Faculty of Health Sciences, Institute of Community Medicine

Psoriasis, overweight and metabolic syndrome

The Tromsø Study

Kjersti Danielsen

A dissertation for the degree of Philosophiae Doctor – January 2014

Preface

After several years working as a senior resident in dermatology at the University Hospital of North Norway, I was introduced to a skilled and innovative multidisciplinary group of scientists, with interests in chronic inflammatory disease, metabolic disturbances, and host-microbe interactions; spanning both basic biological research as well as epidemiological cohort studies. I thereby joined the "Tromsø Staph and Skin Study" group in 2006, and plunged into the world of epidemiological research. I received a grant from the Northern Norway Regional Health Authority to pursue the project leading to this thesis from 2009.

Exploring a PhD has been a great adventure. I found it very stimulating to have the time to deep dig into the literature and take part in generating hypothesis as well as collecting, analyzing and presenting the data. This has been a very rewarding experience, both professionally and personally. I aspire to continue an academic career, as well as returning to tend to my patients.

It has been an eye-opener for me to see how many research questions still lack adequate answers within dermatology, as well as realizing the importance of quality in every step of the research process. This applies not only for those who aspire to work as a scientist, but also for physicians in general, in order to evaluate what is presented to you and making the right decisions for your patients.

"It does happen exceptionally that a practicing doctor makes a contribution to science; but it happens much oftener that he draws disastrous conclusions from his clinical experience because he has no conception of scientific method, and believes, like any rustic, that the handling of evidence and statistics needs no expertise."

(G B Shaw; "The Doctor`s Dilemma". London: Penguin, 1957)

Acknowledgments

I would like to thank the Northern Norway Regional Health Authority and the Arne Klems fund for Norwegian Dermatologists for financial support. Furthermore, thank you to all of you who have inspired and supported me under the process of my PhD. Especially I would like to thank:

My main supervisor Anne-Sofie Furberg: Thank you for finding the time for me and my many questions over several years and in very difficult times. You are a pillar of knowledge and strength; one of the most hardworking people I know, and truly a great inspiration. I look forward to continuing an academic career under your wings.

My co-supervisors Anne Olaug Olsen and Tom Wilsgaard: Thank you for your many inputs in the process of processing the data as well as writing the articles and thesis. You wisdom and kindness throughout the PhD process is much appreciated.

The Tromsø Staph & Skin Study: Thank you for embracing me into your research group. I look forward to further inspiring collaboration. Especially thanks to Karina Olsen for her contributions on common research interests.

Patricia Cassano: A one year research stay at Cornell University was originally planned during my PhD. I did go to Ithaca, NY, but as a new mom of twin girls instead. Luckily we have kept in contact, and our discussions have always been very helpful. I look forward to further collaboration in the near future.

The Tromsø Study: I am very grateful to the founders, personnel and all of the participants of the Tromsø study.

The UiT, Arctic University of Norway, especially the Institute of Community Medicine and research school EpiNOR: Thank you for inspirational lectures. Especially thanks to Inger Thune for your input in the thesis process, and for supporting and guiding me way beyond what could be expected. Also, Anne Elise Eggen, for your aid and collaboration regarding the use of self-reported medication and linkage to the Norwegian Prescription Database. Furthermore, thanks to Rod Wolstenholme for technical assistance in figure preparation.

The Neuro- and Orthopedic Clinic, Department of Dermatology, University Hospital of North Norway: Our head of department, Dagfinn Moseng, who believed in my abilities and allowed me to pursue a PhD. Also, I would like to thank my colleagues for their contributions in making working with dermatology so much fun.

My dear husband Dag: For your devoted love, friendship and stimulating conversation. You are the smartest and most caring man I know, and a wonderful father and partner.

Our lovely children; Gabriel, Elias, Cornelia and Alva: You mean the world to me! Thank you for allowing me to see what matters most in life. Also, thanks to the lovely, intelligent and hardworking Lisa and Ida who are such great big sister.
My parents, friends and extended family: Thank you for all the love you give to me and my family. I am so grateful for always having you cheering me on and being so eager to help out where ever you can.

Contents

Summary

Recently it has been suggested that the chronic inflammatory disease psoriasis is *more than skin deep*, as it has been associated with several diseases, including diabetes and cardiovascular disease. Psoriasis can be attributed to genetic liability as well as environmental risk factors. The overall aim of the thesis was to study time trends in psoriasis prevalence and investigate whether excess weight was associated with psoriasis development, including potential synergisms with smoking. Furthermore, the association between psoriasis and the metabolic syndrome, a predictor for diabetes and cardiovascular disease, was explored; all within the population-based North-Norwegian Tromsø study cohort from 1979 to 2008.

We observed an increase in the self-reported prevalence of psoriasis over the past 30 years among adults above age 29; with more than doubled odds of psoriasis reported in 2007-08 as compared with 1979-80, independent of the investigated birth cohort and population ageing. The lifetime prevalence of psoriasis was 11% among adults in the 2007-08 survey. This increasing trend could partially be due to increased awareness of the disease in the population; however, our results are also supported by others, indicating a global trend.

Overweight above a threshold of body mass index (BMI) 27-28 kg/m^2 increased the risk of psoriasis by 32-41% in 7-13 years follow-up in both genders combined, with even higher risk among overweight and obese non-smokers 62-71%. In Tromsø 4 (1994-95), adult weight-gain led to up to 90% increased risk of psoriasis development from age 45, regardless of weight category. Smoking almost doubled the risk of psoriasis, but there was no indication of a multiplicative effect of overweight and smoking. The cumulative effect from smoking and obesity on psoriasis development may explain some of the increase in psoriasis observed in our study and in comparable populations.

When investigating the association between psoriasis and the metabolic syndrome, 32% of psoriatics versus 24% of the reference population met the criteria for the metabolic syndrome. Men with psoriasis had a stable 35% increased odds of metabolic syndrome compared to persons without psoriasis, while young women with psoriasis displayed a four times increased odds of developing the metabolic syndrome. We observed a dose-response relationship between the severity of psoriasis and the odds of abdominal overweight in women. Further studies to evaluate the potential benefit from screening for the metabolic syndrome in patients with psoriasis are warranted.

Sammendrag

Nyere kunnskap tyder på at psoriasis ikke bare er en kronisk inflammatorisk sykdom begrenset til huden, da psoriasis også kan være forbundet med økt risiko for andre sykdommer som diabetes og hjertekar sykdom. Utvikling av psoriasis betinger genetisk predisposisjon, men miljøfaktorer kan påvirke debut og senere forløp. Den overordnede målsetningen for avhandlingen var derfor å studere tidstrender av psoriasisforekomst, samt å evaluere hvorvidt overvekt, vektøkning og kombinasjon av røyking og overvekt kan øke risiko for psoriasis hos begge kjønn og i ulike aldersgrupper. Vi ønsket også å se nærmere på sammenhengen mellom psoriasis og metabolsk syndrom, en kjent risikofaktor for diabetes og hjertekarsykdom, i en populasjonsbasert kohort i Nord-Norge, Tromsø undersøkelsen, undersøkt ved fem tidspunkt i Tromsø 2-6 fra 1979 til 2008.

Vi fant en økning i selvrapportert psoriasis, med mer enn doblet risiko for psoriasis i 2007-08 sammenlignet med i 1979-80 uavhengig av hvilken fødselskohort eller aldersgruppe som ble undersøkt, fra fylte 29 år. I 1979-80 rapporterte 11% av voksne å ha eller ha hatt psoriasis. Økningen i psoriasisforekomst kan dels skyldes økt bevissthet rundt sykdommen i befolkningen. Det er imidlertidig rapportert doblet forekomst av psoriasis også i andre befolkninger, noe som indikerer en global trend.

Overvekt med kroppsmasseindeks (BMI) fra 27-28 kg/m^2 ga en 32-41% økt risiko for utvikling av psoriasis i løpet av 7-13 år oppfølgingstid hos begge kjønn kombinert og opptil 62-71% økt risiko hos ikke-røykere med overvekt og fedme. Hos deltakere som var 45 år eller eldre i Tromsø 4 (1994-95), ga vektøkning fra 25-årsalder en opptil 90% økt risiko for psoriasis. Røykere hadde doblet risiko for psoriasis, men det var ingen synergistisk effekt av røyk og overvekt. Den samlede effekten av overvekt og røyking, kan muligens forklare noe av økningen i psoriasis både i Tromsø kohorten og i sammenlignbare populasjoner.

I Tromsø 6, 2007-08, påviste vi betydelig høyere forekomst av metabolsk syndrom hos deltakere med psoriasis; 32% versus 24% hos øvrige deltakere. Menn med psoriasis hadde en 35% økt odds for metabolsk syndrom sammenlignet med menn uten psoriasis. Den sterkeste sammenhengen fant vi blant unge kvinner, der psoriasis var forbundet med fire ganger økt odds for metabolsk syndrom. Vi fant et dose-respons forhold mellom alvorlighetsgrad av psoriasis og odds for abdominal overvekt hos kvinner. Studier som vurderer nytten av screening for metabolsk syndrom hos psoriatikere, er berettiget.

