multifactorial and associated with both genetic and environmental factors as inactivity and over-nutrition, causing a slowly progressing hyperglycaemia and altered lipid metabolism [5]. The gradual onset of symptoms may result in several years of undiagnosed type 2 diabetes [3].

Diagnostic criteria of diabetes

In 1965, the World Health Organization (WHO) published guidelines for diabetes, and since then the diagnostic criteria have been revised several times. The current WHO criteria is based on the presence of diabetic retinopathy and uses fasting plasma glucose ≥ 7.0 mmol/l and two hour plasma glucose ≥ 11.1 mmol/l [6]. Recently a WHO report from 2011 recommended glycosylated haemoglobin (HbA1c) 6.5% as an alternative diagnostic criterion for diabetes [7].

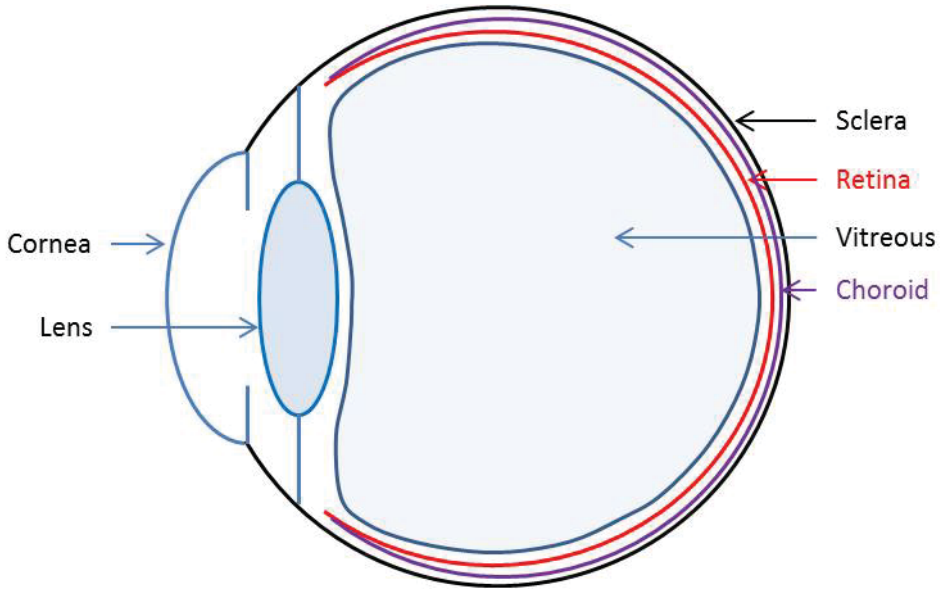
Complications of diabetes

Diabetes increases the risk of many different complications that in general can be divided into macro- and microvascular disease [8]. The macrovascular complications include coronary heart disease and cerebrovascular disease. The microvascular complications include

neuropathy, nephropathy and diabetic retinopathy. Diabetic retinopathy is a major long-term complication of diabetes and the major cause of visual impairment and blindness below 75 years of age in developed countries [9-12]. In addition, diabetes increases the risk for cataract and glaucoma [13].

Due to the risk of visual impairment and blindness caused by diabetic retinopathy, national guidelines recommend annual or biannual eye examination for diabetes patients without retinopathy. In case of retinopathy more frequent examination is recommended [14].

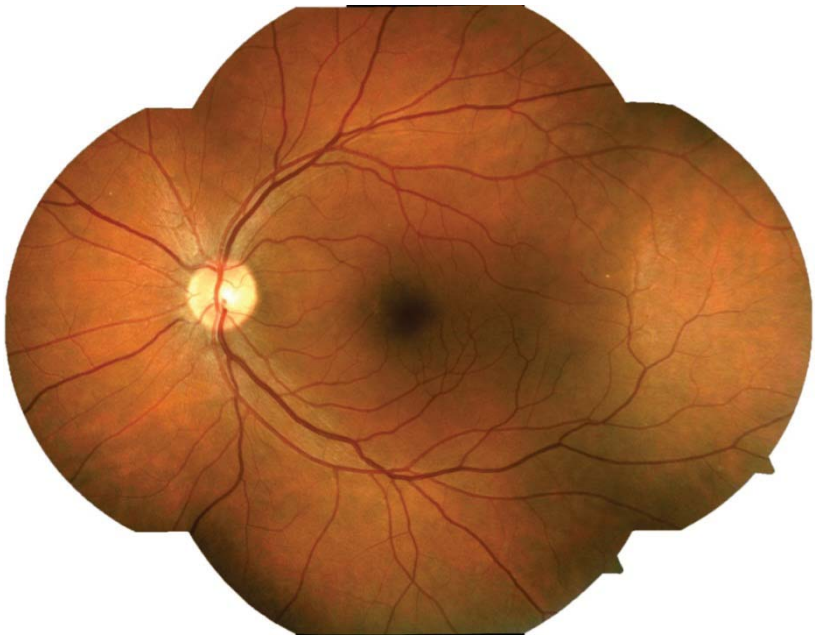
Figure 1: The schematic eye



The eye

A schematic eye is illustrated in figure 1. The eye is often compared to a camera. The cornea, lens and pupil correspond to the camera lens and aperture to create a focused image with adequate amount of light on the neurosensory retina lining the inside posterior 2/3 of the eye (Figure 2). In the retina, rods and cones converts the photons into electrical signals by photo transduction. This process corresponds to the image sensor in a modern camera.

Figure 2: The normal human retina. (Photo: Tromsø Eye Study 2007-8)



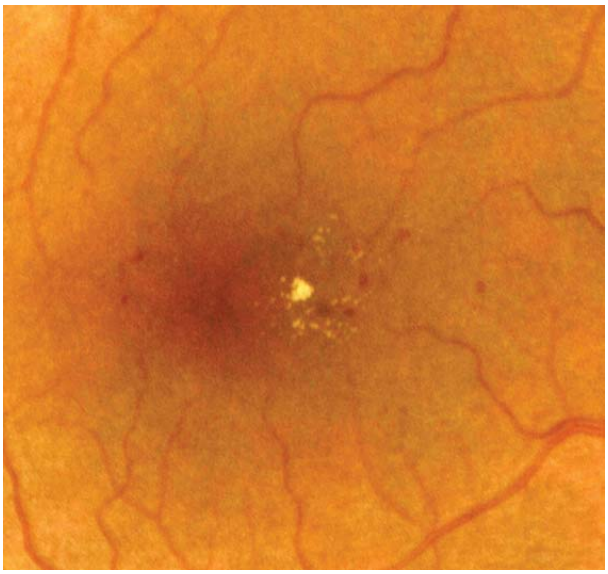
Diabetic retinopathy

Diabetic retinopathy is a multifactorial disease of the retina, and the underlying pathological mechanisms are complex. Several biochemical pathways leading to the hyperglycaemia induced abnormalities seen in diabetic retinopathy have been identified and probably interact. Pathological biochemical mechanisms including Advanced Glycation End-products (AGEs), Protein Kinase C (PKC), the polyol pathway, the hexosamine pathway, angiogenic factor expression and oxidative stress probably cause damage to all major retinal cells leading to neuroglial and microvascular damage [15]. The relative contribution of the different biochemical abnormalities is unclear. The progressive neuroglial and microvascular damage are also affected by an interplay of factors such as blood pressure, impaired retinal autoregulation and hormones to develop the clinical manifestation of diabetic retinopathy where inflammation, leucostasis, ischemia and structural alterations are important features [15-17]. Histopathology studies of diabetic retinopathy show thickening of the capillary basement membrane, loss of pericytes, microaneurysms, endothelial cell death and capillary loss [16].

Retinopathy is clinically characterised by microaneurysms, haemorrhages, venous beading, cotton wool spots, intra retinal microvascular abnormalities and new proliferative vessels. The retinal abnormalities range from changes not visible on a retinal photo to severe proliferative retinopathy with pathological angiogenesis resulting in fibrovascular proliferation on top of the retina or into the vitreous, and eventually vitreous haemorrhage and tractional retinal detachment.

Diabetic macular oedema

Figure 3: Diabetic macular oedema. (Photo: Tromsø Eye Study 2007-8)



The retina lacks lymphatic drainage, and fluid transportation across the capillaries must be balanced by capillary reuptake and transportation across the pigment epithelium separating the retina and underlying choroid. In diabetic macular oedema hyperglycaemia induced capillary dysfunction and damage causes excess vasopermeability, hypoxia and retinal oedema resulting in decreased visual acuity. Key components in the pathophysiology include altered hemodynamics, breakdown of blood retina barrier, angiogenic factor expression, inflammation and oxidative stress [18]. The centre of the macula is prone to oedema due to the high metabolic turnover and the foveal avascular zone limiting both the blood supply and capillary reuptake of extracellular fluid. In a retinal image, macular oedema is characterised by hard exudates consisting of lipid and protein deposits. Figure 3 illustrates macular oedema with hard exudates, microaneurysms and haemorrhages.

Prevalence of diabetic retinopathy

There are inconsistencies between epidemiological studies and differences in study methods contribute to conflicting reports on prevalence of diabetic retinopathy [12, 19]. A recent study used pooled data from 35 studies using similar methodology and estimated the world

prevalence (age-standardized) of any diabetic retinopathy to 34.6%, proliferative retinopathy to 7.0% and diabetic macular oedema to 6.8% in subjects aged 20-79 years with diabetes [20].

Risk factors for diabetic retinopathy

Diabetes duration

The most important and consistent risk factor for retinopathy in observational studies is diabetes duration [21-24]. Type 1 diabetes has a higher prevalence of retinopathy compared to type 2 diabetes [20]. In the Wisconsin Epidemiologic Study of Diabetic Retinopathy (WESDR) the prevalence of diabetic retinopathy was 98% for diabetes duration > 14 years in type 1 diabetes. In type 2 diabetes the prevalence of diabetic retinopathy was 85% for insulin users and 58% for non-insulin users for diabetes duration > 14 years [25].

Hyperglycaemia

Hyperglycaemia is an important risk factor for diabetic retinopathy. Clinical trials as the Diabetes Control and Complications Trial (DCCT) and UK Prospective Diabetes Study (UKPDS) have demonstrated the beneficial effect of tight glycaemic control on development and progression of diabetic retinopathy [26, 27]. Longitudinal observational studies as WESDR, the Blue Mountains eye study and others have also documented the relationship between elevated glucose and diabetic retinopathy [28-30].

Blood pressure

In most studies, blood pressure is correlated to retinopathy [31]. Clinical trials as the UKPDS, DCCT, Epidemiology of Diabetes Interventions and Complications (EDIC) and EuroDIAB studies have demonstrated the importance of blood pressure, but the initial blood pressure was relatively high in some studies [32-34]. The ACCORD study failed to demonstrate any effect of intensive blood pressure control in type 2 diabetes suggesting that there might be a lower limit for the beneficial effect of blood pressure control [35]. In observational studies the results are less consistent, but may be confounded by blood pressure treatment [29, 30, 36-39].

Hyperlipidaemia

Observational studies have investigated the relationship between hyperlipidaemia and retinopathy reporting both positive, negative and no associations [36, 40-42]. The ACCORD Lipid study showed that intensive lipid lowering therapy with fenofibrate slowed the progression of retinopathy at four years compared to placebo, indicating an effect of hyperlipidaemia on retinopathy [35].

Renal disease

Kidney disease is a well-known complication of diabetes, and about 50% of diabetes patients will develop microalbuminuria, and 1/3 of the microalbuminuria cases will progress to proteinuria eventually leading to end stage renal disease in many cases [8]. Microalbuminuria and proteinuria are associated with retinopathy in several studies [39, 43, 44].

In addition diabetic retinopathy have been reported to be associated with pregnancy, cardiovascular disease, stroke and cognitive function [45-49]

Retinopathy without diabetes

The knowledge about the pathogenesis leading to retinopathy without diabetes in a general population is limited and mostly derived from observational studies. The concept of retinopathy occurring in a presumably healthy individual makes it difficult to explore the pathogenesis in detail. The retinal lesions found in a retinal image include the same as in diabetic retinopathy, although usually more discrete and limited to a few haemorrhages, microaneurysms or cotton wool spots. Although hypertension and diabetes are seemingly well defined clinical entities, in reality they both probably represent parts of a continuum with progressive dysfunction. Studies of diabetic retinopathy and hypertensive retinopathy may therefore provide important clues about the pathogenesis of retinopathy without diabetes which probably is a mixture of several pathological mechanisms when studied in a general population.

Prevalence of retinopathy without diabetes

Retinopathy lesions are relatively common in subjects without diabetes. Several studies have reported the prevalence in non-diabetic populations ranging from 4.8-17.2% in different ethnic populations, but the results are confounded by differences in age distribution, methodology and number of images used in the retinopathy grading [43, 50-54].

Risk factors for retinopathy without diabetes

Studies have found associations between several risk factors and non-diabetic retinopathy including blood pressure, age, microalbuminuria, body mass index, carotid artery intima-media thickness, smoking, cardiovascular disease, stroke, cognitive impairment and impaired glucose metabolism below the current diagnostic threshold for diabetes [43, 50, 52-61]. Even though the results differ between the studies, hypertension seems to be the most consistent risk factor in the non-diabetic population. In general the risk factors for retinopathy are similar in diabetic and non-diabetic populations although diabetes duration and severity are obviously not relevant in non-diabetic populations. The wide range of associations between retinopathy and vascular disease in various organ systems suggests that retinopathy is a result of systemic processes.

Aim of the thesis

- To investigate the prevalence of visual impairment in diabetes
- Estimate prevalence of diabetic retinopathy
- Assess risk factors for diabetic retinopathy
- Estimate prevalence of retinopathy in a non-diabetic population
- Assess risk factors for retinopathy without diabetes
- Determine the proportion of diabetes patients following the national guidelines on regular eye examination

Methods paper I-III, Tromsø Eye Study

The Tromsø Study and Tromsø Eye Study

The Tromsø Eye Study is a substudy of the Tromsø Study. The Tromsø Study is a large comprehensive longitudinal population-based study started in 1974. The Tromsø Study and the cohort profile has been described elsewhere [62]. A total of 40,051 subjects have participated in at least one of the six surveys. A description of the large amount of variables collected is presented at: http://tromsoundersokelsen.uit.no/tromso/. Serum samples from each survey and DNA samples from the 4th survey and onwards are stored in a biobank. The Tromsø Study holds several endpoint registers with registration of incident myocardial infarction, stroke, atrial fibrillation, diabetes and non-vertebral fractures from case note reviews at the only local hospital in the region.

The 6th Tromsø Study survey was conducted from October 2007 through December 2008 and consisted of two separate visits [63]. All participants were invited to a 1st visit where they answered a questionnaire (Appendix I) and underwent a physical examination comprising the measurement of blood pressure, height, weight, waist and hip circumference. Blood sampling, bone mineral density and pain threshold tests were also performed. A large subgroup was invited to a 2nd visit a few weeks later. The eye examinations of the Tromsø Eye Study were performed at the 2nd visit. In addition, the 2nd visit comprised a second questionnaire (Appendix II), blood samples, cognitive tests, ultrasound of the carotid artery, 12-lead electrocardiogram, echocardiography, spirometry, and bone mineral densitometry. The Tromsø Study and Tromsø Eye Study followed the tenets of the Declaration of Helsinki for research involving humans and were approved by the Regional Committee for Medical and Health Research Ethics. All participants gave an informed written consent.

Study sample

The study sample was based upon the official population registry and all subjects were residents of the municipality of Tromsø. The sampling strategy for the 6th Tromsø Study survey was complex and a balance between the need for including the participants from

previous visits for longitudinal analyses and the different needs in all substudies for new participants. Therefore the sample consists of a mix of whole birth cohorts, random samples and previous participants.

First visit

A total of 19,762 subjects were invited to the 1st visit. Subjects invited to the 1st visit of the 6th Tromsø Study survey were:

1. All Tromsø residents aged 40-42 or 60-87 years (n=12,578).
2. A 10% random sample of individuals aged 30-39 years (n=1056).
3. A 40% random sample of individuals aged 43-59 years (n= 5787).
4. Subjects who had attended the 2nd visit of the 4th survey, if not already included in the three groups above (n=341).

A total of 12,984 subjects (65.7%) participated.