Abbreviations

BMI	Body mass index
CI	Confidence interval
CDC	Centre for Disease Control
CLA	Cutaneous lymphocyte-associated antigen
CVa	Coefficient of variation
CVD	Cardio vascular disease
DLQI	Dermatological quality of life index
GWAS	Genome wide association studies
HC	Hip circumference
HDL	High-density lipoprotein
HIV	Human Immunodeficiency Virus
HR	Hazard ratio
hs-CRP	High sensitive C reactive protein
HUBRO	Oslo Health Study
HUNT	Health Examination in North-Trøndelag
IDF	International diabetes federation
IL	Interleukin
LDL	Low-density lipoprotein
MetS	Metabolic syndrome
MHC	Major histocompatibility complex
MoBa	Norwegian Mother and Child Cohort Study
NDPA	Norwegian Data Protection Agency
NHS	Nurses' Health Study
NHANES	North American Health and Nutrition Survey
NorPD	Norwegian Prescription Database
NSAIDS	Non-steroidal anti-inflammatory drugs
OR	Odds ratio
PASI	Psoriasis area severity index
PPP	Pustolosis palmo plantaris
PsA	Psoriasis arthritis
PSORS1	Psoriasis susceptibility locus one
Q1-2	Questionnaire one/ two
RCT	Randomized controlled trial
REC	Regional Ethical Committee
RR	Relative risk
SAS	Statistical Analysis System
SNPs	Single-nucleotide polymorphisms
SPSS	Statistical Package for the Social Sciences
Staph	Staphylococcus
T2-6	The Tromsø Study: Tromsø 2-6
Th cell	T helper cell
TNF	Tumor necrosis factor
UK GPRD	UK General Practice Research Database
UV	Ultra violet radiation
WC	Waist circumference
WHO	World Health Organization
WHR	Waist to hip ratio

List of papers

This thesis is based on the following three papers, which are referred to in the text by their Roman numeral.

I. **Danielsen K**, Olsen AO, Wilsgaard T, Furberg A-S. Is the prevalence of psoriasis increasing? A 30 year follow-up of a population-based cohort. British Journal of Dermatology 2013 Jun; 168(6):1303-10.

II. **Danielsen K**, Wilsgaard T, Olsen AO, Furberg A-S. Overweight and weight gain influence psoriasis development in a population-based cohort. Submitted manuscript.

III. **K Danielsen**, T Wilsgaard, AO Olsen, AE Eggen, K Olsen, PA Cassano, and A-S Furberg. Psoriasis and the metabolic syndrome – a population-based study of age and gender differences. Under review, British Journal of Dermatology.

1. Background

Psoriasis is a chronic relapsing inflammatory immune-mediated skin disease leading to substantial morbidity.[1] A condition similar to psoriasis was already described by Hippocrates (460-377 BC) and in the Holy Bible, while the final description and naming of the disease was made by Robert Willan (1757-1812) and Ferdinand Hebra (1816-80).[2] Despite that most cases are mild plaque types which may come and go through life; studies indicate that the impact on a person's quality of life may be substantial.[3,4] Over the past decade psoriasis has been associated with several comorbid conditions including diabetes and cardiovascular disease,[5-7] as well as overall mortality in more severe cases; indicating that the psoriasis plaques seen on the skin surface may represent mere *tips of the iceberg*.[3,8-13] A large part of psoriasis can be attributed to genetic liability; however, a substantial part of the disease phenotype is caused by environmental risk factors, including lifestyle, giving a potential for primary prevention of both the disease itself and possible secondary comorbidities.[14] Changes in environmental exposures, like the obesity epidemic which leads to increased systemic inflammation, may also influence time trends of psoriasis.

1.1 Prevalence and incidence

The debut of psoriasis can appear at all ages, and while some studies describe an increasing prevalence with age up until approximately 60-70 years, others have defined two peaks of onset; one between age 20-39 and another between 50-69 years.[15] Some investigators debate that there is a type I and type II psoriasis, depending on the age of onset before or after middle-age (40-50 years);[1,16] where type I may be more severe and influenced by specific genetic factors, and type II may be milder and more influenced by environmental factors.[17] Traditionally, it has been said that 70-75% of psoriasis cases represent type I.[16] Although a younger debut is described in women, there does not seem to be a gender difference in the predilection for developing psoriasis in a lifelong perspective.[15] In general a young debut and close family members with severe disease may indicate that a more severe course of disease can be expected.[16] Cohort studies from the general population investigating the natural history of psoriasis in modern times are needed.[18]

The prevalence, or prevalence proportion, of psoriasis gives the proportion of the population with psoriasis either at one point in time, point prevalence, or during a defined time period, period prevalence. From population-based samples, psoriasis prevalence is reported spanning from < 0.5 to 8.5%.[15] Among certain native groups like South American Indians, Australian aborigines and inhabitants of isolated Pacific Islands psoriasis rates as low as zero have been suggested; while the world's highest reported prevalence rate of 11.8% comes from Kazaschye, in the former Soviet Union.[15,19] Unfortunately, the methods used to ascertain these results were not available for evaluation.[20] A previous prevalence study from the US found higher psoriasis frequencies in persons with Caucasian versus African heritage, indicating ethnical differences in liability.[21] Low prevalence rates are also consistently reported from Asia.[15] Population-based data are still limited from most of Asia including India, as well as South-America and Africa. Psoriasis in children is rare and scarcely investigated with prevalence reported between 0-2%.[15]

True differences in psoriasis prevalence between geographical regions, countries and populations may be explained by genetic and environmental factors, and may generate hypotheses of disease aetiology.[19] The use of both point prevalence and lifetime prevalence within different age ranges to assess disease frequency across studies is likely one of the reasons why there seems to be large variations in the prevalence of psoriasis throughout the world. Also, many prevalence estimates referred to today come from clinical studies or database samples and may not be truly representative of the general population. The highest lifetime prevalence reported from population-based data comes from two general health surveys in Scandinavia.[22] In the Oslo Health Study (HUBRO, 2000-01), Norway, 8.5% of the sampled adult population reported having received a diagnosis of psoriasis by a physician sometime in their lifetime.[22] In the related time period (2006-08), a Danish general population study reported a lifetime physicians' diagnosed prevalence of 7.1%.[23] However, both studies were criticized due to low attendance (HUBRO, 46%/ Danish study 44%).

The incidence of psoriasis encompasses the number of new psoriasis cases over a fixed time period divided by the population at risk of developing psoriasis.[24] This represents the short-time burden of disease, and provides valuable cases for research in terms of risk factors for new onset of disease. To our knowledge, a limited number of studies have investigated the incidence of psoriasis in the general population, and most of them were based on various health databases.[25-32] Incidence rates among Caucasian adults have been reported to vary between 79 to 230 cases per 100,000 person years.[15]

1.2 Time trends in psoriasis

Changes in environmental and lifestyle exposures may influence the incidence and prevalence of psoriasis, making it necessary to repeat assessment of psoriasis on a regular basis within defined populations. Updated prevalence proportions are important in order to determine the clinical and economic burden related to psoriasis, as well as giving directions in terms of the burden of concomitant disease. Not the least, changes in incidence and prevalence trends within a relatively short timeframe points in the direction of possible influencing modifiable environmental factors which may be of importance in terms of prevention or treatment of psoriasis.

Two US studies investigating trends in psoriasis incidence based on a health service database found that the incidence of psoriasis doubled in both children and adults between the 1970s and today.[29,30] On the other hand, a nationwide study in a Norwegian twin panel sampled in 1992 and 1998, found no indication of increasing psoriasis incidence among young adults in the relatively short time frame observed, also supported by a Dutch study based on general practice data, [26] as well as a study of Swedish conscripts across the 1952-77 birth cohorts.[33] Repeating population-based studies suggested a higher prevalence of psoriasis in both the US adult population as well as the Chinese population over the past 20-30 years.[34,35] Furthermore, a large study from the United Kingdom General Practice Research Database (UK GPRD) found a period prevalence of psoriasis of only 1.5% in the total population from 1987 to 2002;[36] which is comparable to a survey from the UK in the late sixties.[37]

Studies of psoriasis from large general population samples are scarce and longitudinal observations of changing lifetime prevalence within the same population over a longer time period, using the same methodology, are largely lacking. Thus, there is limited evidence regarding trends in psoriasis prevalence and possible influences from age, birth cohort and time period effects. An *age effect* is defined as a change in the frequency of a condition according to age, irrespective of the examined birth cohort or time period.[24] A birth cohort or *cohort effect* is a change in the frequency of a condition according to the year of birth, independent of age and calendar time.[24] A time period or *period effect* applies to a change in the frequency of a condition or trait which affects an entire population over a period of time, irrespective of their age or the year they are born in.[24]

Changes in psoriasis prevalence within a stable population, studied with the same study design over time may largely be explained by environmental factors. The population-based Tromsø study cohort with repeated assessments over three decades allows for the investigation of the trend in psoriasis prevalence according to age, birth cohort and time period. The second Tromsø study in 1979-80 reported a lifetime prevalence of 4.8% of self-reported psoriasis among adults which was the highest figure from a population based study worldwide at that time.[38] Another Norwegian study from the same time period showed large regional differences in psoriasis prevalence with an almost doubled prevalence in the two northernmost counties,[39] raising the question if figures from the Tromsø cohort could now be at even higher levels.