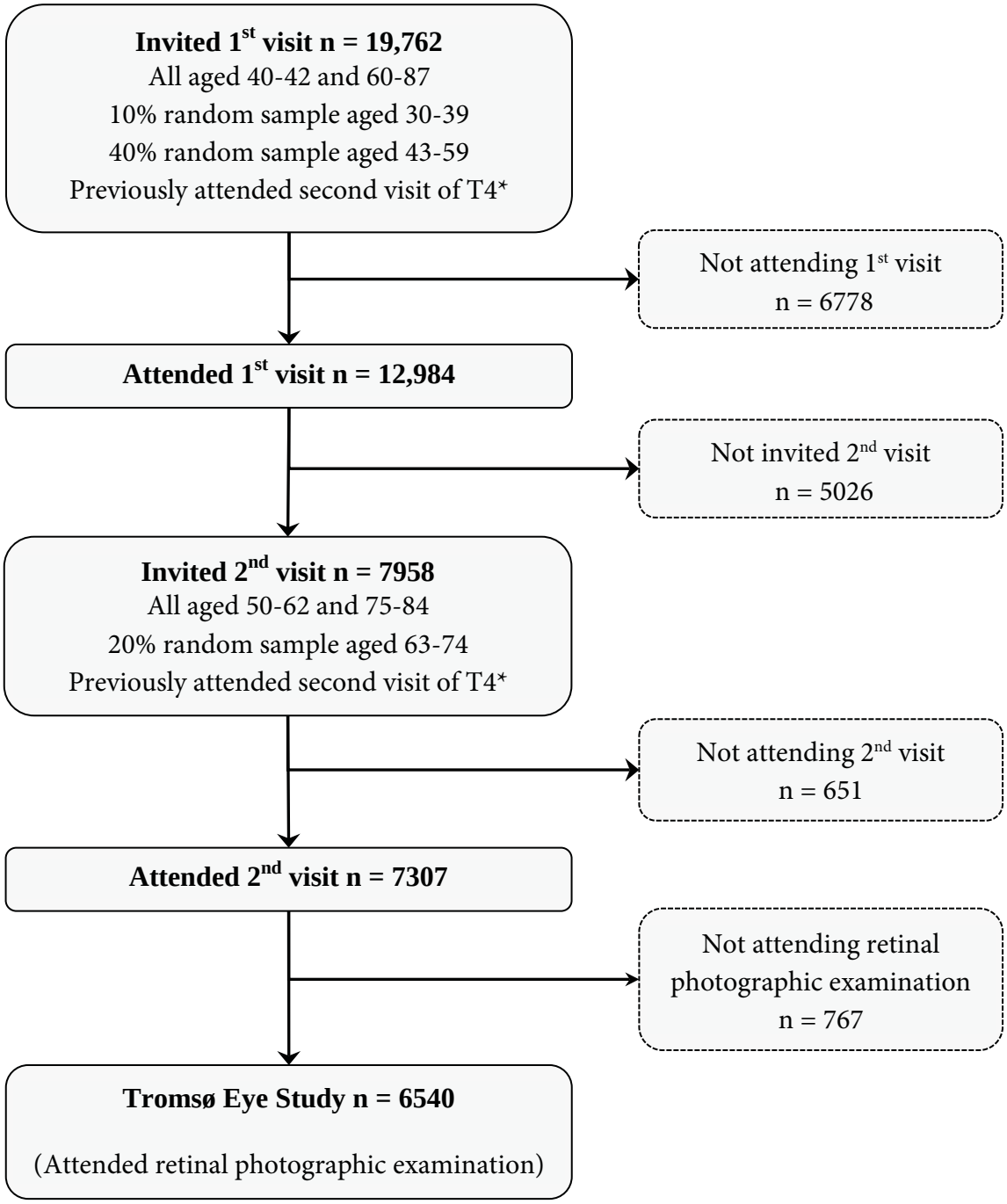
Second visit

The 2nd visit study sample was preselected before the start of the survey, and included:

1. All subjects eligible for the 1st visit aged 50-62 years or aged 75-84 years (n=7657).
2. A 20% random sample of subjects eligible for the 1st visit aged 63-74 years (n=942).
3. Subjects, if not already included in the two groups above, who had attended the 2nd visit of the 4th survey (n=2885).

In addition, participation in the 1st visit was a prerequisite to be reinvited to the 2nd visit [62]. A total of 7958 were invited and 7307 (91.8%) attended the 2nd visit. A total of 6540 attended retinal photography (82.2%). Figure 4, 5 and Table 1 illustrates the study sample and selection process. The participants in the 2nd visit were mainly Caucasians with 91% reporting Norwegian ethnicity and 1.5% reporting Sami ethnicity.

Figure 4: Flow chart illustrating the study sample. Tromsø Study 2007-8



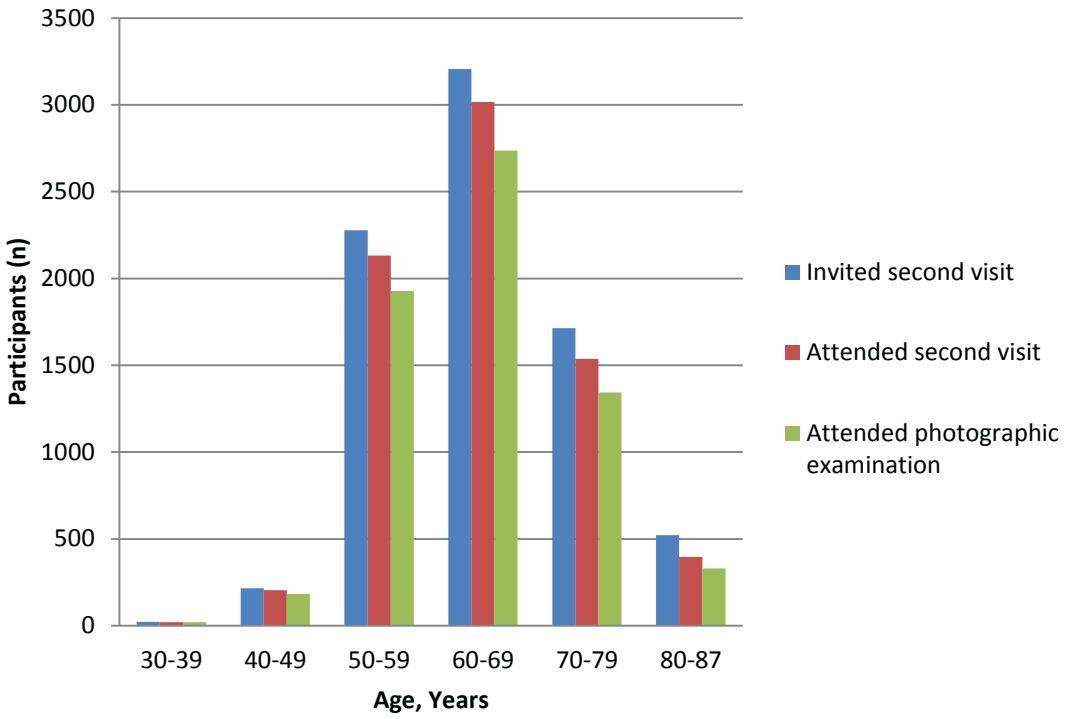
*T4: The 2nd visit of the 4th Tromsø Study survey.

Table 1: Age distribution in invitees and participants in the sixth Tromsø Study 2007-8.

	First visit		Second visit		Tromsø Eye Study*
Age, years	Invited (n)	Attended n (%)	Invited (n)	Attended n (%)	Attended n (%)
30-39	1085	509 (46.9)	23	21 (91.3)	20 (87.0)
40-49	5957	3576 (68.0)	215	205 (95.3)	183 (85.1)
50-59	3407	2436 (71.5)	2278	2132 (93.6)	1927 (84.6)
60-69	5337	4103 (76.9)	3207	3016 (94.0)	2736 (85.3)
70-79	2653	1829 (68.9)	1714	1536 (89.6)	1344 (78.4)
80-87	1323	531 (40.1)	521	397 (76.2)	330 (63.3)
Total	19762	12984 (65.7)	7958	7307 (91.8)	6540 (82.2)

* Participated in retinal photographic examination

Figure 5: Age distribution of participants. Tromsø Eye Study 2007-8.



Data collection and definitions

Anthropometric measurements, blood pressure, blood and urine samples were obtained by physical examination. Blood pressure was measured by trained technicians, using an automated device (Dinamap Vital Signs Monitor, Tampa, FL, USA). Three consecutive measurements were done with one minute intervals and the mean of the two last measurements were used in the analyses. Hypertension was defined as systolic blood pressure > 140 mmHg, diastolic blood pressure > 90mmHg, or use of antihypertensive treatment. Pulse pressure was defined as the difference between systolic and diastolic blood pressure and mean arterial pressure as: 2/3(diastolic blood pressure) + 1/3(systolic blood pressure). Body mass index (BMI) was calculated by dividing body weight (kilograms) with the square of height (meters).

Diabetes was defined as self-reported diabetes, non-fasting blood glucose ≥ 11.1 mmol/l, Hb1Ac > 6.5% or a diabetes diagnosis in the Tromsø Study diabetes registry. Estimated glomerular filtration rate (eGFR) was calculated using the CKD-EPI formula [64].

Smoking habits and medical history were obtained by questionnaires.

Laboratory measurements

All laboratory measurements were performed at the University Hospital of North Norway.

Urinary albumin excretion was assessed as urinary Albumin/Creatinine Ratio (ACR). Three separate urine samples of morning spot urine from three consecutive days were collected and analysed within 20 hours. Urine creatinine was measured using colorimetric methods (Jaffes reaction) with an autoanalyzer (ABX PENTRA, Horiba ABX, Montpellier, France). Urine albumin concentration was measured with immunoturbidimetric method, on an ABX PENTRA autoanalyzer (Horiba ABX, Montpellier, France). ACR was calculated by dividing albumin concentration (mg/L) by creatinine (mmol/L). Mean of the three ACRs from three different days, was defined as ACR. In paper II microalbuminuria was defined as: ACR > 3.4 mg/mmol. Paper III used two alternative microalbuminuria cut-off levels defined as: ACR >

3.4 mg/mmol or ACR > 1.13 mg/mmol (according to KDIGO) [65]. Due to the extremely skewed distribution of ACR, we also analysed log-transformed ACR in paper II and III.

Serum creatinine was analysed on a Hitachi Modular model using an enzymatic method that has been standardized against isotope dilution mass spectroscopy (CREA Plus, Roche Diagnostics, GmbH, Mannheim, Germany).

HbA1c was measured in EDTA whole blood by high performance liquid chromatography (HPLC) using an automated analyser (Variant II, Bio-Rad Laboratories Inc., Hercules, CA, USA).

Non-fasting serum cholesterol, triglycerides and glucose were analysed using an automated clinical chemistry analyser (Modular P, Roche Diagnostics, Mannheim, Germany). Standard enzymatic colorimetric assays were used for cholesterol and triglycerides, and UV test (hexokinase) for glucose.

Eye examinations

The eye examination was divided in two parts and visual acuity was measured in the first part.

Visual acuity

Visual acuity was measured by a Nidek AR 660A auto refractor (Nidek CO., LTD., Gamagori, Japan). "Auto-Shot" and "Auto eye tracking" were enabled and visual acuity recorded using the built in Snellen charts ranging from 20/200 – 20/20 after obtaining stable refraction measurements. In case of visual acuity below 20/200, no attempt on further testing was performed. The visual acuity results were categorized and adapted to WHO criteria as visual impairment (< 20/60) or blindness (< 20/200). For comparison to other studies visual impairment defined as visual acuity < 20/40 was also analysed. Spherical equivalent was calculated as spherical power plus half the cylindrical power in dioptres (D) and presented as the mean value of left and right eye. Visual acuity results and refractive measures were printed on paper, stored and entered in the Tromsø Study database at a later date.

Mydriasis was obtained by application of one drop Tropicamide 0.5% (Chauvin Pharmaceuticals Ltd. Kingston upon Thames, Surrey, England) in both eyes. All participants were informed about the effects and potential risk of pupil dilatation and given the opportunity to withdraw from eye examination prior to application of Tropicamide and still participate in the rest of the survey.

Retinal imaging and interview

In the second part of the eye examination, retinal imaging and interview were performed by the author and three technicians. The technicians were authorised health care personnel and received training before the study started, and two months hands on training at the beginning of the study.

Participants were interviewed by technicians and asked in the Norwegian language if they have or ever have had "age-related macular degeneration", "diabetic retinopathy", "cataract", "glaucoma" or "any other eye diseases or surgery". Norwegian common terms describing the medical terms were also used when necessary. Answers were registered directly in the Tromsø Study database. The interview was followed by retinal photography of both eyes with a Visucam PRONM (Carl Zeiss Meditec, Jena, Germany) 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. To increase the image quality of the macular region in participants with suboptimal mydriasis, a sixth image, (30 degree, resolution 1620x1444 pixels and the "Small pupil" option on the camera activated) centred on the macula was added from the sixth week of the study and onwards. External fixation was used if the internal fixation failed due to low visual acuity. The coverage of the photographic fields is illustrated in Figure 2, which is a composite of the five different photographic fields. Images were stored in the camera and exported as DICOM files to a backup storage immediately after photography. A second backup was downloaded to an image server at the end of each week. Finally the photos were imported to Visupac 4.4.1/4.4.3 (Carl Zeiss Meditec) software for grading.

Grading of images

Grading of the retinal images for diabetic retinopathy was performed using high quality 24" LCD-monitors (Eizo ColorEdge CG241W).

Retinopathy

All participants with retinal images (n=6540) were included in the retinopathy grading. All images were graded for presence or absence, characteristics and severity of retinopathy. The grading was performed by one single grader (the author) and masked for all other variables except for visual acuity, self-reported cataract, glaucoma and AMD. The reason for not using completely masked grading was to be able to identify participants in need of referral to an ophthalmologist when identifying pathology in the photos.

The grading was based on "The International Clinical Diabetic Retinopathy and Diabetic Macular Edema Disease Severity Scales" [66], with minor modifications due to the lack of stereo photos. Macular oedema was therefore defined by the presence or absence of hard exudates or grid laser photocoagulation. The photographs were considered gradable for retinopathy if image quality was sufficient to detect small microaneurysms in at least a total area equivalent of four of the five 45 degrees photographic fields. In addition, microaneurysms, haemorrhages, hard exudates, soft exudates, intra retinal microvascular abnormalities (IRMA), venous beading, New Vessels on the Disk (NVD) and New Vessels Elsewhere (NVE) were quantified. Microaneurysms and haemorrhages were defined according to ETDRS report number 10 [67]. Photographs with haemorrhages but without evidence of microaneurysms were classified as mild retinopathy, but could for analysis purposes be separated into two different categories based on the microaneurysm count. Photos with presence of laser photocoagulation burns indicating panretinal laser photocoagulation were classified as proliferative retinopathy. Other eye diseases known to cause retinal haemorrhages or other findings similar to diabetic retinopathy were also classified, and both eyes on each participant were graded consecutively. The grading was entered in a custom made Access (Microsoft) database and the final grading imported to the Tromsø Study database at the end of the grading.

Prior to the grading of the Tromsø Eye Study, the grader had received training by an experienced retina specialist and achieved kappa 0.75 compared with another experienced retina specialist in a previous study using the same methodology for retinopathy grading [68].

The grading was performed in two stages. In the preliminary grading all photos were graded, and in case of doubt about the presence of a lesion it was graded as present. All photos graded as retinopathy lesions present at first grading were then graded a second time at the end of the study to set a final homogenous grading. At the final grading the grader had to be at least 90% certain that a lesion was present to set a retinopathy grade. For intra grader assessment a random sample of 200 participants (400 eyes) was generated with all stages of pathology represented and mixed with 42.5% normal photos. This sample was graded a third time masked for all other variables and previous grading. Exact agreement was 89% and kappa 0.81 when compared to the final grading.

Statistical analyses

We used t-test for comparison of means and Chi square for comparisons of proportions. Uni- and multivariable logistic regression models were used to calculate odds ratio (OR) and 95% confidence interval (CI) for association between exposure and outcome. For highly skewed ACR, Wilcoxon's rank test and log transformation were used. StataSE/MP version 12 (Stata Corp LP, Texas, USA) was used for statistical analysis. All comparisons used a two-sided significance level of 5%.