1.3 The pathophysiology of psoriasis

Psoriasis is regarded to be a multifactorial immune mediated disease, but the pathophysiology of the condition is not fully understood (Figure 1).[40] Alterations in skin barrier and immune genes facilitate an abnormal response triggered by yet largely unidentified environmental risk factors or antigens.[41] This leads to a complex interplay between the skin epithelium and connective tissue with the innate and adaptive immune system; including activation of antigen presenting cells (e.g. myeloid dendritic cells which produce Interleukine (IL)12 and IL-23) and thereby expansion and activation of T-helper lymphocytes Th1 and Th17. The activated lymphocytes again produce several cytokines, e.g. interferon-γ, tumor necrosis factor (TNF) and leads to further increase of IL-17 and IL-22, as well as antimicrobial peptides and growth factors; which increases the natural turnover of the epidermis and eventually leads to formation of the characteristic psoriasis skin plaques (Figure 2).[1,42]

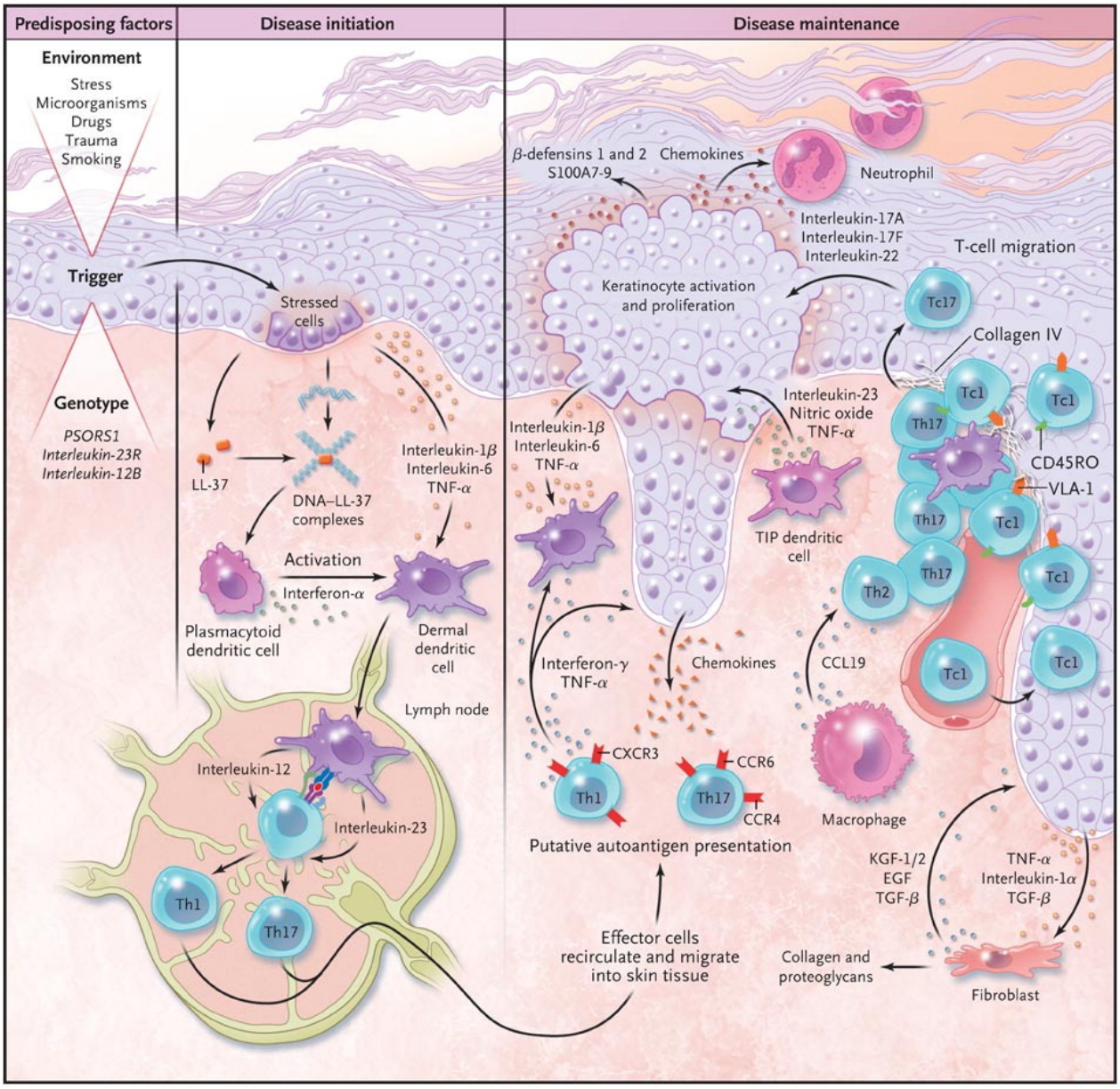

Figure 1. Proposed Schema of the Evolution of a Psoriatic Lesion from Initiation to Maintenance of Disease. *Reproduced with permission from Nestle F et al. N Engl J Med 2009;361:496-509. Copyright Massachusetts Medical Society.*

Genetic aspects

Early studies have shown a greater frequency of psoriasis among both parents and siblings, suggesting a heritable component in the aetiology of the disease.[43-45] Twin studies have shown greater concordance rates for psoriasis in monozygote than in dizygote twins;[46,47] however, the concordance rates for monozygote twins do not reach 100%, something which suggests that environmental factors also play a role. High concordance rates have been found in older twin studies, where the heritability has been suggested to be as high as 80-90%.[46,47] A more recent Norwegian twin cohort study below age 32, suggested that approximately 66% of the phenotypic variance in psoriasis of the early onset type can be attributed to additive genetic effects; while the remaining liability is a result of non-shared environmental factors.[48] A recent Danish study including twins age 20-71 years also supported these findings.[49]

The mode of inheritance seems complex;[50] reaching now 44 known susceptibility loci of major and minor effect mainly involved with the epidermal-barrier, innate immune system, antigen presentation and T-cell function.[14,51] Despite several genome wide association studies (GWAS) a significant proportion of psoriasis heritability remains to be clarified.[14] Additional genetic risk factors may remain to be discovered. Alternatively, the known genetic component in psoriasis may account for far more of the variance in susceptibility than currently recognized, as part of the missing heritability may be due to gene–gene interactions; a known example includes the interaction between risk alleles at HLA-C and *ERAP1* in psoriasis.[52] The main genetic determinant of psoriasis of the early onset type seems to be *PSORS1*, located within the major histocompatibility complex (MHC) on chromosome 6. Three genes within this region have been the major targets for investigations; most importantly *HLA-Cw6* which encodes a class I MHC-protein.[1] Studies suggest that the different clinical phenotypes of psoriasis are genetically heterogeneous, and that there may be a difference in the genetics of plaque psoriasis of the late versus early onset type.[14,53-55]

Gene-environment interaction may also contribute to the missing link in understanding the heritability in psoriasis (Figure 3, page 20). The effect of a certain low-penetrance susceptibility mutation on the development of the psoriasis phenotype may depend on the burden of environmental risk factors. There are known examples of gene-environment interactions in psoriasis;[56] for instance a polymorphism in *IL12B* was associated with increased risk of psoriasis in a nested case-control study, but only among overweight individuals.[57] Recently epigenetic mechanisms have emerged as a putative link between

genetic and environmental factors.[58-60] Differences in DNA methylation and gene expression in psoriatic plaques suggest that epigenetic dysregulation of biological pathways involved with immune response, cell cycle and apoptosis may be involved in the pathogenesis of psoriasis.[58-61]

1.4 The clinical morphology of psoriasis

There are no set diagnostic criteria for psoriasis, and a dermatologist's diagnosis is considered the gold standard. Clinically the epidermis presents with a sharply defined, raised erythematous and silvery scaled, papules or plaques of mostly symmetrical distribution.[1] There is a marked heterogeneity in the clinical morphology of psoriasis. Approximately 90% of psoriasis cases are plaque types,[40] also known as psoriasis vulgaris (Figure 2); and most of the research today applies to this subgroup. Patients with plaque psoriasis usually present with symmetrical distributed, often itchy and painful, plaques from 1 to more than 10 cm in diameter, commonly located on the scalp, elbows, knees and lower back. Other manifestations of psoriasis include guttate psoriasis, which refers to the abrupt onset of multiple small "drop-like" lesions (< 1 cm) mainly on the truncus, and is most commonly seen in children and young adults. Inverse psoriasis is commonly present alongside plaque psoriasis, and refers to the distribution of psoriasis in the intertrigenous areas. In the literature, frequencies of psoriasis patients with nail involvement vary between 10% and 82%.[62,63] Two rare and potentially life threatening forms of psoriasis are generalized pustular psoriasis and erythrodermic psoriasis. Palmoplantar pustulosis (PPP) has traditionally been considered a localized type of pustular psoriasis limited to the palms and plantar area of the feet, mainly affecting women from middle-age; however, many now consider this a distinct entity.[64] Many patients with PPP also have plaque psoriasis.[64]

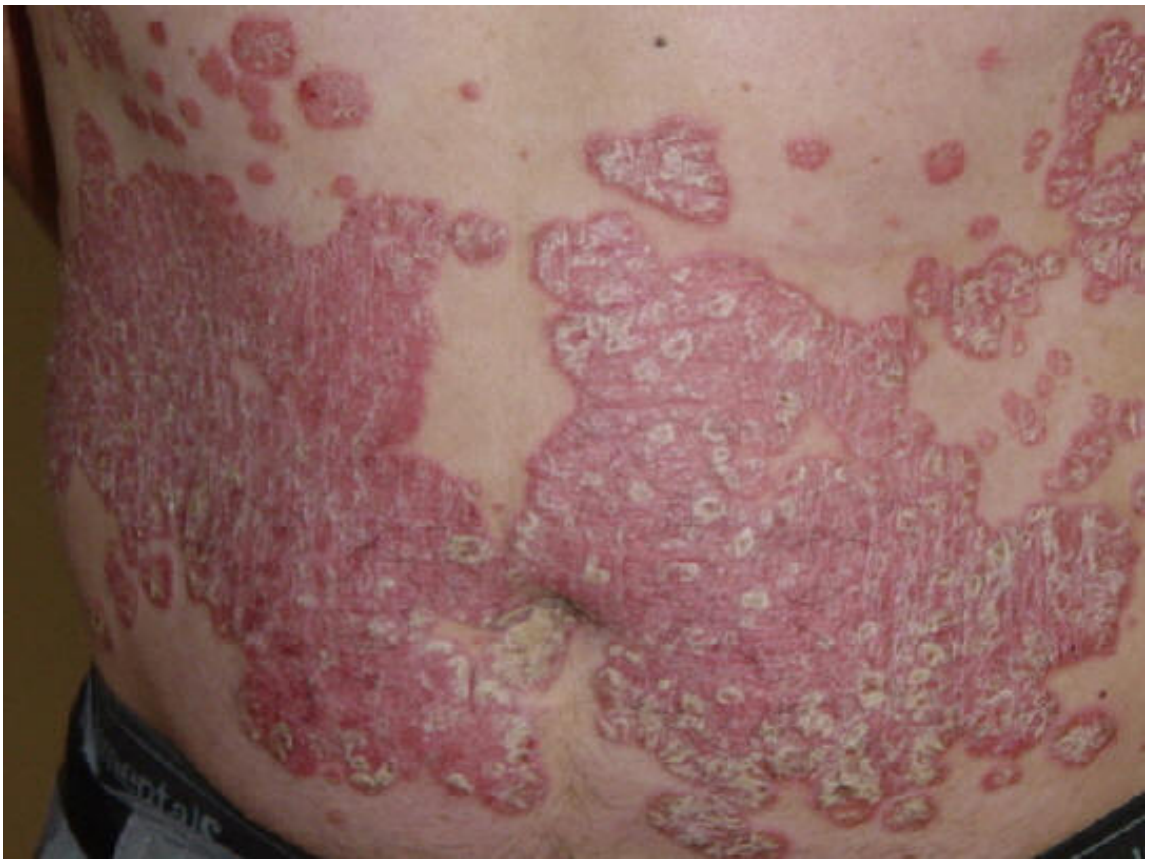

Figure 2. Plaque psoriasis. *Picture courtesy of Wikicommons.com.*

While the appearance of classical plaque psoriasis is distinct, less common subtypes of psoriasis can be confused with other skin conditions. Inverse psoriasis can initially be misdiagnosed as intertrigo or fungal or bacterial infections, however the opposite assumption where intertrigo is referred to a dermatologist as suspected inverse psoriasis is uncommon. The subungual hyperkeratosis and oncholysis which is often found in nail psoriasis can easily be misdiagnosed as fungal disease, and many psoriasis patients are treated with antifungals initially before the right diagnosis is made. Seborrheic dermatitis of the scalp and face may also be confused with psoriasis.

Approximately 70-80% of those affected by plaque psoriasis have mild disease.[65] Severity can be measured by various tools, but the standard measures used in most randomized controlled trials (RCTs) as well as in clinical practice are; the Psoriasis Area Screening Index (PASI),[66] which measures the degree of erythema, induration, scaling and the percentage of affected body surface in various body areas, and the Dermatological Quality of Life Index (DLQI) which is a questionnaire with different questions regarding the impact of psoriasis on daily life.[67] Both measures complement each other, as psoriasis in certain areas like the face, hands

or genitals can have a much larger impact on a person's physical and mental wellbeing than the PASI indicates.

The severity of disease, as well as potential comorbidities and patient compliance, decide what therapeutic interventions are suggested. Traditionally, local therapy with potent steroids, sometimes in combination with topical Vitamin D, is the first-line therapy. With more extensive disease Ultra Violet (UV) therapy, climate therapy, or oral therapy in form of immune suppressants like Methotrexate or more rarely Cyclosporine A; or the retinoid Acitretin is used. In the past decade, biologic agents have proven their efficacy in therapy resistant psoriasis making psoriasis research a "hot topic".

1.5 Environmental risk factors

Several environmental factors have been associated with psoriasis. Firstly, studies have shown higher prevalence of psoriasis closer to the earth's poles.[15,19] Latitude is a likely marker of UV radiation, genetic selection or perhaps a difference in antigen exposure/ infection trends.[19,68] UV radiation has several effects on the immune system; for instance the endogenous production of Vitamin D is directly influenced by UV radiation. Reduced levels of Vitamin D have been seen in psoriasis patients compared to healthy controls in smaller clinic based studies.[69,70] Furthermore, topical Vitamin D has been used in psoriasis treatment for decades. Secondly, both clinical and immunological evidence has suggested a link between an upper respiratory tract infection, mainly with streptococcus species, and the subsequent development of psoriasis, mostly of the guttate subtype and in young people.[28,68,71,72] Severe cases of psoriasis in relation to HIV infection have also been reported.[73] Moreover, clinicians have since long registered that psoriasis plaques can appear in sites of trauma, for instance in the area of an operation wound or after an extensive sunburn. This effect is known as the Köbner phenomenon.[2] It is postulated that damaged DNA from keratinocytes which is released upon injury, forms aggregates with antimicrobial peptides and thereby triggers a cascade of inflammation.[1] In addition, drugs like antibiotics, lithium, antihypertensive agents, and NSAIDS have been questioned to be possible risk factors for psoriasis; however, these assumptions are mainly based on case reports and case series.[74,75] In a large-scale study from the UK GPRD database there was only a weak association between psoriasis and antibiotic

use, however this was likely confounded by the reports of previous infections.[28] More research is needed in order to draw conclusions in this matter.

1.5.1 Lifestyle risk factors: stress, physical activity, alcohol and smoking

There are few longitudinal cohorts investigating risk factors influencing psoriasis development, however a few studies of stress/ depressive state, physical activity, alcohol and smoking in relation to risk of psoriasis have been performed. Further efforts have been made in the time period from we started our data gathering up until today. Interestingly, some changes in potentially important lifestyle factors seem to parallel changes in psoriasis prevalence and incidence, as the major lifestyle epidemics of physical inactivity, overweight and obesity. Importantly, data are still largely lacking in terms of critical age windows and doses of exposure, as well as evaluation of potential gender differences, possible interactions between exposures as well as gene-environment interactions.

Psoriasis patients regularly report increased psychosocial stress as a self-observed reason for disease exacerbation, and it is suggested that stress and an individual's ability to cope with stress can play a role in the exacerbation of the disease, however causality has not been established.[76,77] A recent meta-analysis concluded that the higher prevalence of depression found among persons with psoriasis is most likely due to tertiary study populations and differential misclassification through questionnaires, where psoriasis symptoms are confused with depressive symptoms.[78] However, there is evidence supporting associations between anxiety and depression and risk of psoriasis onset.[79-81] Physical inactivity is linked to both inflammation and oxidative stress, which can potentially influence psoriasis development and severity.[82] There are to date few studies investigating the effect of physical inactivity on psoriasis incidence and severity, and very few of these have been specifically designed to look at physical inactivity as a main predictor of psoriasis.[82] However, an inverse association between vigorous physical activity and risk of psoriasis was recently found in women,[83] and further studies are warranted.

Alcohol may induce psoriasis by affecting the immune system through keratinocyte proliferation, or upregulation of proinflammatory cytokines,[84] as well as being associated with increased infection and trauma risk.[85] Some studies indicate a potential increased risk of psoriasis with increasing intake of alcohol, especially among men who drink large amounts of alcohol.[85-88] However, a recent literature review indicated that although the average alcohol

consumption among psoriatics may be increased in many populations, there is not sufficient evidence to evaluate if alcohol is a risk factor for psoriasis.[89]

Interestingly, smoking has been associated with psoriasis in several cross-sectional studies, and has also been implicated as a risk factor in the debut of disease.[90,91] The biological effect of smoking derives from a complex interplay between several substances, importantly nicotine and carbon monoxide, and can be modulated by genetic vulnerability, gender, and degree of consumption.[77,92] In a US study smoking was observed to influence psoriasis incidence, with a relative risk for current smokers between 1.8 to 2.7, and a positive dose-dependent association.[93] There was also indication of an increased risk among past smokers, which decreased with time.[93] The possible psoriasis subtype, or comorbid condition, PPP has an even higher reported association with smoking; however, few population-based data are available.[64,77] Due to the biological effects of smoking, it has been hypothesized that smoking may act synergistically and potentiate the effect of other exposures. In a study from Italy, a multiplicative effect of the combined exposure to obesity and cigarette smoking on the odds of psoriasis was suggested, with up to tripled odds of psoriasis among those who were both obese and current or prior smokers.[77] More studies are needed to explore this synergism within a longitudinal population-based design.