Methods paper IV

Although exploring similar research questions in paper two and four, the methodology was different.

Study sample

The study was multi-centre study in three different regions of Norway (Tromsø, Tønsberg and Stavanger). In each region randomly selected general practitioners were asked to randomly select 25 patients among those with known diabetes (ICPC-2 diagnose T89 or T90

in the electronic patient record database). A total of 51% of the randomly selected general practitioners participated and had to be supplemented by five additional general practitioners to include a sufficient sample size. Additional patients were included by allowing two of the randomly selected general practitioners to include diabetes patients from colleagues sharing the same electronic patient record database as the randomly selected general practitioners. A total of 591 patients were invited and 299 attended the study (50.6%).

Retinal imaging

Mydriatic retinal imaging was performed at the outpatient hospital clinics in all three sites, using the available camera equipment (Zeiss FF450 plus, Topcon TRC501, Canon CF-60DSi). Two fields 50/60 degrees digital red free images centred on the fovea and optic disk were performed on both eyes by experienced photographers.

Retinopathy grading

Retinopathy grading was performed according to "The International Clinical Diabetic Retinopathy and Diabetic Macular Edema Disease Severity Scales" [66], with minor modifications due to the lack of stereo photos identical to paper I-III. The additional quantification of retinopathy lesions described in paper I-III was not used in paper IV. A preliminary grading was performed at each centre by experienced graders and in case of doubt the image was graded as retinopathy. All images with pathology or questionable pathology at the first grading were graded a second time in a plenary session attended by all graders from all centres to set a final grade after consensus. Retinopathy lesions most likely caused by other diseases than diabetes were graded as either no retinopathy or non-gradable. To validate the grading, a random sample of 10% was regraded by one of the authors masked for previous grading.

Visual acuity

Visual acuity was measured by experienced health care personnel with the participants own spectacles and by the use of Snellen charts. No attempts on refraction were made.

Interview

Participants were interviewed about diabetes type, onset, medication, diabetes care and prior ophthalmological examination using a questionnaire filled in by the investigators (Appendix III). The questionnaire was later used in the retinopathy grading.

The author contribution

In contrast to paper I-III, the author was not the principal investigator in study IV. The author recruited the general practitioners and participants into the study in Tromsø. The author also planned and conducted the clinical examination in Tromsø and participated in a critical review of the paper.

Main results

Paper I: The Tromsø Eye Study: Study design, methodology and results on visual acuity and refractive errors

Paper I describes the study design and general methodology of the Tromsø Eye Study, including a detailed description of the methodology used for retinopathy grading. Intra grader kappa was 0.81 for retinopathy grading. Although not explored further in the present thesis, the age related macular degeneration grading and retinal vessel calibre measurements were also described. Intra and inter grader kappa was 0.66 and 0.58 respectively for age related macular degeneration and all interclass correlation coefficients were above 0.93 for retinal vessel calibre measurements.

A total of 6540 participants had retinal images. Visual acuity was available from 6459 participants and refraction from 6566 participants. Retinopathy was graded in all 6540 participants with retinal images, and 116 had ungradable images on both eyes and 292 had ungradable images in one eye. All 6540 participants with retinal images were also included in the retinal vessel analysis and 6353 had successful grading. Age related macular degeneration was graded in participants 65 years and older, and in this subsample 2653 had retinal images. Of those, a total of 22 had ungradable photos in both eyes and 138 had ungradable photos in one eye.

Vision loss was highest among participants aged 80-87 years, of whom 7.3% (95% CI, 3.3-11.2) had visual acuity < 20/60 in the better-seeing eye compared to 1.2% (95% CI, 0.95-1.5) for the whole study population. When standardizing the study sample to the Tromsø population the prevalence of visual acuity < 20/60 in the better-seeing eye was overall 1.2% among participants aged 50 - 87 years. A total of 25 eyes (0.39% of the participants) had unilateral blindness and two participants had bilateral blindness (0.03%) defined as visual acuity < 20/200.

We found no clinical relevant sex difference in median spherical equivalent. As expected we found a trend towards hyperopia with increasing age.

Paper II: Tromsø Eye Study: Prevalence and risk factors of diabetic retinopathy

The study sample included all 608 (8.3%) participants with diabetes from the Tromsø Eye Study. The overall prevalence of visual impairment (corrected Snellen visual acuity < 20/60) was 1.6% in the better-seeing eye. Corrected Snellen visual acuity < 20/40 was 4.1% in the better-seeing eye. We found no legally blind participants.

The total prevalence of diabetic retinopathy was 26.9% and macular oedema 3.9% in participants with diabetes. Among participants with type 1 diabetes, 77.8% had retinopathy and the mean diabetes duration was 25.2 years, as compared to 25.0% with retinopathy and mean diabetes duration of 5.1 years in type 2 diabetes. The insulin treated group had more than twice the frequency of retinopathy as compared to the group treated with oral antidiabetic medication (53.6% vs. 19.6%). The overall prevalence of proliferative retinopathy was 1.2%. Logistic regression models adjusted for sex and age showed that diabetes duration, insulin use, pulse pressure, microalbuminuria, non-fasting glucose and HbA1c were associated with increased odds for retinopathy. In contrast, higher total- and LDL-cholesterol were associated with decreased odds for retinopathy. In a multivariable logistic regression model, retinopathy was associated with longer diabetes duration (OR per year, 1.07, 95% CI, 1.03-1.11), insulin use (OR, 2.14, 95% CI, 1.19-3.85), non-fasting glucose (OR per mmol/l, 1.07, 95% CI, 1.00-1.15) and microalbuminuria (OR 1.89, 95% CI, 1.28-2.81).

To evaluate microalbuminuria cut-off level for increased retinopathy odds, we substituted log transformed microalbuminuria with tertiles of urine albumin-creatinine ratio (ACR) as a categorical variable in the multivariable model. The lowest ACR tertile was used as reference. When excluding participants with proteinuria (ACR > 30 mg/mmol) the highest ACR tertile was associated with retinopathy (OR third tertile, 2.80, 95% CI, 1.55 -5.05). The third ACR tertile ranged from 1.16-28.5 mg/mmol when proteinuria was excluded.

Paper III: Sex differences in risk factors for retinopathy in non-diabetic men and women. The Tromsø Eye Study.

The study sample included 5869 participants aged 38-87 years from the Tromsø Eye Study without diabetes (self-reported and screening detected). The overall prevalence of retinopathy was 14.8%. Men had a higher prevalence of retinopathy compared to women (15.9% vs. 14.0%, p=0.04). Owing to interaction between sex and risk factors, the regression analyses were done stratified by sex. In age adjusted logistic regression models, retinopathy was associated with all blood pressure variables and HbA1c in men. In women retinopathy was associated with urine albumin excretion (log transformed and dichotomous albumin-creatinine ratio > 3.4 mg/mmol) and all blood pressure variables except for diastolic blood pressure. The sex difference was also found in multivariable logistic regression: In men retinopathy was associated with hypertension (OR, 1.59; 95%CI, 1.24-2.04) and HbA1c (OR per 1%, 1.41; 95% CI, 1.01-1.96). In women retinopathy was associated with age (OR per 10 years, 1.32; 95% CI, 1.14-1.52), log transformed urinary albumin excretion (OR per log unit, 1.46; 95% CI, 1.14-1.87) and hypertension (OR, 1.36; 95% CI, 1.08-1.71). To evaluate microalbuminuria cut-off level for increased retinopathy odds in women, we substituted log transformed microalbuminuria with quartiles of urine albumin-creatinine ratio (ACR) as a categorical variable in the multivariable model. The lowest ACR quartile was used as reference. Retinopathy was associated with the two highest ACR quartiles indicating that even very low levels of urinary albumin excretion (urinary albumin-creatinine ratio > 0.43 mg/mmol) was associated with increased risk for retinopathy (OR third quartile, 1.61; 95% CI, 1.17 -2.22 and OR fourth quartile, 1.42; 95%CI, 1.03-1.97).

Paper IV: Prevalence of diabetic retinopathy in Norway: report from a screening study

The majority of the participants (89.2%) had type 2 diabetes. A total of 93.8% of the type 1 diabetes and 58.0% of the type 2 diabetes patients (62.0% for type 1 and 2 combined) had attended eye examination during the last two years as recommended by the national guidelines. A total of 96.9% of the type 1 diabetes and 62.3% of the type 2 diabetes patients had attended eye examination during the last three years. Overall, 26.1% had never had an eye examination. All type 1 diabetes patients had attended at least one eye examination by an ophthalmologist.

The overall prevalence of any diabetic retinopathy was 28.2%. In type 1 diabetes, a total of 65.6% had any retinopathy, and 37.5% had proliferative retinopathy. In type 2 diabetes, a total of 23.7% had any retinopathy and 1.5% had proliferative retinopathy. As expected the prevalence of retinopathy among type 2 diabetes patients was highest in the insulin treated group and lowest in the diet only group. In the diet only group where only 34.7% attended at least biannual eye examination, a total of 11.0% had retinopathy.

Diabetic macular oedema was present in 9% of type 1 diabetes and in 11% of insulin treated type 2 diabetes, the rest had low prevalence.

The prevalence of visual impairment (defined as visual acuity < 20/40 in the better-seeing eye) was 5.4%, similar to the results in paper II. One participant was legally blind on both eyes due to diabetic retinopathy.

General discussion

Methodology considerations paper I-III, Tromsø Eye Study

Study design

The Tromsø Eye study was planned and conducted by the author in collaboration with the principal investigators of the 6th Tromsø Study. The Tromsø Study has in general a solid experience with conducting population based surveys. In contrast the Tromsø Eye Study had

no experience with setting up a large population based ophthalmologic study. In the initial planning other Scandinavian studies were consulted for advice, but it became soon clear that each study was unique and adapted to local traditions, logistics and pre-existing facilities. The Tromsø Eye Study therefore had to make independent choices based on the available recourses. In contrast to other well-known population based eye studies, the present study was a sub-study of a larger multipurpose study and not an ophthalmology driven study. This limited the possibility for extensive eye examinations due to logistics and time concerns, but gave a huge advantage in terms of a large amount of available data and relevant adjustment variables collected in the rest of the Tromsø Study.

One of the strengths of the Tromsø Study is the longitudinal design, but paper I-III only analysed cross-sectional data from the 6th Tromsø Study and thus limits the possibilities for exploring causality. Although the attendance rates in The Tromsø Study as in many other population based studies are decreasing, the relatively high (in an epidemiological context) attendance rate and large sample size are strengths of the study [62].

Internal validity

The term "internal validity" refers to how the study results reflects or mirrors the actual study population, in other words how close to the truth are the results [69]. The main concerns are selection bias, information bias and confounding.

Selection bias

The term "bias" is often used to describe systematic errors in science [70]. An important source of systematic error in cross sectional surveys is selection bias, occurring if there is any systematic difference in the characteristics between those who take part in the study and those who do not [71].

The sampling strategy in paper I-III, using birth year and being a resident of Tromsø as selection criteria combined with relatively high attendance rates reduces the potential for selection bias.

A general concern in cross-sectional surveys is the healthy participant effect. Legal restrictions preclude detailed analyses of mortality or morbidity according to attendance in The Tromsø study. Previous data showed that subjects who attended all Tromsø 2-4 surveys had lower mortality compared to those invited to all three, but only attended Tromsø 4 and indicate some degree of healthy participant effect [62].

A total of 767 participants in the second visit of the Tromsø Study did not participate in retinal imaging. The majority was due to logistics and random events, not likely to contribute to selection bias. When comparing all participants without retinal imaging to participants with retinal imaging we found similar results although the participants without photos were slightly older (63.4 vs. 65.0 years), had slightly higher HbA1c (5.73% vs. 5.80%) and reported higher prevalence of all eye diseases. A reason for this may be that the oldest and most disabled participants did not manage to have retinal images taken and may contribute to selection bias. In addition, among the 767 participants without photos, a total of 209 chose not to participate in retinal imaging and were probably not random events. Compared to the final sample, they reported significantly higher prevalence of all eye-diseases except for diabetic retinopathy, but were otherwise similar with regard to the relevant variables presented in this thesis. The 209 participants reported 2.3% higher prevalence of age related macular degeneration compared to participants with photos, and if included in the final sample they would have generated only five excess cases of age related macular degeneration.

In conclusion, our data indicated a minor healthy participant effect that most likely does not affect the results substantially.

Information bias and misclassification

Information bias is a result of systematic errors in the measurement of either exposure or outcome or both. This may lead to both underestimating and overestimating the associations [70].

Definition of diabetes

Due to logistic concerns, fasting blood samples were not feasible, and the sensitivity of self-reported diabetes is moderate [72, 73]. We therefore used self-reported diabetes diagnose supplemented with data from the Tromsø Study diabetes registry and laboratory measurements using both non-fasting glucose and HbA1c to detect diabetes. Paper II and III used HbA1c > 6.5%, but a recent study suggests that some diabetes participants are missed using this cut off value and thus underestimating the diabetes prevalence although this is controversial [74].

Questionnaires:

Questionnaires are susceptible for bias. It is well known that some questions are answered incorrectly by a large number of the participants, especially on topics that might be linked to socially unfavourable behaviour such as alcohol consumption which very often is underestimated [75]. In the present study smoking status was explored by questionnaires and one might suspect similar effects, but studies in general find self-reported smoking to give valid information [76, 77]. Self-reported stroke was also explored. One might suspect cerebral pathology to reduce the accuracy of information, but a study from the 4th Tromsø survey concluded that self-reported stroke can be used to assess the prevalence of stroke [78]. Other variables on cardiovascular disease and supplements have not been thoroughly validated, but we do not suspect substantial bias.

Grading of photographs:

There are several methods for describing the retinal lesions involved in retinopathy, and to compare results with other studies it is important to use similar methodology. The most common grading protocol is probably the classification from the Early Treatment Diabetic Retinopathy Study Research Group (ETDRS) [67]. It was developed from the earlier work of the "Airlie House" and the Diabetic Retinopathy Study Research Group (DRS) [79] to be able to detect small steps of progression in a intervention study. The grading is detailed with evaluation of 17 different lesions, some of them with several severity steps in multiple images and is therefore a very time consuming protocol not suitable for a large population based

study. To overcome the excess workload of the ETDRS grading, simpler grading schemes have been proposed. In 2003 "The International Clinical Diabetic Retinopathy and Diabetic Macular Edema Disease Severity Scales" (Table 2 and 3) was published as a result of an expert consensus panel. It was adopted by the American Academy of Ophthalmology and is widely used [66]. It is a five step scale (when including no retinopathy) and initially developed for clinical ophthalmoscopy, but easily adaptable to retinal images.

Table 2: The International Clinical Diabetic Retinopathy Severity Scales

Proposed disease severity level	**Findings observable on dilated ophthalmoscopy.**
No apparent retinopathy	No abnormalities
Mild retinopathy	Microaneurysms only
Moderate retinopathy	More than just microaneurysms, but less than severe retinopathy
Severe retinopathy	Any of the following: - More than 20 intraretinal haemorrhages in each quadrant - Definite venous beading in 2+ quadrants - Prominent intraretinal microvascular abnormalities (IRMA) in 1 + quadrant
Proliferative retinopathy	Any of the following: - Neovascularization - Vitreous haemorrhage - Preretinal haemorrhage

Table 3: The International Clinical Diabetic Macular Edema Severity Scales

Proposed disease severity level	**Findings observable on dilated ophthalmoscopy**
Diabetic macular oedema apparently absent	No apparent retinal thickening or hard exudates in the posterior pole.
Diabetic macular oedema apparently present	Some apparent retinal thickening or hard exudates in the posterior pole.
Mild	Some retinal thickening or hard exudates in the posterior pole, but distant to the centre of the macula.
Moderate	Retinal thickening or hard exudate approaching the centre of the macula, but not involving centre.
Severe	Retinal thickening or hard exudates involving the centre of the macula.

By using "The International Clinical Diabetic Retinopathy and Diabetic Macular Edema Disease Severity Scales" we are able to compare our prevalence results to other studies using similar methodology. In many cross-sectional studies using the ETDRS, the majority of statistical analyses use a dichotomous retinopathy grade (retinopathy yes/no), making comparison to our data possible. A disadvantage is the limited ability to detect small changes in follow-up studies. To expand the possibilities for analyses, retinal lesions were quantified as previously described.