1.5.2 Overweight, obesity, weight gain and psoriasis

Overweight and obesity has reached epidemic proportions worldwide during the last decades.[94] Globally approximately 35% of adults were overweight in 2008 (body mass index, BMI = 25-<30 kg/m^2), while 11% were obese (BMI ≥ 30 kg/m^2).[95] In Norway, the proportion of persons defined as obese has increased from 8-10% in 1985 to approximately 20-23%. In 2007-08, both in the sixth Tromsø study, as well as in the Health Examination in North Trøndelag (HUNT) study, over 50% of the adult population was overweight.[96] There is a growing interest in the contribution of excess weight to systemic low grade chronic inflammation, which may also influence the risk of psoriasis.[14,97] Basic research indicates that adipocytes and activated inflammatory macrophages can play a role in both psoriasis and excess weight; however, the exact mechanisms behind the association remain unclear.[97]

The relationship between overweight, obesity and psoriasis has long been discussed, after Lindegård first described this association within a Swedish hospital-based cohort.[98] Since then numerous, mainly cross-sectional, studies have found positive associations.[90,99] A recent meta-analysis showed that individuals with psoriasis have an over 50-60% increased odds of

being obese compared to the general population,[97] with a clear dose-response relationship between the severity of psoriasis and the odds of obesity.[97] Traditionally the higher BMI found in psoriasis patients was attributed to high energy intake combined with a sedentary lifestyle secondary to the skin disease. However, there is only one longitudinal study, from the UK GPRD, investigating the risk of obesity among patients with psoriasis. Within this study population, individuals with newly diagnosed psoriasis had an 18% increased risk of developing obesity compared to the control subjects during follow-up for up to ten years, but to our understanding, this analysis was not adjusted for baseline BMI.[100] More recently, it has been suggested that excess weight is an independent risk factor for psoriasis.[77,86] A publication from the UK GPRD found that overweight and obesity, increased the risk of psoriasis by 10-30%.[28] Two later publications containing data from the renown US Nurses' Health Study (NHS) cohort showed a dose-response relationship with up to two- to threefold increasing risk among severely obese women compared to normal weight women, as well as associations between adult weight gain and risk of psoriasis.[25,101] The relationship between excess weight, weight gain and incident psoriasis has not yet been investigated in a longitudinal cohort representing both genders over time. Interestingly, others have also suggested that the observed increased risk of psoriasis among those who are overweight could lead to secular changes in the incidence and prevalence of psoriasis.[102]

1.6 Psoriasis and comorbidities

Over the past decade psoriasis has been increasingly associated with a whole range of comorbidities including among others depression, autoimmune disease (Mb Crohn), lymphoma and some other cancers, obesity, hypertension, dyslipidemia, metabolic syndrome (MetS), type II diabetes, thromboembolic disease, cardiovascular disease (myocardial infarction and stroke) and increased mortality.[5,6,12,13,103-105]

The traditional comorbid condition associated with psoriasis is psoriasis arthritis (PsA).[5] PsA is characterized by the presence of mostly sero-negative inflammatory arthritis in a psoriasis patient which fulfils the as of 2006 internationally agreed on Classification criteria for psoriatic arthritis (CASPAR criteria).[5,106] Clinically the patients develop pain, swelling and tenderness of the joints and surrounding ligaments/ tendons, which in worst case can lead to joint destruction. A study from the UK GPRD found a total prevalence of PsA of 0.2% in the

general population, while the prevalence was 8.6% among psoriasis patients, with higher numbers among those with more severe psoriasis or longer disease duration.[107] A European multicentre trial found that approximately 20% of psoriasis patients develop psoriasis arthritis within a 30 year period, and that those with more severe disease were more likely to develop PsA.[108] Most patients who present with PsA already have established psoriasis. However, the severity of plaque psoriasis does not necessarily correlate with the severity of PsA.[109] PsA is difficult to study as it is not easy to separate if the risk factors apply to the whole disease continuum of psoriasis and PsA or for PsA as an isolated component and more studies are needed.[110] Importantly, persons who also have PsA may have a greater risk of cardiovascular disease, compared to those with psoriasis alone.[105]

The increased burden of comorbidities among persons with psoriasis has led to the hypothesis that psoriasis is a *systemic* inflammatory condition.[6] One may hypothesize that there could be common pathophysiological mechanisms operating for psoriasis as well as for several other chronic diseases. A recent meta-analysis of four GWAS psoriasis cohorts from Sweden and the US found that patients with psoriasis share common genetic single nucleotide polymorphisms (SNPs) which are suggested to increase the risk of dyslipidemia, hypertension and coronary artery disease in itself.[111] Another meta-analysis found that over 677 genes were up-regulated and 443 were down-regulated in psoriasis plaques compared to non-lesional skin, enlightening the complexity of the genetic aspects of the condition.[112] The multitude of activated genes in psoriasis plaques indicates that multiple biomarkers are produced locally and likely released into systemic circulation, depending on the extent of the affected body surface.[113,114] The Th-1 and Th-17 inflammatory cytokines which are increased in psoriasis pathogenesis (Figure 1, page 11) may influence angiogenesis, insulin signaling, adipogenesis, lipid metabolism and immune cell trafficking, and thereby potentially impact other conditions like obesity, diabetes, thrombosis and atherosclerosis. Vice versa, inflammatory cytokines and hormones produced by adipose tissue may influence psoriasis debut or severity by induction of a systemic pro-inflammatory state (Figure 3).[42,115]

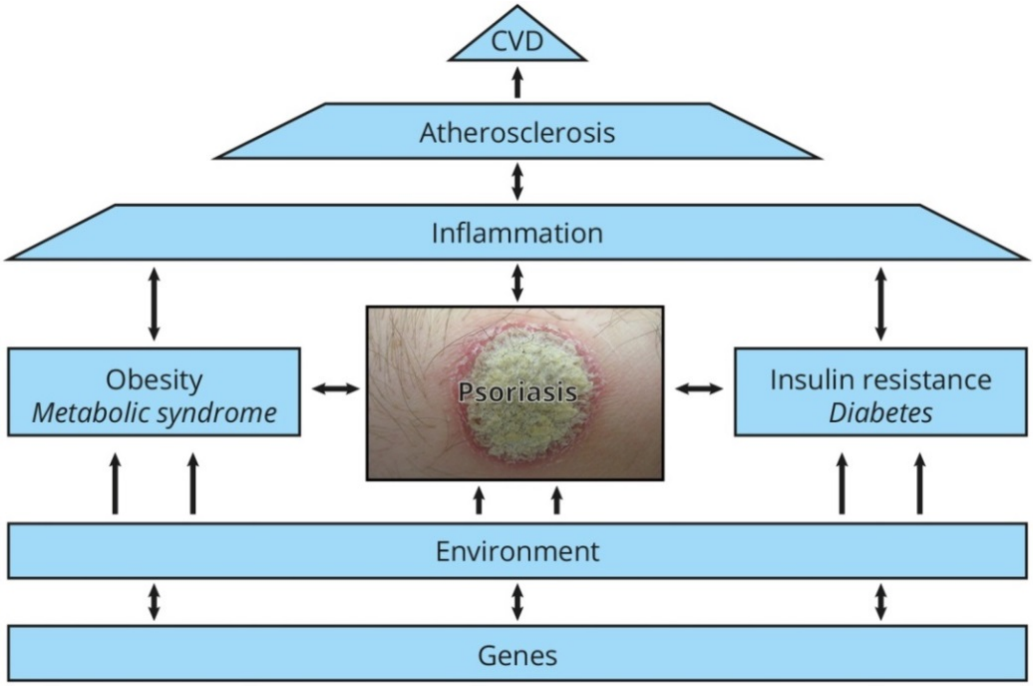

Figure 3. The proposed interplay between psoriasis, chronic inflammation and cardiovascular disease.

1.6.1 Psoriasis and the metabolic syndrome

There is growing evidence of an association between psoriasis and the metabolic syndrome (MetS),[116-118] The MetS is a cluster of risk factors (overweight/obesity, dyslipidemia, insulin resistance, and hypertension) associated with a doubling of cardiovascular disease risk and a five times greater risk of developing type II diabetes.[119,120] Overlapping inflammatory pathways as well as shared genetic susceptibility may be potential biological mechanisms behind the association between psoriasis and the MetS;[121] however, the exact mechanisms remain unclear. Apart from obesity, recent meta-analyses have demonstrated a relationship between psoriasis and dyslipidemia (odds ratio (OR) 1.5),[105] diabetes (OR 1.59),[13] as well as hypertension (OR 1.58).[122] There was also indication of a positive dose-response relationship with all components; finding increasing odds with greater severity of psoriasis.[13,122,123]

A recent meta-analysis reported an odds ratio for MetS of 2.3 among patients with psoriasis compared to their reference groups.[118] However, a limitation of this analysis was the scarcity of data from truly population-based studies, lack of uniform screening procedures for psoriasis and MetS, as well as missing information on potential confounding lifestyle factors. Two fairly small population-based health surveys have provided conflicting results. The

North-American National Health and Nutrition Examination Survey (NHANES; 2003-06, n= 2,456) reported a two-fold increase in the risk of MetS among persons with self-reported psoriasis, and an even higher risk among women.[116] In contrast, in a comparable Danish study (n= 3,374) no association was observed.[23] Interestingly, a positive dose-response association between the severity of psoriasis and odds of MetS was seen in a large case-control study from the UK GPRD.[117]

Questions remain concerning the link between psoriasis and the MetS in the general unselected population and the extent to which age and gender influences the risk of the MetS in psoriasis. Furthermore, abdominal obesity measured through waistline has become the preferred component of the MetS, and a new and lower waistline cut-off for abdominal obesity has been suggested.[124] There are few studies investigating psoriasis and risk of MetS which have had data on waistline measurements. The first-ever public health agenda for psoriasis recently released by the United States Centers for Disease Control and Prevention (CDC) points to needs for more population-based cohort studies, including analysis of age and gender disparities, of relationships between psoriasis and obesity, metabolic- and cardiovascular disease,[125] also underlined by others.[18,126,127] In recent meta-analyses discrepancies between population-based and clinic-/register-based study populations, as well as lack of adequate adjustment for relevant cardiovascular risk factors have been pointed out.[105,128,129]

2. Aims of Thesis

The overall aim of the thesis was to investigate time trends in psoriasis prevalence, and exploring overweight and weight increase as an environmental risk factor for psoriasis development; as well as investigating the association between psoriasis and the metabolic syndrome, including age and gender variations, within a population-based cohort.

More specifically the aims were to examine the following:

- Whether the prevalence of self-reported psoriasis increased over the time period from 1979 to 2008 in a population-based cohort. Moreover, whether there were changes across the surveys (time period effects) and birth cohorts (birth cohort effects), independent of population aging.

- How overweight and weight gain, as well as overweight in combination with smoking, influenced the odds of psoriasis, and whether these associations may be modified by age and gender within a population-based cohort.

- How psoriasis is related to the metabolic syndrome and whether this association varies by age and gender within a population-based sample.

3. Population and methods

Figure 4. The city of Tromsø, Norway, 69°N, our research laboratory. Private picture.

3.1 The Tromsø Study

The Tromsø Study (www.tromsostudy.com) is a single centre multipurpose researcher initiated population-based study with repeated high quality health surveys inviting inhabitants in the municipality of Tromsø, Norway (Figure 4).[130] Tromsø is the largest city in North Norway and a modern regional capital with the world's northernmost university. The municipality of Tromsø is thought to be representative of a Northern European, white, urban population.[131] Tromsø has grown from 42,253 in 1974 at the study start-up, to close to 70,000 in the last Tromsø survey. The great majority of the city inhabitants, and thereby study participants are ethnic Norwegian/ Caucasian, but also includes an indigenous Sami and Kven

minority (3-4%, according to the 2007-08 Tromsø study). There was limited immigration from non-ethnic Norwegians or non-Europeans in the time period.

The Tromsø study was initiated in the early seventies as a combined effort between the University of Tromsø, Tromsø University Hospital and the Norwegian Health Authorities in search of explanations for the high levels of cardiovascular disease in North Norway.[132,133] It is now run and owned by the University of Tromsø. The design and cohort profile of the six surveys from the adult population have been described in detail (Paper I-III).[130,131] I will therefore only briefly summarize the main patterns of data collection included in the present work.

All measurements have been made according to standardized procedures by trained health professionals in each survey attempting minimal diversity in the time period. The first survey was carried out in 1974 (T1) on men only and is not included in the present studies. Further studies were performed in 1979-80 (Tromsø 2, T2), 1986-87 (Tromsø 3, T3), 1994-95 (Tromsø 4, T4), 2001 (Tromsø 5, T5) and 2007-08 (Tromsø 6, T6) in both genders (Figure 5).[130]

The aim of the Tromsø study has been to include large representative samples of the population, with invitation to whole birth cohorts and random samples based on the official population registry. The total sample size has varied somewhat. In T2-4 and T6 new birth cohorts were consecutively added. Detailed information regarding the sampling strategy is described elsewhere.[130,131] In T5, a larger portion of those invited was selected from T4 participants, making this survey slightly different from a sampling point of view. The overall participation rate has been 66-85% and somewhat declining,[130] but is still relatively high.[131]

3.2 Study design and study population

The total number of participants with valid consent for study participation from the five surveys were; 16,554 in T2, 21,734 in T3, 26,957 in T4, 8,039 in T5, and 12,982 in T6. Tromsø 1 was not included in any of our analysis because it did not include data on self-reported psoriasis.

The analysis of trends in psoriasis prevalence in **Paper I** was based on five cross-sectional surveys.[130] All attendees from Tromsø 2-6 with the following exceptions were included: to

reduce the risk of recall bias in older ages, a total of 1,400 participants above 79 years old in T4-6 were excluded from the analysis. Further, to avoid selection bias due to non-random invitation of youngsters in T3, 1,134 participants under 20 years old were excluded. An additional 90 participants in T2-3 were excluded because they did not belong to the invited birth cohorts in these surveys. In T5, 538 participants below age 30 were excluded, because this age group was represented by only one birth cohort (1971) and may not be representative for all individuals age 20-30.

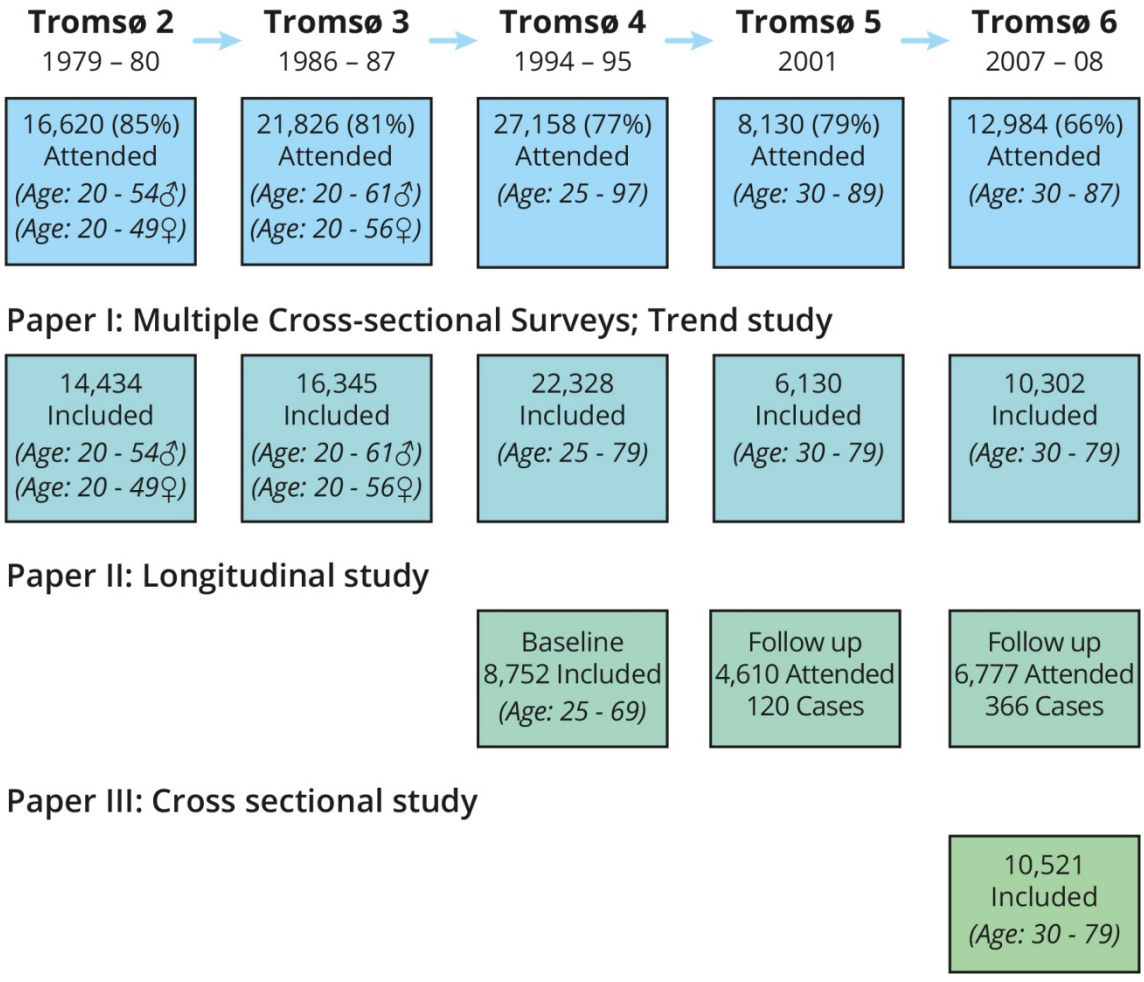

Figure 5. Methodological approach and study samples for Papers I-III. Study inclusion criteria are described in the main text and Papers I-III.