Misclassification of retinopathy

Variations are common in interpreting the findings of a photo, and may lead to misclassification of retinopathy [67, 80]. To reduce this problem, some studies use a second grader, with a third grading if the first two were not identical. Due to the large sample size and high cost for grading at a professional grading centre all photos were graded by the author. The author has experience from both research and clinical work using photographic grading of diabetic retinopathy, and the intragrader kappa and previous intergrader kappa was high. In addition, a second and final grading was done at the end of the study on all participants with suspected lesions at the first grading to reduce temporal drift. We therefore do not suspect any substantial misclassification of retinopathy. The grading was also done in random order and masked for all other variables except for self-reported eye disease, and any possible misclassification will therefore most likely be non-differential.

Ungradable images

Ungradable images may cause a systematic error and may also be classified as selection bias. In general the oldest and most medically disabled participants are more difficult to image and resulting in a higher proportion of ungradable images among the oldest participants. The prevalence of age related macular degeneration, diabetic retinopathy, cataract and glaucoma is related to age, and thus missing photos may cause underestimation of the population prevalence [81, 82]. Diabetes is also associated with an increased risk of cataract, a common feature resulting in ungradable images [83]. This may lead to an underestimation of diabetic retinopathy.

Visual acuity

In paper I-III corrected visual acuity was measured with an auto refractor (Nidek AR 660). The gold standard is the "ETDRS"-method for testing visual acuity in interventional studies [84]. Unfortunately this method is very time consuming, and not feasible in our study. The Nidek AR 660A has been validated and compared to subjective refraction with no statistically significant difference between two examinations or between estimated refraction and subjective refraction [85]. Although the auto refractor uses Snellen charts, the charts sizes are equivalent to logMar steps and can easily be converted to logMar. A major drawback is the lack of three steps in acuity measurement between Snellen 20/200 and 20/80 and limits the possibility to compare the results to other studies using the complete logMar scale. Another drawback is the use of the same charts on both eyes. The visual acuity was therefore categorized as impaired vision and blindness. The visual acuity measured on the auto refractor also generated more missing values in participants with reduced vision due to opaque media and must be considered as a systematic error leading to underestimating the prevalence of visual impairment and blindness. Initially the participants who failed the auto refractor exam underwent an alternative visual acuity test using a logMAR visual acuity chart and their own spectacles, but this part of the examination eventually had to be discontinued due to logistic and time concerns.

Due to the large sample size the results on visual acuity > 20/40 is probably less affected by the methodological limitations, supported by the similar finding in paper II and IV (4.1% vs. 5.4% visual acuity < 20/40). In conclusion we found the visual acuity tests most suitable for confirming visual acuity > 20/40 and the results on visual impairment are probably underestimated due to systematic errors. In future studies the assessment of visual impairment must be improved.

Fundus camera

Several fundus cameras are commercially available. For diabetic retinopathy grading, the Zeiss FF450 plus with 35 mm colour slides has been used in several large interventional and epidemiological studies and must be considered one of the "gold standard" cameras. The Zeiss

FF450 plus and similar cameras have major drawbacks, requiring experience and technical skills of the photographer and some limitations with suboptimal mydriasis. In addition the extensive logistics of using colour slides compared to digital images is a huge disadvantage and not feasible in our setting.

The non-mydriatic Visucam PRONM digital camera used in the Tromsø Eye Study has been validated against the Zeiss FF450 plus with kappa 0.87 for diabetic retinopathy grading and 0.80 for macular oedema grading. It produced in fact better quality photos in subjects with suboptimal mydriasis (pupil size < 7 mm), common in an older population using Tropicamide for mydriasis [86]. It also provides focusing aid and internal fixation to secure high quality images and consistent photographic fields. Non-mydriatic cameras have also been shown to produce good quality photos with very little photographic training [87]. We conclude that the camera was suitable for the study and are not likely to cause any bias.

Retinal imaging logistics:

The retinal imaging was done by three technicians and the author. Due to limited resources, the technicians in some cases had to be allocated to other tasks and the eye examination site closed, resulting in missing images. As the participants were invited in a random order and the closing of the eye examination site were random events we conclude that it did not lead to a systematic error.

Blood samples:

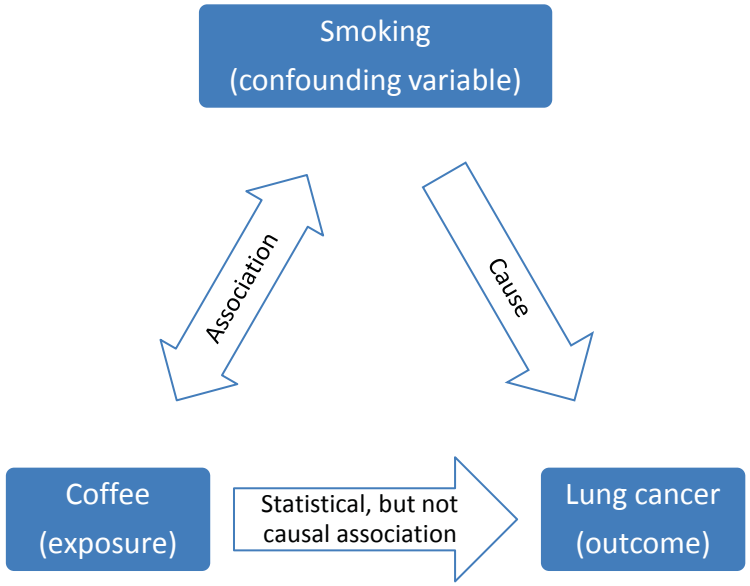
The collection and analysis of blood samples followed strict protocols and there were no differences in collection or analysis routine between potential cases and controls. The participants were invited to the survey in a random order and the blood samples were collected in consecutive order according to when the participants attended the survey, so the potential cases and controls should be randomly distributed among the technicians. The same concept also applies to the analysis. On the other hand participant characteristics may affect analyses, as exemplified by an effect of smoking on measured serum vitamin D levels dependent on the spectrometry assay used [88]. To the best of our knowledge there are no

other similar correlations between the laboratory analyses and participant characteristics in the present study. Blood analyses were performed at the University Hospital of North Norway with strict quality control.

Confounding

Confounders are factors independently associated with both the outcome and the exposure [70, 71, 89]. Bhopal uses an example where alcohol drinking is associated with smoking and smoking is associated with lung cancer. In this situation smoking is the confounder and if not included in the analysis, alcohol drinking is statistically (but not causally) associated with lung cancer [70]. A similar example is illustrated in Figure 6. Confounding can lead to both under and overestimation of the associations studied. In our risk factor analyses we adjusted for known confounders by multiple regression analyses. Still there is always the possibility of residual confounding by unknown or unmeasured factors.

Figure 6: Confounding illustrated by coffee, smoking and lung cancer



External validity

The concept of external validity refers to the generalizability of the study, or in other terms if the results are applicable to other populations [69]. Due to the sampling strategy and age

related differences in attendance rates, there is a discrepancy between the relative sizes of the attending age groups and the Tromsø population. However this can be solved by age-standardizing the study sample to the Tromsø population. This was done in visual impairment analyses but did not change the original results. Similar analyses were done on retinopathy with almost identical results (unpublished) and we believe that our results are applicable to the Tromsø population. Using data from Statistics Norway, the cardiovascular death rates and all-cause mortality are slightly higher in Troms County, but comparable to the general Norwegian population. Furthermore, the prevalence of diabetic retinopathy in subjects with diabetes in the Tromsø Eye Study was similar to the prevalence in Tønsberg and Stavanger indicating that our results, with some caution, can be applied to the Norwegian population [23, 90].

Previous studies have found ethnical differences in diabetic retinopathy and refraction and thus limit the generalizability to other populations [12, 53, 91]. We do not have any indication of the Norwegian population being substantially different to other Western Caucasian populations with regard to the major risk factors and outcome explored and the results are probably generalizable to other Western Caucasian populations. Our prevalence data on diabetic retinopathy supports this conclusion.

Statistical considerations

Although statistical significant results were found in several analyses, the clinical relevance may be limited when including a large sample size. As is common in population based studies using multivariable logistic regression models, the "pseudo R^2's" were in general low, indicating that the model is not suitable for individual prediction.

Methodological considerations paper IV

In general the methodological considerations in paper I-III apply to the fourth paper, although some additional topics must be addressed.

Study sample

The study sample was generated from the electronic patient records of general practitioners and not validated in any other way than through the patient interview. We were not allowed access to the patient records and were therefore not able to validate the diabetes diagnosis set by the general practitioners. By not including screening detected diabetes the duration of diabetes will be longer in paper IV compared to paper II-III and thus a higher proportion of diabetic retinopathy was found.

Due to a heavy work load only about half of the randomly selected general practitioners participated. If non-participating general practitioners had less interest in diabetes one might suspect poorer compliance with the national diabetes guidelines recommendations. This may cause a selection bias where diabetes patients with above average diabetes care were included, resulting in a possible overestimation of the proportion of patients refereed to eye examination and underestimation of diabetic retinopathy.

As only 50.6% attended the study, a healthy participant effect may have occurred. On the other hand, subjects already attending regular eye examinations and receiving high quality care may not wish to spend time on an extra eye examination as required by the study protocol, while participants with suboptimal diabetes care may want to use the opportunity to receive an eye examination resulting in an "unhealthy" participant effect. We were not allowed access to any data on the nonparticipants and were therefore unable to explore this issue further.

Retinal imaging

Paper IV used only two fields 50/60 degrees compared to five fields 45 degrees in paper I-III. The total retinal area examined was therefore smaller in paper IV and may result in an underestimation of diabetic retinopathy. On the other hand, red free images have a higher sensitivity for detecting retinopathy lesions compared to colour images [92].

Retinopathy grading

The plenary masked grading used in paper IV was performed by experienced graders and consensus were made for all images. The inter grader validation also showed excellent correspondence and we believe that misclassification of retinopathy is limited.

Visual acuity

The visual acuity was measured using the participants own spectacles and we must suspect at least some degree of suboptimal refraction and underestimation of best corrected visual acuity. A recent Norwegian study in a mixed diabetic and non-diabetic population found 3% correctable visual impairment (visual impairment defined as visual acuity < 20/40) [68]. This suggests that our data on visual impairment might be overestimated compared to best corrected visual acuity. On the other hand the results reflect the actual visual acuity performance as experienced in the population and also give important information.

Conclusions

Visual impairment in participants with diabetes was assessed in two different Norwegian populations and was low, but the methodology for assessment of visual acuity was not optimal.

The prevalence of diabetic retinopathy was assessed in two different Norwegian populations and found to be similar, almost 30%. The prevalence of retinopathy in a population without diabetes was 14.8%.

The present studies are the first large scale studies using retinal imaging to provide valid estimates of diabetic retinopathy in Norway. Diabetic retinopathy was associated with diabetes duration, insulin use, non-fasting glucose and urine albumin excretion.

A sex difference in risk factor profiles for retinopathy was observed in the non-diabetic population.

The current situation for ophthalmological examination among diabetes patients in Norway is suboptimal and about one third of the diabetic patients claimed not to have attended eye examination at least biannually as recommended by the national guidelines.

Implications for public health

Risk factors for retinopathy

We found urine albumin excretion to be a risk factor for retinopathy in both diabetic and non-diabetic populations. Our data suggest that with some caution, a lower microalbuminuria cut-off level than the current clinical practice may be used in the diabetes care to identify patients with higher risk of retinopathy and thus in need of more intensive treatment.

Screening

A total of 26.1% of the participants claimed not to have attended eye examination indicating that the current diabetes care is not optimal and national guidelines is not followed. Studies have shown the benefits and cost-effectiveness of screening for diabetic retinopathy [93, 94]. This gives an imperative to develop more robust programs for eye examination among diabetes patients in Norway.

Further research

The present research on retinopathy has been done on cross-sectional data. Further research will take advantage of data collected in the previous Tromsø surveys and explore how HbA1c from previous surveys predicts diabetic retinopathy in the sixth Tromsø survey. The preparations for the seventh Tromsø study have already started, and will provide a unique opportunity to explore incidence and causality of retinopathy.

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Paper I

The Tromsø Eye Study: study design, methodology and results on visual acuity and refractive errors.

Bertelsen G, Erke MG, von Hanno T, Mathiesen EB, Peto T, Sjølie AK, Njølstad I.

Acta Ophthalmol. 2012; [Epub ahead of print].

Paper II

Tromsø eye study: prevalence and risk factors of diabetic retinopathy.

Bertelsen G, Peto T, Lindekleiv H, Schirmer H, Solbu MD, Toft I, Sjølie AK, Njølstad I.

Acta Ophthalmol. 2012; [Epub ahead of print].

Paper III

Tromsø Eye Study: Sex difference in risk factors for retinopathy without diabetes.

Bertelsen G, Peto T, Lindekleiv H, Schirmer H, Solbu MD, Toft I, Sjølie AK, Njølstad I.

[Submitted].

Paper IV

Prevalence of diabetic retinopathy in Norway: Report from a screening study.

Kilstad HN, Sjølie AK, Gøransson L, Hapnes R, Henschien HJ, Alsbirk KE, Fossen K, Bertelsen G, Holstad G, Bergrem H.

Acta Ophthalmol 2012; 90:609-12.

Appendix I

Questionnaire I

Tromsø-undersøkelsen

Skjemaet skal leses optisk. Vennligst bruk blå eller sort penn. Du kan ikke bruke komma, bruk blokkbokstaver.

2007 – 2008 KONFIDENSIELT

HELSE OG SYKDOMMER

1 **Hvordan vurderer du din egen helse sånn i alminnelighet?**

- ☐ Meget god
- ☐ God
- ☐ Verken god eller dårlig
- ☐ Dårlig
- ☐ Meget dårlig

2 **Hvordan synes du at helsen din er sammenlignet med andre på din alder?**

- ☐ Mye bedre
- ☐ Litt bedre
- ☐ Omtrent lik
- ☐ Litt dårligere
- ☐ Mye dårligere

3 **Har du eller har du hatt?**

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

4 **Har du langvarige eller stadig tilbakevendende smerter som har vart i 3 måneder eller mer?**

☐ Ja ☐ Nei

5 **Hvor ofte har du vært plaget av søvnløshet de siste 12 måneder?**

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

6 **Under finner du en liste over ulike problemer. Har du opplevd noe av dette den siste uken (til og med i dag)?** (Sett ett kryss for hver plage)

	Ikke plaget	Litt plaget	Ganske mye	Veldig mye
Plutselig frykt uten grunn	☐	☐	☐	☐
Føler deg redd eller engstelig	☐	☐	☐	☐
Matthet eller svimmelhet	☐	☐	☐	☐
Føler deg anspent eller oppjaget	☐	☐	☐	☐
Lett for å klandre deg selv	☐	☐	☐	☐
Søvnproblemer	☐	☐	☐	☐
Nedtrykt, tungsindig	☐	☐	☐	☐
Følelse av å være unyttig, lite verd	☐	☐	☐	☐
Følelse av at alt er et slit	☐	☐	☐	☐
Følelse av håpløshet mht. framtida	☐	☐	☐	☐

BRUK AV HELSETJENESTER

7 **Har du i løpet av de siste 12 måneder vært hos:** Hvis JA; Hvor mange ganger?