All persons with missing psoriasis data were excluded from the analysis in each cross sectional survey. A total of 13,565 observations in T2-6 with missing self-reported psoriasis data were omitted. This leaves, 14,434 observations from T2, 16,345 observations from T3, 22,328 observations from T4, 6,130 observations from T5, and 10,302 observations from T6 eligible to enter the analysis, and represents a total of 69,539 observations from 33,387 unique individuals born from 1915 to 1977 (Figure 5).

For the analysis of how overweight/obesity, weight gain, and overweight and smoking combined, may influence the risk of psoriasis, a prospective study design was used (**Paper II)** (Figure 5). Tromsø 4 was used as baseline and the response to the question regarding psoriasis status in follow-up surveys up to 7 years (Tromsø 5, 2001) to 13 years later (Tromsø 6, 2007-08) was the outcome variable. In Tromsø 4 all subjects age 25-97 years were invited, and a total of 27,158 subjects (77%) attended.[130] A total of 26,957 attendees with valid consent were available for the analysis. In this cohort, follow-up data on psoriasis status was available for 11,328 individuals. The following exclusion criteria were applied using baseline data in T4: age $\geq$ 70 years (n=547); missing data on self-reported psoriasis (n=1,106); self-reported psoriasis diagnosis (prevalent disease) (n=739); being pregnant (n=100); missing measured BMI (n=7); and missing smoking status T4 (n=8) or smoking only cigars and pipe (n=69); giving a total of 8,752 included in the analysis with baseline BMI as main predictor. In analysis of adult gain in BMI based on self-reported weight at age 25 years and measured height at baseline, 26 individuals with age < 26 years at baseline were excluded to insure that they did not have psoriasis within one year of study enrollment, and 384 individuals were excluded due to missing report of weight at 25 years, giving a study sample of 8,342 individuals.

A validation of self-reported weight at age 25 was performed among 900 repeat attendees who had their weight measured at age 24-26 years in T2, T3, or T4, and recalled their weight at age 25 years in T5 or T6.

In **Paper III**, the association between psoriasis and odds of MetS was investigated within a cross-sectional study design (Figure 5). The sampling strategy in the sixth Tromsø study is described in detail (Paper III).[131] In total 9,625 men and 10,137 women aged 30-87 years were invited, and 12,984 participants attended (66%).[131] Two participants have since withdrawn their consent. Moreover, all subjects over the age of 79 (n=531), were excluded due to risk of recall bias as well as healthy survivor bias. In addition pregnant women (n=28), and

participants with missing data on both self-reported lifetime psoriasis and doctor's diagnosis of psoriasis (n=1,176) or measured MetS components (n=726) were excluded; leaving a total of 10,521 individuals, 5,499 women and 5,022 men, for the analysis.

3.3 Data Collection

3.3.1. Questionnaire and register data

In all surveys, the subjects have been invited through an invitation letter, and a first questionnaire (Q1) has been enclosed with the invitation. A second questionnaire (Q2) was handed out at the screening centre; which was to be returned either on site or through the mail; approximately 90-96% of attendees did so.[130,131] Q2 in T4 and Q1 in T5 differed slightly for attendees from age 70 years. Over the years both questionnaires have expanded and include information on a wide range of exposures, symptoms, diseases and medications (Appendix I-V). The original Norwegian-language versions are available at the study website (www.tromsostudy.com). Also, a short interview was made, in order to check the questionnaires for inconsistency, as well as focusing on medications and women's reproductive health.

Assessment of psoriasis

Life-time self-reported psoriasis was assessed in Q2 using the following question; in T2 and T3: "Do you have or have you had the skin disease psoriasis?" In T4 and T5 the question was: "Do you have or have you had psoriasis?" and in T6: "Do you have or have you ever had psoriasis?" Answers were; yes or no. In T6, the question "Have you ever been diagnosed with psoriasis by a physician?" was added for validation and comparability purposes.

In Paper I and II the self-reported psoriasis was used for consistency within the surveys. In Paper III self-reported psoriasis and/ or self-reported doctors`s diagnosed psoriasis was combined. Persons who answered yes to any or both of these questions were classified as having lifetime psoriasis.

Also in T6 (Q2), a question to self-evaluation of present disease severity was added. "Answer on a scale from 0 to 10, where 0 corresponds to no symptoms and 10 correspond to worst imaginable complaints; "If you answered YES to that you have or have had psoriasis: How

much are you affected by your psoriasis today: Scale 0-10 with 0=No complaint, 10=worst possible complaint" (Paper III). Furthermore, information on medication from the Norwegian Prescription Database (NorPD) was used as a proxy for disease severity (Paper III). Information on all prescriptions for outpatient treatment of psoriasis from 1 October 2006 to 1 June 2009 was linked with data on a selected set of variables from T6. This analysis included all individuals age 30-79 with self-reported psoriasis and measured waist circumference (WC), n=1,192. Persons who received systemic drugs were considered to have moderate to severe psoriasis.

Assessment of lifestyle variables

Socioeconomic status

Questions on marital status, total household income, and educational level were available, and educational level reflecting variations in socioeconomic status was mainly used in our analyses.[134]

Alcohol consumption

In all surveys, participants who were not teetotalers indicated their usual frequency of drinking sessions (in T2 and T3 also separated by type of beverage). In Paper I and III we dichotomized those reporting a weekly number of drinking sessions of 2-3 or more as higher alcohol consumers versus all others. In T4 (Paper II), the average daily gram intake of alcohol was computed from number of units of intake of wine (16.6 g/unit), beer (11.7 g/unit) and spirits (7.4 g/unit) within a two week period. The validity of self-reported data on alcohol consumption was examined in the fourth Tromsø study, where a strong positive association was found between self-reported alcohol use and measured gamma-glutamyltransferase.[135]

Smoking

In all surveys, participants indicated whether they were present daily smokers (T4 split by type of tobacco; the vast majority were cigarette smokers) and smoking history including previous daily smoking, years since stopped smoking, total number of smoke-years, and average daily number of cigarettes or weekly number of tobacco packs. Smoking status was described through a dichotomous variable in form of present versus never or past smokers (Paper I and II). In Paper II and III, smoking status was also reported with three categories; current daily smoking, former daily smoking and never smoking. In Paper II, smoking at

baseline (T4) was further elaborated in pack years defined as number of cigarettes per day x number of years smoked divided by twenty; this was further categorized into four pack-year categories: 0, 1-9, 10-19, 20+. The validity of self-reported smoking has been evaluated in other Norwegian cohorts (see discussion of Methodology).[136,137]

Physical activity

In all surveys apart from Tromsø 4, the participants indicated their usual level of leisure activity in the past year using one of four response categories: level 1: reading, watching television, or engaging in sedentary, activities; level 2: at least 4 hours a week of walking, bicycling, or engaging in other types of physical activity; level 3: at least 4 hours a week exercising to keep fit and participating in recreational athletics; and level 4: regular, vigorous training or participating in competitive sports several times a week. This self-reported physical activity variable has been validated,[138] and was further validated within a subsample of Tromsø 6 attendees, with acceptable concurrence with heart rate, metabolic profile and the level of measured physical fitness.[139] There was also an acceptable degree of tracking between the previously reported physical activity level over time among repeat attendees.[140] In Paper I and III we dichotomized those reporting sedate lifestyles (level 1) versus all others. In T4, participants indicated their usual level of recreational physical activity as the average weekly number of hours (0, <1, 1-2, 3+ hours) spent doing light activities (not sweating or out of breath) and hard activities (sweating/ out of breath) separately. This question on physical activity has been used in prior Scandinavian studies.[141] In Paper II the physical activity score was calculated as a combined variable of the sum of hours of light and heavy physical activity in spare time per week, with heavy physical activity given double weight.[142] Work place physical activity in terms of four categories of work from sitting still to hard manual labor was reported in all surveys. Due to the relatively large degree of missing related to those who were seniors, unemployed or on disability pension, this question was not used in multivariable analysis and only used to describe the population (Paper I).

3.3.2. Clinical measurements and body composition

When measuring ***blood pressure*** the used cuff was selected after measurement of the circumference of the right upper arm. Blood pressure was recorded three times with one minute intervals in a sitting position after two minutes rest, by the use of an automatic blood pressure measurement device and the mean of the two last readings was generated. In T4 a

Dinamap Vital Signs Monitor 1846, Critikon, GE Healthcare, Norway, was used while in T6 a Dinamap Pro care 300 Monitor from the same company was used.

BMI and waist circumference

In all surveys, ***height*** and ***weight*** were measured to the first decimal amongst participants, who wore light clothing and no shoes. In T6 an electrical scale; Jenix DS 102 stadiometer; Dong Sahn Jenix, Seoul, Korea, was used. ***Body mass index*** (BMI) was computed as weight divided by height squared (kg/m^2). In T6 and in the second visit of T4 and T5, ***waist circumference*** (WC) was measured at the umbilical line to the nearest centimetre, without outerwear, by using a measuring tape. ***Hip circumference*** was measured around the widest part of the thigh to the nearest centimetre, and the waist to hip ratio was computed.