	Ja	Nei	Ant ggr
Fastlege/allmennlege	☐	☐	
Psykiater/psykolog	☐	☐	
Legespesialist utenfor sykehus *(utenom fastlege/allmennlege/psykiater)*	☐	☐	
Fysioterapeut	☐	☐	
Kiropraktor	☐	☐	
Annen behandler *(homøopat, akupunktør, fotsoneterapeut, naturmedisiner, håndspålegger, healer, synsk el.l)*	☐	☐	
Tannlege/tannpleier	☐	☐	

8 **Har du i løpet av de siste 12 måneder vært på sykehus?**

	Ja	Nei	Ant ggr
Innlagt på sykehus	☐	☐	
Konsultasjon ved sykehus uten innleggelse;			
Ved psykiatrisk poliklinikk	☐	☐	
Ved annen sykehuspoliklinikk	☐	☐	

9 **Har du gjennomgått noen form for operasjon i løpet av de siste 3 årene?**

☐ Ja ☐ Nei

BRUK AV MEDISINER

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

	Aldri brukt	Nå	Før	Alder første gang
Medisin mot høyt blodtrykk	☐	☐	☐	
Kolesterolsenkende medisin	☐	☐	☐	
Medisin mot hjertesykdom	☐	☐	☐	
Vanndrivende medisin	☐	☐	☐	
Medisin mot beinskjørhet *(osteoporose)*	☐	☐	☐	
Insulin	☐	☐	☐	
Diabetesmedisin *(tabletter)*	☐	☐	☐	
Stoffskiftemedisinene Thyroxin/levaxin	☐	☐	☐	

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

	Ikke brukt siste 4 uker	Sjeldnere enn hver uke	Hver uke, men ikke daglig	Daglig
Smertestillende på resept	☐	☐	☐	☐
Smertestillende reseptfrie	☐	☐	☐	☐
Sovemidler	☐	☐	☐	☐
Beroligende medisiner	☐	☐	☐	☐
Medisin mot depresjon	☐	☐	☐	☐

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

Får du ikke plass til alle medisiner, bruk eget ark.

VED FRAMMØTE vil du bli spurt om du har brukt antibiotika eller smertestillende medisiner de siste 24 timene. Om du har det, vil vi be om at du oppgir preparat, styrke, dose og tidspunkt

FAMILIE OG VENNER

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

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

14 **Kryss av for de slektninger som har eller har hatt**

	Foreldre	Barn	Søsken
Hjerteinfarkt	☐	☐	☐
Hjerteinfarkt før fylte 60 år	☐	☐	☐
Angina pectoris *(hjertekrampe)*	☐	☐	☐
Hjerneslag/hjerneblødning	☐	☐	☐
Beinskjørhet *(osteoporose)*	☐	☐	☐
Magesår/tolvfingertarmsår	☐	☐	☐
Astma	☐	☐	☐
Diabetes	☐	☐	☐
Demens	☐	☐	☐
Psykiske plager	☐	☐	☐
Rusproblemer	☐	☐	☐

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

☐ Ja ☐ Nei

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

☐ Ja ☐ Nei

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

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

ARBEID, TRYGD OG INNTEKT

18 **Hva er din høyeste fullførte utdanning?** (Sett ett kryss)

☐ Grunnskole, framhaldsskole eller folkehøyskole
☐ Yrkesfaglig videregående, yrkesskole eller realskole
☐ Allmennfaglig videregående skole eller gymnas
☐ Høyskole eller universitet, mindre enn 4 år
☐ Høyskole eller universitet, 4 år eller mer

19 **Hva er din hovedaktivitet?** (Sett ett kryss)

☐ Yrkesaktiv heltid
☐ Yrkesaktiv deltid
☐ Arbeidsledig
☐ Hjemmeværende
☐ Pensjonist/trygdet
☐ Student/militærtjeneste

20 **Mottar du noen av følgende ytelser?**

- ☐ Alderstrygd, førtidspensjon (AFP) eller etterlattepensjon
- ☐ Sykepenger (er sykemeldt)
- ☐ Rehabiliterings-/attføringspenger
- ☐ Uføreytelse/pensjon, hel
- ☐ Uføreytelse/pensjon, delvis
- ☐ Dagpenger under arbeidsledighet
- ☐ Overgangstønad
- ☐ Sosialhjelp/-stønad

21 **Hvor høy var husholdningens samlede bruttoinntekt siste år?** Ta med alle inntekter fra arbeid, trygder, sosialhjelp og lignende.

- ☐ Under 125 000 kr
- ☐ 125 000-200 000 kr
- ☐ 201 000-300 000 kr
- ☐ 301 000-400 000 kr
- ☐ 401 000-550 000 kr
- ☐ 551 000-700 000 kr
- ☐ 701 000 -850 000 kr
- ☐ Over 850 000 kr

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

- ☐ Ja
- ☐ Nei

FYSISK AKTIVITET

23 **Hvis du er i lønnet eller ulønnet arbeid, hvordan vil du beskrive arbeidet ditt?**

- ☐ For det meste stillesittende arbeid *(f.eks. skrivebordsarbeid, montering)*
- ☐ Arbeid som krever at du går mye *(f.eks ekspeditørarbeid, lett industriarbeid, undervisning)*
- ☐ Arbeid der du går og løfter mye *(f.eks postbud, pleier, bygningsarbeider)*
- ☐ Tungt kroppsarbeid

24 **Angi bevegelse og kroppslig anstrengelse i din fritid. Hvis aktiviteten varierer meget f eks mellom sommer og vinter, så ta et gjennomsnitt. Spørsmålet gjelder bare det siste året.** (Sett kryss i den ruta som passer best)

- ☐ Leser, ser på fjernsyn eller annen stillesittende beskjeftigelse
- ☐ Spaserer, sykler eller beveger deg på annen måte minst 4 timer i uken *(her skal du også regne med gang eller sykling til arbeidsstedet, søndagsturer med mer)*
- ☐ Driver mosjonsidrett, tyngre hagearbeid, snømåking e.l. *(merk at aktiviteten skal vare minst 4 timer i uka)*
- ☐ Trener hardt eller driver konkurranseidrett regelmessig og flere ganger i uka

25 **Hvor ofte driver du mosjon?** (Med mosjon mener vi at du f.eks går en tur, går på ski, svømmer eller driver trening/idrett)

- ☐ Aldri
- ☐ Sjeldnere enn en gang i uken
- ☐ En gang i uken
- ☐ 2-3 ganger i uken
- ☐ omtrent hver dag

26 **Hvor hardt mosjonerer du da i gjennomsnitt?**

- ☐ Tar det rolig uten å bli andpusten eller svett.
- ☐ Tar det så hardt at jeg blir andpusten og svett
- ☐ Tar meg nesten helt ut

27 **Hvor lenge holder du på hver gang i gjennomsnitt ?**

- ☐ Mindre enn 15 minutter
- ☐ 15-29 minutter
- ☐ 30 minutter – 1 time
- ☐ Mer enn 1 time

ALKOHOL OG TOBAKK

28 **Hvor ofte drikker du alkohol?**

- ☐ Aldri
- ☐ Månedlig eller sjeldnere
- ☐ 2-4 ganger hver måned
- ☐ 2-3 ganger pr. uke
- ☐ 4 eller flere ganger pr.uke

29 **Hvor mange enheter alkohol** (en øl, et glass vin, eller en drink) **tar du vanligvis når du drikker?**

- ☐ 1-2
- ☐ 3-4
- ☐ 5-6
- ☐ 7-9
- ☐ 10 eller flere

30 **Hvor ofte drikker du 6 eller flere enheter alkohol ved en anledning?**

- ☐ aldri
- ☐ sjeldnere enn månedlig
- ☐ månedlig
- ☐ ukentlig
- ☐ daglig eller nesten daglig

31 **Røyker du av og til, men ikke daglig?**

- ☐ Ja
- ☐ Nei

32 **Har du røykt/røyker du daglig?**

- ☐ Ja, nå
- ☐ Ja, tidligere
- ☐ Aldri

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

Antall år ☐☐

34 **Hvis du røyker daglig nå eller har røykt tidligere: Hvor mange sigaretter røyker eller røykte du vanligvis daglig?**

Antall sigaretter ☐☐

35 **Hvor gammel var du da du begynte å røyke daglig?**

Antall år ☐☐

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

Antall år ☐☐

37 **Bruker du, eller har du brukt, snus eller skrå?**

- ☐ Nei, aldri
- ☐ Ja, men jeg har sluttet
- ☐ Ja, av og til
- ☐ Ja, daglig

KOSTHOLD

38 **Spiser du vanligvis frokost hver dag?**

☐ Ja ☐ Nei

39 **Hvor mange enheter frukt og grønnsaker spiser du i gjennomsnitt per dag?** (Med enhet menes f.eks. en frukt, glass juice, potet, porsjon grønnsaker)

Antall enheter ☐☐

40 **Hvor mange ganger i uken spiser du varm middag?**

Antall ☐☐

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

	0-1 g pr. mnd	2-3 g pr.mnd	1-3 g pr.uke	4-6 g pr.uke	1-2 g pr. dag
Poteter	☐	☐	☐	☐	☐
Pasta/ris	☐	☐	☐	☐	☐
Kjøtt *(ikke kvernet)*	☐	☐	☐	☐	☐
Kvernet kjøtt *(pølser, hamburger o.l)*	☐	☐	☐	☐	☐
Grønnsaker, frukt, bær	☐	☐	☐	☐	☐
Mager fisk	☐	☐	☐	☐	☐
Feit fisk	☐	☐	☐	☐	☐

(f.eks.laks, ørret, makrell, sild, kveite,uer)

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

	Sjelden/ aldri	1-6 glass pr. uke	1 glass pr. dag	2-3 glass pr. dag	4 glass el. mer pr. dag
Melk, kefir, yoghurt	☐	☐	☐	☐	☐
Fruktjuice	☐	☐	☐	☐	☐
Brus/leskedrikker med sukker	☐	☐	☐	☐	☐

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

	Antall kopper
Filterkaffe	☐☐
Kokekaffe/presskanne	☐☐
Annen kaffe	☐☐
Te	☐☐

44 **Hvor ofte spiser du vanligvis fiskelever?**
(For eksempel i mølje)

☐ Sjelden/aldri ☐ 1-3 g i året ☐ 4-6 g i året
☐ 7-12 g i året ☐ Oftere

45 **Bruker du følgende kosttilskudd?**

	Daglig	Iblant	Nei
Tran, trankapsler	☐	☐	☐
Omega 3 kapsler *(fiskeolje,selolje)*	☐	☐	☐
Kalktabletter	☐	☐	☐

SPØRSMÅL TIL KVINNER

46 **Er du gravid nå?**

☐ Ja ☐ Nei ☐ Usikker

47 **Hvor mange barn har du født?**

Antall ☐☐

48 **Hvis du har født, fyll ut for hvert barn: fødselsår og vekt samt hvor mange måneder du ammet.**
(Angi så godt som du kan)

Barn	Fødselsår	Fødselsvekt i gram	Ammet ant.mnd
1	☐☐☐☐	☐☐☐☐	☐☐
2	☐☐☐☐	☐☐☐☐	☐☐
3	☐☐☐☐	☐☐☐☐	☐☐
4	☐☐☐☐	☐☐☐☐	☐☐
5	☐☐☐☐	☐☐☐☐	☐☐
6	☐☐☐☐	☐☐☐☐	☐☐

49 **Har du i forbindelse med svangerskap hatt for høyt blodtrykk?**

☐ Ja ☐ Nei

50 **Hvis Ja, i hvilket svangerskap?**

☐ Første ☐ Senere

51 **Har du i forbindelse med svangerskap hatt protein (eggehvite) i urinen?**

☐ Ja ☐ Nei

52 **Hvis Ja, i hvilket svangerskap?**

☐ Første ☐ Senere

53 **Ble noen av disse barna født mer enn en måned for tidlig (før termin) pga. svangerskapsforgiftning?**

☐ Ja ☐ Nei

54 **Hvis Ja, hvilke(t) barn**

Barn 1	Barn 2	Barn 3	Barn 4	Barn 5	Barn 6
☐	☐	☐	☐	☐	☐

55 **Hvor gammel var du da du fikk menstruasjon første gang?**

Antall år ☐☐

56 **Bruker du for tiden reseptpliktige legemidler som påvirker menstruasjonen?**

P-pille, hormonspiral eller lignende ☐ Ja ☐ Nei
Hormonpreparat for overgangs-alderen ☐ Ja ☐ Nei

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

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

Appendix II

Questionnaire II

Tromsø 6

- en del av Tromsøundersøkelsen

SLIK FYLLER DU UT SKJEMAET:

Skjemaet vil bli lest maskinelt, det er derfor viktig at du krysser av riktig:

☒ Riktig

☑ Galt

☒ Galt

■ Om du krysser feil, retter du ved å fylle boksen slik

Skriv tydelige tall 1 2 3 4 5 6 7 8 9 0

7 | 4 Riktig

7 | 4 Galt

Bruk kun sort eller blå penn, bruk ikke blyant eller tusj

1. BESKRIVELSE AV DIN HELSETILSTAND

Vis hvilke utsagn som passer best på din helsetilstand i dag ved å sette ett kryss i en av rutene utenfor hver av de fem gruppene nedenfor:

1.01 **Gange**

- ☐ Jeg har ingen problemer med å gå omkring
- ☐ Jeg har litt problemer med å gå omkring
- ☐ Jeg er sengeliggende

1.02 **Personlig stell**

- ☐ Jeg har ingen problemer med personlig stell
- ☐ Jeg har litt problemer med å vaske meg eller kle meg
- ☐ Jeg er ute av stand til å vaske meg eller kle meg

1.03 **Vanlige gjøremål** (f.eks. arbeid, studier, husarbeid, familie- eller fritidsaktiviteter)

- ☐ Jeg har ingen problemer med å utføre mine vanlige gjøremål
- ☐ Jeg har litt problemer med å utføre mine vanlige gjøremål
- ☐ Jeg er ute av stand til å utføre mine vanlige gjøremål

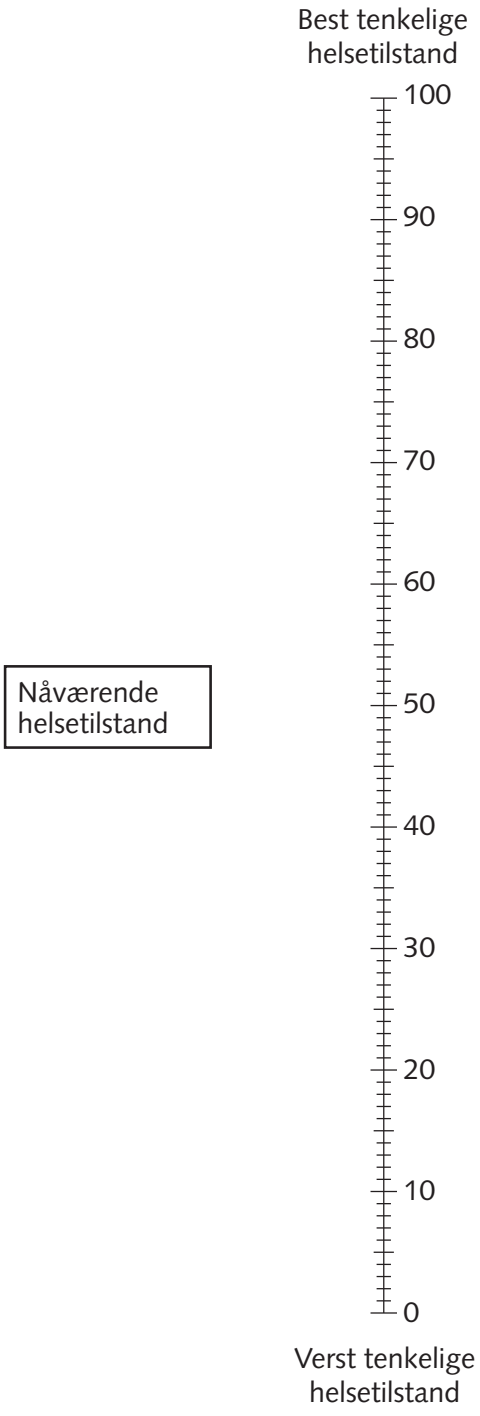
1.04 **Smerte og ubehag**

- ☐ Jeg har verken smerte eller ubehag
- ☐ Jeg har moderat smerte eller ubehag
- ☐ Jeg har sterk smerte eller ubehag

1.05 **Angst og depresjon**

- ☐ Jeg er verken engstelig eller deprimert
- ☐ Jeg er noe engstelig eller deprimert
- ☐ Jeg er svært engstelig eller deprimert

1.6 For at du skal kunne vise oss hvor god eller dårlig din helsetilstand er, har vi laget en skala (nesten som et termometer), hvor den beste helsetilstanden du kan tenke deg er markert med 100 og den dårligste med 0. Vi ber om at du viser din helsetilstand ved å trekke ei linje fra boksen nedenfor til det punkt på skalaen som passer best med din helsetilstand.



2. OPPVEKST OG TILHØRIGHET

2.01 **Hvor bodde du da du fylte 1 år?**

- ☐ I Tromsø *(med dagens kommunegrenser)*
- ☐ I Troms, men ikke i Tromsø
- ☐ I Finnmark fylke
- ☐ I Nordland fylke
- ☐ Annet sted i Norge
- ☐ I utlandet

2.02 **Hvordan var de økonomiske forhold i familien under din oppvekst?**

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

2.03 **Hvilken betydning har religion i ditt liv?**

- ☐ Stor betydning
- ☐ En viss betydning
- ☐ Ingen betydning

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

- ☐ Norsk
- ☐ Samisk
- ☐ Kvensk/Finsk
- ☐ Annet

2.05 **Hvor mange søsken og barn har du/har du hatt?**

Antall søsken ..... ☐☐

Antall barn ..... ☐☐

2.06 **Lever din mor?**

☐ Ja ☐ Nei

Hvis NEI: hennes alder ved død ..... ☐☐

Lever din far?

☐ Ja ☐ Nei

Hvis NEI: hans alder ved død ..... ☐☐

2.07 **Hva var/er den høyeste fullførte utdanning til dine foreldre og din ektefelle/samboer?** (sett ett kryss i hver kolonne)

	Mor	Far	Ektefelle/ samboer
Grunnskole 7-10 år, framhaldsskole eller folkehøyskole	☐	☐	☐
Yrkesfaglig videregående, yrkesskole eller realskole	☐	☐	☐
Allmennfaglig videregående skole eller gymnas	☐	☐	☐
Høyskole eller universitet (mindre enn 4 år)	☐	☐	☐
Høyskole eller universitet (4 år eller mer)	☐	☐	☐

3. TRIVSEL OG LIVSFORHOLD

3.01 **Nedenfor står tre utsagn om tilfredshet med livet som et hele. Deretter står to utsagn om syn på din egen helse. Vis hvor enig eller uenig du er i hver av påstandene ved å sette et kryss i rubrikken for det tallet du synes stemmer best for deg.** (sett ett kryss for hvert utsagn)

	Helt uenig	1	2	3	4	5	6	7	Helt enig
På de fleste måter er livet mitt nær idealet mitt		☐	☐	☐	☐	☐	☐	☐	
Mine livsforhold er utmerkede		☐	☐	☐	☐	☐	☐	☐	
Jeg er tilfreds med livet mitt		☐	☐	☐	☐	☐	☐	☐	
Jeg ser lyst på min framtidige helse		☐	☐	☐	☐	☐	☐	☐	
Ved å leve sunt kan jeg forhindre alvorlige sykdommer		☐	☐	☐	☐	☐	☐	☐	

3.02 **Nedenfor står fire utsagn om syn på forhold ved din nåværende jobb, eller hvis du ikke er i arbeid nå, den jobben du hadde sist** (sett ett kryss for hvert utsagn)

	Helt uenig	1	2	3	4	5	6	7	Helt enig
Arbeidet mitt er for belastende, fysisk eller følelsesmessig		☐	☐	☐	☐	☐	☐	☐	
Jeg har tilstrekkelig innflytelse på når og hvordan arbeidet mitt skal utføres		☐	☐	☐	☐	☐	☐	☐	
Jeg blir mobbet eller trakassert på arbeidsplassen min		☐	☐	☐	☐	☐	☐	☐	
Jeg blir rettferdig behandlet på arbeidsplassen min		☐	☐	☐	☐	☐	☐	☐	

3.03 **Jeg opplever at yrket mitt har følgende sosiale status i samfunnet:** (dersom du ikke er i arbeid nå, tenk på det yrket du hadde sist)

- ☐ Meget høy status
- ☐ Ganske høy status
- ☐ Middels status
- ☐ Ganske lav status
- ☐ Meget lav status

3.04 **Har du over lengre tid opplevd noe av det følgende?** (sett ett eller flere kryss for hver linje)

	Nei	Ja, som barn	Ja, som voksen	Ja, siste år
Blitt plaget psykisk, eller truet med vold	☐	☐	☐	☐
Blitt slått, sparket eller utsatt for annen type vold	☐	☐	☐	☐
Noen i nær familie har brukt rusmidler på en slik måte at dette har vært til *bekymring* for deg	☐	☐	☐	☐

Dersom du har opplevd noen av disse forholdene, hvor mye plages du av dette nå?

☐ Ingen plager ☐ Noen plager ☐ Store plager

4. SYKDOMMER OG PLAGER

4.01 **Har du i løpet av den siste måneden følt deg syk eller hatt en skade?**

☐ Ja ☐ Nei

Hvis JA: har du i den samme perioden?
(sett ett kryss for hver linje)

	Ja	Nei
Vært hos allmennlege/fastlege	☐	☐
Vært hos spesialist	☐	☐
Vært på legevakt	☐	☐
Vært innlagt i sykehus	☐	☐
Vært hos alternativ behandler *(kiropraktor, homøopat eller lignende)*	☐	☐

4.02 **Har du merket anfall med plutselig endring i pulsen eller hjerterytmen siste året?**

☐ Ja ☐ Nei

4.03 **Blir du tungpustet i følgende situasjoner?**
(sett ett kryss for hvert spørsmål)

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

4.04 **Hoster du omtrent daglig i perioder av året?**

☐ Ja ☐ Nei

Hvis JA: Er hosten vanligvis ledsaget av oppspytt?

☐ Ja ☐ Nei

Har du hatt slik hoste så lenge som i en 3 måneders periode i begge de to siste årene?

☐ Ja ☐ Nei

4.05 **Hvor ofte er du plaget av søvnløshet?**
(sett ett kryss)

☐ Aldri, eller noen få ganger i året
☐ 1-3 ganger i måneden
☐ Omtrent 1 gang i uka
☐ Mer enn 1 gang i uka

Hvis du er plaget av søvnløshet månedlig eller oftere, når på året er du mest plaget?
(sett ett eller flere kryss)

☐ Ingen spesiell tid
☐ Mørketida
☐ Midnattsoltida
☐ Vår og høst

4.06 **Har du i de siste par ukene hatt vansker med å sove?**

☐ Ikke i det hele tatt
☐ Ikke mer enn vanlig
☐ Heller mer enn vanlig
☐ Mye mer enn vanlig

4.07 **Har du de siste par ukene følt deg ulykkelig og nedtrykt (deprimert)?**

☐ Ikke i det hele tatt
☐ Ikke mer enn vanlig
☐ Heller mer enn vanlig
☐ Mye mer enn vanlig

4.08 **Har du i de siste par ukene følt deg ute av stand til å mestre dine vanskeligheter?**

☐ Ikke i det hele tatt
☐ Ikke mer enn vanlig
☐ Heller mer enn vanlig
☐ Mye mer enn vanlig

4.09 **Nedenfor ber vi deg besvare noen spørsmål om din hukommelse:** (sett ett kryss for hvert spørsmål)

	Ja	Nei
Synes du at din hukommelse har blitt dårligere?	☐	☐
Glemmer du ofte hvor du har lagt tingene dine?	☐	☐
Har du problemer med å finne vanlige ord i en samtale?	☐	☐
Har du fått problemer med daglige gjøremål som du mestret tidligere?	☐	☐
Har du vært undersøkt for sviktende hukommelse?	☐	☐

Hvis JA på minst ett av de fire første spørsmålene ovenfor: Er det et problem i hverdagen?

☐ Ja ☐ Nei

4.10 **Har du i løpet av det siste året vært plaget med smerter og/eller stivhet i muskler og ledd som har vart i minst 3 måneder sammenhengende?** (sett ett kryss i hver linje)

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

4.11 **Har du vært plaget med smerter og/eller stivhet i muskler og ledd i løpet av de siste 4 ukene?** (sett ett kryss i hver linje)

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

4.12 **Har du noen gang hatt:**

	Ja	Nei	Alder siste gang
Brudd i håndledd/ underarm?	☐	☐	
Lårhalsbrudd?	☐	☐	

4.13 **Har du fått stilt diagnosen slitasjegikt av lege?**

☐ Ja ☐ Nei

4.14 **Har eller har du hatt noen av følgende:**

	Aldri	Litt	Mye
Nikkelallergi	☐	☐	☐
Pollenallergi	☐	☐	☐
Andre allergier	☐	☐	☐

4.15 **Har du opplevd ufrivillig barnløshet i mer enn 1 år?**

☐ Ja ☐ Nei

Hvis JA, skyldtes dette:

	Ja	Nei	Vet ikke
Forhold hos deg selv?	☐	☐	☐
Forhold hos partneren?	☐	☐	☐

4.16 **I hvilken grad har du hatt følgende plager i de siste 12 måneder?**

	Aldri	Litt	Mye
Kvalme	☐	☐	☐
Halsbrann/sure oppstøt	☐	☐	☐
Diare	☐	☐	☐
Treg mage	☐	☐	☐
Vekslende treg mage og diare	☐	☐	☐
Oppblåsthet	☐	☐	☐
Smerter i magen	☐	☐	☐

4.17 **Hvis du har hatt smerter i eller ubehag fra magen siste året:**

	Ja	Nei
Er disse lokalisert øverst i magen?	☐	☐
Har du hatt plagene så ofte som 1 dag i uka eller mer de siste 3 måneder?	☐	☐
Blir plagene bedre etter avføring?	☐	☐
Har plagene sammenheng med hyppigere eller sjeldnere avføring enn vanlig?	☐	☐
Har plagene noen sammenheng med løsere eller fastere avføring enn vanlig?	☐	☐
Kommer plagene etter måltid?	☐	☐

4.18 **Har du noen gang hatt:**

	Ja	Nei	Alder siste gang
Sår på magesekken	☐	☐	
Sår på tolvfingertarmen	☐	☐	
Magesår-operasjon	☐	☐	

4.19 **Til kvinnen: Har du spontanabortert?**

☐ Ja ☐ Nei ☐ Vet ikke

Hvis JA, antall ganger

4.20 **Til mannen: Har din partner noen gang spontanabortert?**

☐ Ja ☐ Nei ☐ Vet ikke

Hvis JA, antall ganger

4.21 **Bruker du glutenfri diett?**

☐ Ja ☐ Nei ☐ Vet ikke

4.22 **Har du fått stilt diagnosen Dermatitis Herpetiformis (DH)?**

☐ Ja ☐ Nei ☐ Vet ikke

4.23 **Har du fått stilt diagnosen cøliaki på bakgrunn av en vevsprøve fra tynntarmen tatt under en undersøkelse der du svelget en slange (gastroskopi)?**

☐ Ja ☐ Nei ☐ Vet ikke

4.24 **Har du egne tenner?**

☐ Ja ☐ Nei

4.25 **Hvor mange amalgamfyllinger har du/har du hatt?**

☐ 0 ☐ 1-5 ☐ 6-10 ☐ 10+

4.26 **Har du vært plaget av hodepine det siste året?**

☐ Ja ☐ Nei

Hvis NEI, gå til del 5, kosthold

4.27 **Hva slags hodepine er du plaget av?**

☐ Migrene ☐ Annen hodepine

4.28 **Omtrent hvor mange dager per måned har du hodepine?**

☐ Mindre enn 1 dag
☐ 1-6 dager
☐ 7-14 dager
☐ Mer enn 14 dager

4.29 **Er hodepinen vanligvis:**
(sett et kryss for hver linje)

	Ja	Nei
Bankende/dunkende smerte	☐	☐
Pressende smerte	☐	☐
Ensidig smerte *(høyre eller venstre)*	☐	☐

4.30 **Hvor sterk er hodepinen vanligvis?**

☐ Mild *(hemmer ikke aktivitet)*
☐ Moderat *(hemmer aktivitet)*
☐ Sterk *(forhindrer aktivitet)*

4.31 **Hvor lenge varer hodepinen vanligvis?**

☐ Mindre enn 4 timer
☐ 4 timer – 1 døgn
☐ 1-3 døgn
☐ Mer enn 3 døgn

4.32 **Dersom du er plaget av hodepine, når på året er du plaget mest?** (sett ett eller flere kryss)

☐ Ingen spesiell tid
☐ Mørketida
☐ Midnattsoltida
☐ Vår og/eller høst

4.33 **Før eller under hodepinen, kan du da ha forbigående:**

	Ja	Nei
Synsforstyrrelse? *(takkede linjer, flimring, tåkesyn, lysglimt)*	☐	☐
Nummenhet i halve ansiktet eller i hånden?	☐	☐
Forverring ved moderat fysisk aktivitet	☐	☐
Kvalme og /eller oppkast	☐	☐

4.34 **Angi hvor mange dager du har vært borte fra arbeid eller skole siste måned på grunn av hodepine:**

Antall dager ☐☐

5. KOSTHOLD

5.01 **Hvor ofte spiser du vanligvis følgende?** (sett ett kryss i hver linje)

	0-1 g per mnd	2-3 g per mnd	1-3 g per uke	Mer enn 3 g per uke
Ferskvannsfisk *(ikke oppdrett)*	☐	☐	☐	☐
Saltvannsfisk *(ikke oppdrett)*	☐	☐	☐	☐
Oppdrettsfisk *(laks, røye, ørret)*	☐	☐	☐	☐
Tunfisk *(fersk eller hermetisert)*	☐	☐	☐	☐
Fiskepålegg	☐	☐	☐	☐
Skjell	☐	☐	☐	☐
Den brune innmaten i krabbe	☐	☐	☐	☐
Hvalkjøtt/sel/kobbekjøtt	☐	☐	☐	☐
Innmat fra rein eller elg	☐	☐	☐	☐
Innmat fra rype	☐	☐	☐	☐

5.02 **Hvor mange ganger i året spiser du/spiste du vanligvis følgende?** (antall ganger)

	Som voksen	I din barndom
Mølje *(Antall ganger i året)*	☐☐	☐☐
Måsegg *(Antall egg i året)*	☐☐	☐☐
Reinsdyrkjøtt *(Antall ganger i året)*	☐☐	☐☐
Selvplukket sopp og bær *(blåbær/tyttebær/multe) (Antall ganger i året)*	☐☐☐	☐☐☐

5.03 **Hvor mange ganger i måneden spiser du hermetiske matvarer (fra metallbokser)?**

Antall ☐☐

5.04 **Bruker du vitaminer og/eller mineraltilskudd?**

☐ Ja, daglig ☐ Iblant ☐ Aldri

5.05 **Hvor ofte spiser du?**

	Aldri	1-3 g per mnd	1-3 g per uke	4-6 g. per uke	1-2 g. per dag	3 g. per dag eller mer
Mørk sjokolade	☐	☐	☐	☐	☐	☐
Lys sjokolade/melkesjokolade	☐	☐	☐	☐	☐	☐
Sjokoladekake	☐	☐	☐	☐	☐	☐
Andre søtsaker	☐	☐	☐	☐	☐	☐

5.06 **Hvis du spiser sjokolade, hvor mye pleier du vanligvis å spise hver gang?**
Tenk deg størrelsen på en Kvikk- Lunsj sjokolade, og oppgi hvor mye du spiser i forhold til den.

¼	½	1	1 ½	2	Mer enn 2
☐	☐	☐	☐	☐	☐

5.07 **Hvor ofte drikker du kakao/varm sjokolade**

Aldri	1-3 g per mnd	1-3 g per uke	4-6 g. per uke	1-2 g. per dag	3 g. per dag eller mer
☐	☐	☐	☐	☐	☐

6. ALKOHOL

6.01 **Hvor ofte har du det siste året:**	Aldri	Sjeldnere enn månedlig	Månedlig	Ukentlig	Daglig, eller nesten daglig
Ikke klart å stoppe og drikke alkohol når du først har begynt?	☐	☐	☐	☐	☐
Ikke klart å gjøre det som normalt forventes av deg fordi du har drukket?	☐	☐	☐	☐	☐
Trengt en drink om morgenen for å få komme i gang etter en rangel?	☐	☐	☐	☐	☐
Følt skyld eller anger etter at du har drukket?	☐	☐	☐	☐	☐
Ikke klart å huske hva som skjedde kvelden før på grunn av at du hadde drukket?	☐	☐	☐	☐	☐

	Aldri	Ja, men ikke det siste året	Ja, det siste året
6.02 **Har du eller andre noen gang blitt skadet på grunn av at du har drukket?**	☐	☐	☐
Har en slektning, venn, lege, eller annet helsepersonell vært bekymret for din drikking, eller foreslått at du reduserer inntaket?	☐	☐	☐

7. VEKT

7.01 **Har du ufrivillig gått ned i vekt siste 6 måneder?**

☐ Ja ☐ Nei

Hvis JA: Hvor mange kilo? ☐☐

7.02 **Anslå din vekt da du var 25 år gammel:**

Antall hele kg ☐☐☐

7.03 **Er du fornøyd med vekta di nå?**

☐ Ja ☐ Nei

7.04 **Hvilken vekt ville du være tilfreds med (din trivselsvekt):**

Antall kg ☐☐☐

8. LØSEMIDLER

8.01 **Hvor mange timer i uka driver du med følgende fritids- eller yrkesaktiviteter:**
Bilreparasjoner/lakkering, keramikkarbeid, maling/lakkering/løsemidler, frisør, glassmester, elektriker (Sett 0 om du ikke driver med slike fritids eller yrkesaktiviteter)

Antall timer per uke i gjennomsnitt ☐☐

8.02 **Bruker du hårfargemidler?**

☐ Ja ☐ Nei

Hvis JA, hvor mange ganger per år? ☐☐

9. BRUK AV HELSETJENESTER

9.01 **Har du noen gang opplevd at sykdom er blitt mangelfullt undersøkt eller behandlet, og at dette har gitt alvorlige følger?**

- ☐ Ja, det har rammet meg selv
- ☐ Ja, det har rammet en nær pårørende *(barn, foreldre, ektefelle/samboer)*
- ☐ Nei

Hvis JA, hvor mener du årsaken ligger? (sett ett eller flere kryss):

- ☐ hos fastlege/allmennlege
- ☐ hos legevaktslege
- ☐ hos privatpraktiserende spesialist
- ☐ hos sykehuslege
- ☐ hos annet helsepersonell
- ☐ hos alternativ behandler
- ☐ hos flere på grunn av svikt i rutiner og samarbeid

9.02 **Har du noen gang følt deg overtalt til å godta undersøkelse eller behandling som du selv ikke ønsket?**

☐ Ja ☐ Nei

Hvis JA, mener du dette har hatt uheldige helsemessige følger?

☐ Ja ☐ Nei

9.03 **Har du noen gang klaget på behandling du har fått?**

- ☐ Har aldri vært aktuelt
- ☐ Har vurdert å klage, men ikke gjort det
- ☐ Har klaget muntlig
- ☐ Har klaget skriftlig

9.04 **Hvor lenge har du hatt din nåværende fastlege/annen lege?**

- ☐ Mindre enn 6 måneder
- ☐ 6 til 12 måneder
- ☐ 12 til 24 måneder
- ☐ Mer enn 2 år

9.05 **Ved siste legebesøk hos fastlegen, snakket legen(e) til deg slik at du forsto dem?** Svar på en skala fra 0 til 10, hvor 0=de var vanskelige å forstå og 10=de var alltid enkle å forstå

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

9.06 **Hvordan vil du karakterisere behandlingen eller rådgivingen du fikk siste gang du var hos lege?** Svar på en skala fra 0 til 10, hvor 0= meget dårlig behandling og 10 = meget god behandling

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

9.07 **Har du i løpet av de siste 12 måneder opplevd at det har vært vanskelig å bli henvist til spesielle undersøkelser (som røntgen eller liknende) eller til spesialist-helsetjenesten (privatpraktiserende spesialist eller ved sykehus)?**

- ☐ Ikke aktuelt
- ☐ Intet problem
- ☐ Noe problem
- ☐ Stort problem

9.08 **Har du i løpet av de siste 12 måneder opplevd at det er vanskelig å bli henvist til fysioterapeut, kiropraktor eller liknende?**

- ☐ Ikke aktuelt
- ☐ Intet problem
- ☐ Noe problem
- ☐ Stort problem

9.09 **Alt i alt, har du opplevd at det er vanskelig eller enkelt å bli henvist til spesialisthelse-tjenesten?**

- ☐ Ikke aktuelt
- ☐ Meget vanskelig
- ☐ Noe vanskelig
- ☐ Rimelig enkelt
- ☐ Meget enkelt

9.10 **Har du i løpet av de siste 12 måneder vært til undersøkelse eller behandling i spesialist-helsetjenesten?**

☐ Ja ☐ Nei

Hvis JA, snakket legen(e) til deg slik at du forstod dem? Svar på en skala fra 0 til 10, hvor 0=de var vanskelige å forstå og 10=de var alltid enkle å forstå

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

9.11 **Hvordan vil du karakterisere behandlingen eller rådgivningen du fikk siste gang du var hos spesialist?** Svar på en skala fra 0 til 10, hvor 0=meget dårlig og 10=meget god

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

9.12 **Har du noen gang før 2002 gjennomgått en operasjon på sykehus eller spesialist-klinikk?**

☐ Ja ☐ Nei

9.13 **Har du i løpet av de siste 12 måneder brukt urtemedisin , naturmidler eller naturlegemidler?**

☐ Ja ☐ Nei

9.14 **Har du i løpet av de siste 12 måneder brukt meditasjon, yoga, qi gong eller thai chi som egenbehandling?**

☐ Ja ☐ Nei

10. BRUK AV ANTIBIOTIKA

10.01 **Har du brukt antibiotika i løpet av de siste 12 måneder?** (all penicillinliknende medisin i form av tabletter, mikstur eller sprøyter)

☐ Ja ☐ Nei ☐ Husker ikke

Hvis JA, hva fikk du behandling mot? Har du tatt flere antibiotikakurer, sett ett kryss for hver kur.

	Kur 1	Kur 2	Kur 3	Kur 4	Kur 5	Kur 6
· Urinveisinfeksjon *(blærebetennelse, blærekatarr)*	☐	☐	☐	☐	☐	☐
· Luftveisinfeksjon *(øre-, bihule- hals- eller lungebetennelse, bronkitt)*	☐	☐	☐	☐	☐	☐
· Annet	☐	☐	☐	☐	☐	☐
Antall dagers antibiotika kur						

Hvordan skaffet du deg antibiotikakuren? Har du tatt flere kurer, sett ett kryss for hver kur.

Etter resept fra lege/tannlege	☐	☐	☐	☐	☐	☐
Uten kontakt med lege/uten resept:						
· Kjøp direkte fra apotek i utlandet	☐	☐	☐	☐	☐	☐
· Kjøp gjennom Internett	☐	☐	☐	☐	☐	☐
· Rest fra tidligere kur tilgjengelig hjemme	☐	☐	☐	☐	☐	☐
· Fått av familie/venner	☐	☐	☐	☐	☐	☐
· Andre måter	☐	☐	☐	☐	☐	☐

10.02 **Har du antibiotika hjemme?**

☐ Ja ☐ Nei

Hvis JA, er dette etter avtale med lege for å behandle kronisk eller hyppig tilbakevendende sykdom?

☐ Ja ☐ Nei

Hvis Nei, hvordan skaffet du deg dette legemiddelet? (Flere kryss er mulig)

Kjøpt direkte fra apotek i utlandet ☐
Kjøpt over Internett ☐
Rest fra tidligere kur ☐
Fått av familie/venner ☐
Andre måter ☐

10.03 **Kan du tenke deg å bruke antibiotika uten å kontakte lege først?**

☐ Ja ☐ Nei

Hvis JA, hvilke tilstander vil du i så fall behandle? (Flere kryss mulig)

Forkjølelse ☐
Hoste ☐
Bronkitt ☐
Halsbetennelse ☐
Bihulebetennelse ☐
Feber ☐
Influensa ☐
Ørebetennelse ☐
Diaré ☐
Blærebetennelse ☐
Andre infeksjoner ☐

11. DIN DØGNRYTME

Vi vil stille deg noen spørsmål som handler om dine søvnvaner.

11.01 **Har du hatt skiftarbeid de tre siste månedene?**

☐ Ja ☐ Nei

11.02 **Antall dager i løpet av uken hvor du ikke kan velge fritt når du vil sove (f.eks arbeidsdager)?**

0 1 2 3 4 5 6 7

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

Da går jeg til sengs klokken ..... ☐☐:☐☐

Jeg gjør meg klar til å sove klokken ..... ☐☐:☐☐

Antall minutter jeg trenger på å sovne ..... ☐☐

Jeg våkner klokken ..... ☐☐:☐☐

Ved hjelp av: ☐ Vekkeklokke ☐ annen ytre påvirkning *(støy, familie etc)* ☐ av meg selv

Antall minutter jeg trenger på å stå opp ..... ☐☐

11.03 **Antall dager i løpet av uken hvor du fritt kan velge når du vil sove** (f.eks helger eller fridager)

0 1 2 3 4 5 6 7

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

Da går jeg til sengs klokken ..... ☐☐:☐☐

Jeg gjør meg klar til å sove klokken ..... ☐☐:☐☐

Antall minutter jeg trenger på å sovne ..... ☐☐

Jeg våkner klokken ..... ☐☐:☐☐

Ved hjelp av: ☐ Vekkeklokke ☐ annen ytre påvirkning *(støy, familie etc)* ☐ av meg selv

Antall minutter jeg trenger på å stå opp ..... ☐☐

12. HUD OG HUDSYKDOMMER

12.01 **Hvor ofte dusjer eller bader du vanligvis?** (sett ett kryss)

- ☐ 2 eller flere ganger daglig
- ☐ 1 gang daglig
- ☐ 4-6 ganger per uke
- ☐ 2-3 ganger per uke
- ☐ 1 gang per uke
- ☐ sjeldnere enn 1 gang per uke

12.02 **Hvor ofte vasker du vanligvis hendene med såpe i løpet av en dag?** (sett ett kryss)

- ☐ 0 ganger
- ☐ 1-5 ganger
- ☐ 6-10 ganger
- ☐ 11-20 ganger
- ☐ Mer enn 20 ganger

12.03 **Har du noen gang fått antibiotikakur (penicillin og liknende medisin) på grunn av en hudlidelse, for eksempel betent eksem, kviser, leggsår som ikke vil gro, tilbakevendende verkebyll?**

☐ Ja ☐ Nei

Hvis JA, hvor mange ganger i gjennomsnitt per år fikk du antibiotika i den perioden du var mest plaget (sett ett kryss)

☐ 1-2 ☐ 3-4 ☐ Mer enn 4 ganger

12.04 **Har du eller har du noen gang hatt følgende hudlidelser?** (sett ett kryss for hver linje)

	Ja	Nei
Psoriasis	☐	☐
Atopisk eksem (barneeksem)	☐	☐
Tilbakevendende håndeksem	☐	☐
Tilbakevendende kviser over flere måneder	☐	☐
Legg- eller fotsår som ikke ville gro i løpet av 3-4 uker	☐	☐

Hvis JA på spørsmål om legg-og/eller fotsår, har du leggsår i dag?

☐ Ja ☐ Nei

12.05 **Har du ofte eller bestandig noen av følgende plager?** (sett ett kryss for hver linje)

	Ja	Nei
Hevelse i ankler og legger, særlig om kvelden	☐	☐
Åreknuter	☐	☐
Eksem (rødt, kløende utslett) på leggene	☐	☐
Smerter i beina når du går, men som forsvinner når du står stille	☐	☐

12.06 **Har du noen gang fått følgende diagnoser av lege?** (sett ett kryss for hver linje)

	Ja	Nei
Psoriasis	☐	☐
Atopisk eksem	☐	☐
Rosacea	☐	☐

12.07 **Har du tilbakevendende store kviser/ verkebyller som er ømme/smertefulle og som ofte tilheler med arr på følgende steder?** (sett ett kryss for hver linje)

	Ja	Nei
Armhulene	☐	☐
Under brystene	☐	☐
Magefolden/navlen	☐	☐
Rundt kjønnsorganet	☐	☐
Rundt endetarmsåpningen	☐	☐
Lyskene	☐	☐

Hvis JA, har du noen gang oppsøkt lege på grunn av verkebyller?

☐ Ja ☐ Nei

Hvis JA, fikk du da noen av følgende behandlinger? (sett ett kryss for hver linje)

	Ja	Nei
Antibiotika salve/krem	☐	☐
Antibiotika tabletter	☐	☐
Kirurgisk åpning/tømming	☐	☐
Større kirurgisk inngrep med fjerning av hud	☐	☐
Kirurgisk laserbehandling	☐	☐

Oppfølgingsspørsmål

INFORMASJON TIL OPPFØLGINGSSPØRSMÅL

De neste sidene med spørsmål skal ikke besvares av alle. Dersom du har svart ja på ett eller flere av spørsmålene under, ber vi deg om å gå videre til oppfølgingsspørsmål om emnet eller emnene du har svart ja på. De fire første emnene er fra det første spørreskjemaet og det siste spørsmålet er fra dette skjemaet.

Vi har for enkelhetsskyld markert emnene med ulike farger slik at du lett skal finne frem til de spørsmålene som gjelder for deg.

Dersom du svarte JA på at du har: langvarige eller stadig tilbakevendende smerter som har vart i 3 måneder eller mer, ber vi deg svare på spørsmålene på side 19 og 20. Margen er markert med grønn.

Dersom du svarte JA på at du har gjennomgått noen form for operasjon i løpet av de siste 3 årene, ber vi deg svare på spørsmålene på side 21 og 22. Margen er markert med lilla.

Dersom du svarte JA på at du arbeider utendørs minst 25% av tiden, eller i lokaler med lav temperatur, som for eksempel lager/industrihaller, ber vi deg svare på spørsmålene på side 23. Margen er markert med rød.

Dersom du svarte JA på at du har brukt reseptfrie smertestillende medisiner, ber vi deg svare på spørsmålene på side 24. Margen er markert med orange.

Dersom du svarte JA på at du har eller noen gang har hatt plager med hud (som psoriasis, atopisk eksem, legg- eller fotsår som ikke vil gro, tilbakevendende håndeksem, kviser eller verkebyll), ber vi deg svare på spørsmålene på side 25. Margen er markert med gul.

Har du svart **NEI** på disse fem spørsmålene, er du ferdig med besvarelsen din. Spørreskjemaet returneres i svarkonvolutten du fikk utlevert på undersøkelsen. Portoen er allerede betalt.

Skulle du ønske å gi oss en skriftlig tilbakemelding om enten spørreskjema eller Tromsøundersøkelsen generelt, er du hjertelig velkommen til det på side 26.

Har du noen spørsmål, kan du ta kontakt med oss på telefon eller på e-post. Du finner kontaktinformasjon på baksiden av skjemaet. **TUSEN TAKK** for at du tok deg tid til undersøkelsen og til å svare på spørsmålene fra oss.

13. OPPFØLGINGSSPØRSMÅL OM SMERTE

Du svarte i det første spørreskjemaet at du har langvarige eller stadig tilbakevendende smerter som har vart i 3 måneder eller mer. Her ber vi deg beskrive de smertene litt nærmere.

13.01 **Hvor lenge har du hatt disse smertene?**

Antall år..... ☐☐ måneder..... ☐☐

13.02 **Hvor ofte har du vanligvis disse smertene?**

- ☐ Hver dag
- ☐ En eller flere ganger i uken
- ☐ En eller flere ganger i måneden
- ☐ Sjeldnere enn 1 gang i måneden

13.03 **Hvor er det vondt?** (Kryss av for alle steder der du har langvarige eller stadig tilbakevendende smerter)

- ☐ Hode/ansikt
- ☐ Kjeve/kjeveledd
- ☐ Nakke
- ☐ Rygg
- ☐ Skulder
- ☐ Arm/albue
- ☐ Hånd
- ☐ Hofte
- ☐ Lår/kne/legg
- ☐ Ankel/fot
- ☐ Bryst
- ☐ Mage
- ☐ Underliv/kjønnsorganer
- ☐ Hud
- ☐ Annet sted

13.04 **Hva mener du er årsaken til smertene?** (Kryss av for alle kjente årsaker)

- ☐ Ulykke/akutt skade
- ☐ Langvarig belastning
- ☐ Kirurgisk inngrep/operasjon
- ☐ Skiveutglidning *(prolaps)*/lumbago
- ☐ Nakkesleng *(whiplash)*
- ☐ Migrene/hodepine
- ☐ Slitasjegikt *(artrose)*
- ☐ Leddgikt
- ☐ Bechterews sykdom
- ☐ Fibromyalgi
- ☐ Angina pectoris *(hjertekrampe)*
- ☐ Dårlig blodsirkulasjon
- ☐ Kreft
- ☐ Nerveskade/nevropati
- ☐ Infeksjon
- ☐ Helvetesild
- ☐ Annen årsak *(beskriv under)*
- ☐ Vet ikke

Beskriv annen årsak:

.....

13.05 **Hvilke former for behandling har du fått for smertene?** (Kryss av for alle typer smertebehandling du har mottatt)

- ☐ Ingen behandling
- ☐ Smertestillende medisiner
- ☐ Fysioterapi/kiropraktikk
- ☐ Behandling ved smerteklinikk
- ☐ Operasjon
- ☐ Smerteskole/avspenning/psykoterapi
- ☐ Akupunktur
- ☐ Alternativ behandling *(homøopati, healing, aromaterapi, m.m.)*
- ☐ Annen behandling

13.06 **På en skala fra 0 til 10, der 0 tilsvarer ingen smerte og 10 tilsvarer den verst tenkelige smerten du kan forestille deg:**

Hvor sterke vil du si at smertene vanligvis er?	Ingen smerte	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	Verst tenkelige smerte
Hvor sterke er smertene når de er på sitt sterkeste?	Ingen smerte	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	Verst tenkelige smerte
I hvor stor grad påvirker smertene søvnen din?	Påvirker ikke	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	Umulig å få sove
I hvor stor grad hindrer smertene deg i å utføre vanlige aktiviteter hjemme og i arbeid?	Påvirker ikke	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	Kan ikke gjøre noe

14. OPPFØLGINGSSPØRSMÅL OM OPERASJON

I det første spørreskjemaet svarte du at du har gjennomgått en operasjon i løpet av de siste 3 årene.

14.01 **Hvor mange operasjoner har du totalt gjennomgått de siste 3 årene?**

Antall ..... ☐

Nedenfor ber vi deg beskrive operasjonen. Dersom du har gjennomgått flere operasjoner i løpet av de siste 3 årene gjelder disse spørsmålene den siste operasjonen du gjennomgikk.

14.02 **Hvor i kroppen ble du operert?** (Dersom du samtidig ble operert flere steder i kroppen, settes flere kryss)

Operasjon i hode/nakke/rygg
- Hode/ansikt ☐
- Nakke/hals ☐
- Rygg ☐

Operasjon i brystregionen
- Hjerte ☐
- Lunger ☐
- Bryster ☐
- Annen operasjon i brystregionen ☐

Operasjon i mage/underliv
- Mage/tarm ☐
- Lyskebrokk ☐
- Urinveier/kjønnsorganer ☐
- Galleblære/galleveier ☐
- Annen operasjon i mage/underliv ☐

Operasjon i hofte/ben
- Hofte/lår ☐
- Kne/legg ☐
- Ankel/fot ☐
- Amputasjon ☐

Operasjon i skulder og arm
- Skulder/overarm ☐
- Albue/underarm ☐
- Hånd ☐
- Amputasjon ☐

14.03 **Bakgrunn for operasjonen:**
- Akutt sykdom/skade ☐
- Planlagt ikke-kosmetisk operasjon ☐
- Planlagt kosmetisk operasjon ☐

14.04 **Hvor ble du operert?**
- Sykehuset i Tromsø ☐
- Sykehuset i Harstad ☐
- Annet offentlig sykehus ☐
- Privat klinikk ☐

14.05 **Hvor lenge er det siden du gjennomgikk operasjonen?**

Antall år ..... ☐ måneder ..... ☐

14.06 **Har du nedsatt følsomhet i et område nær operasjonsarret?**

☐ Ja ☐ Nei

14.07 **Er du overfølsom for berøring, varme eller kulde i et område nær operasjonsarret?**

☐ Ja ☐ Nei

14.08 **Kan lett berøring av klær, dusj og lignende fremkalle ubehag/smerte?**

☐ Ja ☐ Nei

14.09 **Hvis du hadde smerter på operasjonsstedet før du ble operert, har du samme type smerte nå?**

☐ Ja ☐ Nei

14.10 **Smerte fra operasjonsstedet:** Svar på en skala fra 0 til 10, hvor 0=ingen smerte og 10=verst tenkelige smerte

Hvor sterke smerter hadde du fra operasjonsstedet før operasjonen.....	Ingen smerte	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	Verst tenkelige smerte
Hvor sterke smerter har du vanligvis fra operasjonsstedet nå.....	Ingen smerte	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	Verst tenkelige smerte
Hvor sterke smerter har du nå fra operasjonsstedet når smertene er på det sterkeste.....	Ingen smerte	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	Verst tenkelige smerte

15. OPPFØLGINGSSPØRSMÅL OM ARBEID I KALDT KLIMA

I det første spørreskjemaet svarte du ja på at du arbeidet i kaldt klima. Her er noen oppfølgingsspørsmål vi håper du vil svare på.

15.01 **Fryser du på jobb?**

☐ Ja, ofte
☐ Ja, noen ganger
☐ Nei, aldri

15.02 **Hvor lenge har du vært utsatt for kalde omgivelser under 0°C sist vinter?**

Fritid/hobby *(timer/uke)* ..... ☐☐
Arbeid *(timer/uke)* ..... ☐☐
Utendørs, godt kledd *(timer/uke)* ..... ☐☐
Utendørs, tynnkledd *(timer/uke)* ..... ☐☐
Innendørs, uten oppvarming *(timer/uke)* ..... ☐☐
I kalde omgivelser, med våte klær *(timer/uke)* ..... ☐☐
Kontakt med kalde gjenstander/ verktøy *(timer/uke)* ..... ☐☐

15.03 **Hvilken omgivelsestemperatur forhindrer deg i å:**

	Under °C
Arbeide utendørs	☐☐
Trene utendørs	☐☐
Utføre andre aktiviteter utendørs	☐☐

15.04 **Har du hatt forfrysninger siste 12 måneder, med blemmer, sår eller skader i huden?**

☐ Ja ☐ Nei

Hvis JA, hvor mange ganger? ..... ☐☐

15.05 **Har du opplevd kløe og/eller utslett i forbindelse med kulde?**

☐ Ja ☐ Nei

15.06 **Har du i løpet av de siste 12 måneder vært involvert i ulykke som krevde medisinsk behandling der kulde var en viktig faktor?**

	Ja	Nei
På arbeid	☐	☐
I fritiden	☐	☐

15.07 **Opplever du noen av følgende symptomer mens du oppholder deg i kalde omgivelser? I så fall, ved hvilken temperatur oppstår symptomene?**

	Ja	Nei	Under °C
Pusteproblemer	☐	☐	☐☐
Pipende pust	☐	☐	☐☐
Slim fra lungene	☐	☐	☐☐
Brystsmerter	☐	☐	☐☐
Forstyrrelse i hjerterytmen	☐	☐	☐☐
Nedsatt blodsirkulasjon i hender/føtter	☐	☐	☐☐
Synsforstyrrelse *(kortvarig/ forbigående)*	☐	☐	☐☐
Migrene *(kortvarig/forbigående)*	☐	☐	☐☐
Hvite fingre *(kortvarig/ forbigående)*	☐	☐	☐☐
Blå, blå-røde fingre *(kortvarig/forbigående)*	☐	☐	☐☐

15.08 **Hvordan påvirker kalde omgivelser og kulderelaterte symptomer din yteevne?**

	Nedsatt	Uforandret	Forbedret
Konsentrasjon	☐	☐	☐
Hukommelse	☐	☐	☐
Fingerfølsomhet *(følelse)*	☐	☐	☐
Fingerferdighet *(motorikk)*	☐	☐	☐
Kontroll av bevegelse *(for eksempel skjelving)*	☐	☐	☐
Tungt fysisk arbeid	☐	☐	☐
Langvarig fysisk arbeid	☐	☐	☐

16. BRUK AV RESEPTFRIE SMERTESTILLENDE LEGEMIDLER

I det første spørreskjemaet svarte du at du hadde brukt reseptfrie smertestillende legemidler de siste 4 ukene. Her er noen oppfølgingsspørsmål vi håper du vil svare på.

16.01 **Hvilke typer reseptfrie smertestillende legemidler har du brukt?**

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

- ☐ Ikke brukt
- ☐ Sjeldnere enn hver uke
- ☐ Hver uke, men ikke daglig
- ☐ Daglig

Hvor mye tar du vanligvis daglig når du bruker midlene?
(Antall tabletter, stikkpiller)..... ☐

Acetylsalisylsyre: (*Aspirin,Dispril, Globoid)*

- ☐ Ikke brukt
- ☐ Sjeldnere enn hver uke
- ☐ Hver uke, men ikke daglig
- ☐ Daglig

Hvor mye tar du vanligvis daglig når du bruker midlene?
(Antall tabletter)..... ☐

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

- ☐ Ikke brukt
- ☐ Sjeldnere enn hver uke
- ☐ Hver uke, men ikke daglig
- ☐ Daglig

Hvor mye tar du vanligvis daglig når du bruker midlene?
(Antall tabletter, stikkpiller)..... ☐

Naproksen: *(Ledox, Naproxen)*

- ☐ Ikke brukt
- ☐ Sjeldnere enn hver uke
- ☐ Hver uke, men ikke daglig
- ☐ Daglig

Hvor mye tar du vanligvis daglig når du bruker midlene?
(Antall tabletter)..... ☐

Fenazon med koffein: *(Antineuralgica ,Fanalgin Fenazon-koffein, Fenazon-koffein sterke)*

- ☐ Ikke brukt
- ☐ Sjeldnere enn hver uke
- ☐ Hver uke, men ikke daglig
- ☐ Daglig

Hvor mye tar du vanligvis daglig når du bruker midlene?
(Antall tabletter)..... ☐

16.02 **Mot hvilke plager bruker du reseptfrie smertestillende midler: (**Flere kryss er mulig)

- ☐ Hodepine
- ☐ Menssmerter
- ☐ Migrene
- ☐ Ryggsmerter
- ☐ Muskelsmerter/leddsmerter
- ☐ Tannsmerter
- ☐ Annet

16.03 **Mener du å ha opplevd bivirkninger av noen av legemidlene?** (sett ett kryss for hver linje)

	Ja	Nei
Paracetamol	☐	☐
Acetylsalisylsyre	☐	☐
Ibuprofen	☐	☐
Naproksen	☐	☐
Fenazon med koffein	☐	☐

16.04 **Hvor pleier du å kjøpe slike legemidler?**

- ☐ Apotek
- ☐ Dagligvare
- ☐ Bensinstasjon
- ☐ Utenlands
- ☐ Internett

16.05 **Kombinerer du behandlingen med bruk av reseptbelagte smertestillende midler?**

☐ Ja ☐ Nei

17. OPPFØLGINGSSPØRSMÅL OM HUDSYKDOMMER

På side 15 i dette spørreskjemaet svarte du at du har eller har hatt en hudsykdom. Her er noen oppfølgingsspørsmål vi håper du vil svare på.

Svar på en skala fra 0 til 10, der 0 tilsvarer ingen plager og 10 tilsvarer verst tenkelige plager. Dersom du svarte JA på at du har eller har hatt:

Ingen plager 0 1 2 3 4 5 6 7 8 9 10 Verst tenkelige plager

17.01 **Psoriasis**
- Hvor mye plaget er du av din psoriasis i dag? ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
- Hvor mye plaget er du av din psoriasis når den er som verst? ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

17.02 **Atopisk eksem**
- Hvor mye plaget er du av ditt atopiske eksem i dag? ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
- Hvor mye plaget er du av ditt atopiske eksem når det er som verst? ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

17.03 **Håndeksem**
- Hvor mye plaget er du av ditt håndeksem i dag? ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
- Hvor mye plaget er du av ditt håndeksem når det er som verst? ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

17.04 **Kviser**
- Hvor mye plaget er du av dine kviser i dag? ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
- Hvor mye plaget er du av dine kviser når de er som verst? ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

17.05 **Verkebyller**
- Hvor mye plaget er du av dine verkebyller i dag? ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐
- Hvor mye plaget er du av dine verkebyller når de er som verst? ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

17.06 **Her er en liste over faktorer som kan tenkes å utløse eller forverre verkebyller, kryss av for hva du synes gjelder for deg:**

	Ja	Nei
Stress/psykisk påkjenning	☐	☐
Trange/tette klær	☐	☐
Menstruasjonssyklus	☐	☐
Svangerskap	☐	☐
Annet	☐	☐

17.07 **Hvor mange utbrudd av verkebyller har du vanligvis i løpet av ett år?** (sett ett kryss)

☐ 0-1 ☐ 4-6
☐ 2-3 ☐ Mer enn 6

17.08 **Hvor gammel var du da du fikk verkebyller første gang?**

☐ 0-12 år ☐ 26-35 år
☐ 13-19 år ☐ 36-50 år
☐ 20-25 år ☐ Over 50 år

17.09 **Dersom du ikke lenger har verkebyller, hvor gammel var du da plagene forsvant?**

☐ 0-12 år ☐ 26-35 år
☐ 13-19 år ☐ 36-50 år
☐ 20-25 år ☐ Over 50 år

TILBAKEMELDING

Skulle du ønske å gi oss en skriftlig tilbakemelding om enten spørreskjema eller Tromsøundersøkelsen generelt, er du hjertelig velkommen til det her:

Takk for hjelpen!

Tromsø-
undersøkelsen

Tromsøundersøkelsen
Institutt for samfunnsmedisin, Universitetet i Tromsø
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epost: tromsous@ism.uit.no
www.tromso6.no

Appendix III

Questionnaire III

NORGES DIABETESFORBUND

DIABøye – SCREENING FOR DIABETESRETINOPATI I NORGE

REGISTRERINGSSKJEMA

1	**Senter nummer**				
2	Navn på pasient				
3	Fødselsnummer		4	Pasient prosjektnr. (4 siffer)	
5	Kjønn	☐ KVINNE ☐ MANN	6	Diabetes debut år (4 siffer)	
7	Diabeteskontroll hos	☐ FASTLEGE ☐ INDREMEDISINER/DIABETESSYKEPLEIER ☐ PRIVATPRAKTISERENDE INDREMEDISINER ☐ ANNEN:			
8	Type diabetes	☐ TYPE 1 ☐ TYPE 2 KOSTREGULERT ☐ TYPE 2 TABLETTREGULERT ☐ TYPE 2 MED INSULIN (med eller uten tabletter samtidig)			

9	Startet insulinbehandling innen 12 mnd etter diabetesdebut?	☐ JA ☐ NEI
10	Foto-/øyelegeundersøkelse på utvidet pupille ved øyelege noensinne?	☐ JA ☐ NEI
11	Hvis JA, undersøkt siste 36 måneder?	☐ JA ☐ NEI
12	Hvis JA, undersøkt siste 24 måneder?	☐ JA ☐ NEI
13	Hvis JA, undersøkt siste 12 måneder?	☐ JA ☐ NEI
14	Deltar i fast kontrollopplegg hos øyelege utenfor sykehus?	☐ JA ☐ NEI
15	Hvis JA, navn på øyelege	
16	Deltar i fast kontrollopplegg hos øyelege ved sykehuspoliklinikk?	☐ JA ☐ NEI
17	Registrert / målt visus	HØYRE: VENSTRE:
18	Annen hovedårsak til synstap enn diabetesretinopati? Hvis JA, angi årsak:	☐ JA ☐ NEI ÅRSAK:
19	Retinopatistatus (0 – 5)	☐ 0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5
20	Bilder med god nok kvalitet for bedømming?	HØYRE: ☐ JA ☐ NEI VENSTRE: ☐ JA ☐ NEI
21	Makulaødem?	☐ JA ☐ NEI
22	Tidligere glasslegemekirurgi på grunn av diabetes?	HØYRE: ☐ JA ☐ NEI VENSTRE: ☐ JA ☐ NEI ÅRSAK:
23	Laserbehandlet for proliferasjon?	☐ JA ☐ NEI
24	Laserbehandlet for maculaødem?	☐ JA ☐ NEI
25	Laserbehandlet på annet / ukjent grunnlag?	☐ JA ☐ NEI
26	Ledet den aktuelle kontroll til henvisning for nærmere øyebunnsundersøkelse?	☐ JA ☐ NEI

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