In T5 and T6, self-reported ***weight at age 25 years*** was reported. "Estimate your body weight when you were 25 years old?" (kg). In the analysis in Paper II, the first survey with available data was chosen in order to estimate weight change from age 25 up till the date of participation in T4 (for individuals age 26 years or more in T4). Among 900 attendees who had their weight measured at age 24-26 years in T2 (1979-80), T3 (1986-87), or T4 (1994-95), and recalled their weight at age 25 years in T5 (2001) or T6 (2007-08), Pearson correlation coefficient was 0.89 (women, n=532, R=0.80; mean self-reported weight at 25 years = 57.7 kg and measured at 24-26 years = 59.7 kg; men, n=368, R=0.79, mean self-reported weight at 25 years = 74.9 kg and measured at 24-26 years = 75.2 kg). The validity of recalled weight has been investigated in prior publications, and found to be acceptable, (See discussion of methodology).[143,144]

Laboratory analysis

All blood samples were taken non-fasting; however, during the visit at the survey centre they were only allowed to drink water or black coffee/tea. The time since last meal was recorded. The specimens were taken from the antecubital vein with the subjects sitting in an upright position.

In T4, serum was prepared by centrifugation after 1 h rest at room temperature, and further analyzed at the Department of Clinical Chemistry, University Hospital of North Norway:
Serum total cholesterol and ***triglyceride*** analyses were performed by enzymatic colorimetric methods with commercial kits (CHOD-PAP for cholesterol and GPO-PAP for triglycerides;

Boehringer–Mannheim, Mannheim, Germany). ***Serum high-density (HDL) cholesterol*** was measured after the precipitation of lower density lipoprotein with heparin and manganese chloride.

In T6, within 30 minutes in room temperature the blood samples were centrifuged and transferred within one hour to plastic tubes kept between 1-10 degrees Celsius. Twice a day, the samples were sent to the accredited Department of Laboratory Medicine at the University Hospital of North-Norway for analysis (ISO-standard 17025).[131] ***Total cholesterol*** (Coefficient of Variation, CVa: 1.5%) and ***triglycerides*** (CVa: 3.7%) were analyzed within 10 hours using an enzymatic colorimetric method. ***HDL*** (CVa: 3.3%) was analyzed using a homogenous enzymatic colorimetric method. ***High sensitivity CRP*** (CVa: 1.2%) was analyzed by a particle-enhanced immunoturbidimetric assay. These analysis were performed on a Modal PPE auto-analyzer using regents from Roche Diagnostics AS, Norway. ***HbA1c*** (CVa: 2.0%) was analyzed the next day on blood samples collected in EDTA anticoagulation vessels. The analysis was performed by high-performance liquid chromatography (HPLC) with an automated analyzer (Variant II, Bio-Rad Laboratories, Hercules, CA, USA).

Assessment of metabolic syndrome

The metabolic syndrome was assessed using the new unified definition of the International Diabetes Federation (IDF) as well as the National Heart, Lung and Blood Institute, and others.[120] In order to be defined as having the MetS participants were required to have minimum three of the five criteria related to MetS; central obesity defined by waistline using two different waist criteria, raised triglyceride, reduced HDL-C, raised blood pressure, and raised fasting plasma glucose. The specific cut-off values for each component are described in Paper III, Supplementary material. Due to non-fasting of participants raised fasting glucose was replaced with HbA1c $\geq$ 6.1% according to established cut-off value for pre-diabetes 6.1–6.4% (Paper III).[145] HbA1c $\geq$ 6.0% was the best cut-off for impaired glucose tolerance among 3,476 participants undergoing an oral glucose tolerance test in T6.[146]

Medication use

In 2006-2007 (Tromsø 6), present use of antidiabetic medication (insulin and pills), antihypertensive and cholesterol lowering (statin use) medication were reported, and data on present use was included in the analysis (Paper III).

3.4 Statistical analysis

To investigate time trends in psoriasis prevalence, exploring overweight and obesity as an environmental risk factor for psoriasis development; as well as investigating the association between psoriasis and the metabolic syndrome, within The Tromsø study cohort the Statistical packages, SAS 9.2 (SAS Institute, Inc., Cary, NC) and SPSS 20-21 (SPSS Inc., Chicago, IL) were used. Two-sided p-values below 0.05 were considered statistically significant. Most analyses were stratified by gender, due to the known gender differences in lifestyle, body composition and metabolic risk factors in the adult and elderly population. Descriptive characteristics of the study population were presented as means (SD) or proportions (%). When comparing the means of continuous variables between groups, Student's t-test was used, and when comparing the distribution of categorical variables between groups, Pearson's chi-squared test was used. Correlations between covariates were assessed using Pearson's correlation coefficient.

When evaluating associations of demographic, lifestyle and metabolic risk factors with psoriasis, univariable and multivariable logistic regression models were used. In general, variables of statistical significance, variables with a biologically plausible explanation, and variables that were known risk factors for psoriasis from former studies, were kept in the multivariable models. Statistical interaction was evaluated by the inclusion of multiplicative interaction terms in the logistic regression models. Subjects with missing values for exposures, outcome, or covariates were excluded from the analyses.

In **Paper I**, the statistical methods were chosen in order to try to disentangle age, birth cohort and time period effects in the trends of psoriasis prevalence.[147] Data were first presented graphically in six different panels in order to visualize and explore age, birth cohort and time period trends according to the epidemiological method described by Palmore.[148,149] We then examined three different designs: *cross-sectional* differences in psoriasis prevalence between

10-year age groups in each of the surveys; indicating birth cohort or age effects, *time-lag* differences in psoriasis prevalence between the surveys for 10-year age groups; indicating birth cohort or time period effects, and *longitudinal* changes in psoriasis prevalence within 10-year birth cohorts followed over time; indicating time period or age effects. The irregular intervals between the surveys T2-6 made it necessary to approximate some of the data points in the graphs following birth cohorts. When there are corresponding patterns in two of the designs and no changes in the third, there is only one kind of effect. When changes are seen in all three designs, two or three effects are present. When there are no measurable changes in any design, there is no effect.

Odds ratios for self-reported psoriasis per 10 year increase in age, per 10 year increase in birth cohort and between time periods were estimated by generalized linear models (PROC GENMOD in SAS). Response probability distribution 'binomial' and link function 'logit' were chosen. In order to control for possible dependencies between repeated observations within subjects an unstructured covariance matrix was used in all models. As there was no clear pattern of interactions in the graphical presentation of data (almost no crossing lines), interaction terms were not included in the models. In order to increase the validity of the results sensitivity analysis were performed. When adjusting for age as a continuous variable in the multivariable model, the OR estimates were minimally changed. When subjects with missing psoriasis data were recoded to negative responders in the same multivariable model, almost identical OR estimates were observed.

In the prospective analysis of BMI and adult weight gain (from age 25 to baseline) in relation to odds of psoriasis, T4 was used as baseline and response to question about psoriasis in follow-up surveys up to 7 years (T5) to 13 years later (T6) as outcome variable (**Paper II)**. Incidence proportions (number of incident psoriasis in T5 and T6/ total number in the baseline population without psoriasis) in the total population, and by gender, BMI and weight change category were estimated. Logistic regression models were used to estimate the odds of psoriasis and adjust for potential confounders. BMI at baseline was investigated both as a continuous, dichotomous (cut-off 27-28 kg/m^2, close to upper BMI quartile), as well as a categorical variable (modified WHO classification, category one and two combined) in both age-adjusted and multivariable analysis including also gender, present smoking (yes/no), average daily alcohol intake (g/day), and a score of recreational physical activity. For the analysis of adult BMI/ weight change as predictor of psoriasis, gender and age specific Z-

scores and quartiles of BMI/ weight change were calculated within 5 year age groups (age at baseline; 26-<30, 30-<35, …65-<70) and the same multivariable logistic regression models were used without age and gender as covariates, including also mean of BMI at age 25 and at baseline. Potential interactions with gender, age and smoking status were tested in the regression analyses as described above. We also investigated 'biological interactions' between overweight and smoking as defined by Rothman;[150] interactions were analysed using the Synergy index (S) scores (**Paper II**).[150]

In a sensitivity analysis, observations with missing psoriasis data at baseline were recoded as not having psoriasis, which lead to slightly higher effect estimates. We also performed separate age-adjusted analysis for persons with incomplete data on covariates, which did not influence the results. In a further sensitivity analysis persons who only attended T5 were excluded, without this leading to any major influences on the results. Furthermore, those who reported to quit smoking within the last year prior to baseline were redefined as present smokers, without this leading to any changes in the results.

Comparisons of the prevalence of MetS and its components by psoriasis status were done in age-stratified analysis; i.e. 30-44, 45-59, and 60-79 years, according to approximate cut-off for premenopause in women (<45 years) and premature cardiovascular disease (<60 years) (**Paper III)**. The odds ratio (OR) for MetS according to the presence of psoriasis, was assessed in an age-adjusted logistic regression model (n=10,521 and n=9,662), and in a multivariable model adjusted for age, gender, smoking, educational level and physical activity in leisure time (n=9,662; observations with missing covariates excluded). Physical activity was included both using a binary variable (sedate versus others) and using an indicator variable for each category, without this influencing the model. Alcohol and statin use did not influence the analysis and were not included in the final model. The association between psoriasis and MetS may vary by age and the variation in effect size (odds ratio) may be non-linear. Therefore we included second-degree fractional polynomial terms of age in the logistic regression model,[151] both as main effects and as two-way interactions terms with psoriasis (**Paper III**).

Sample size and statistical power

The Tromsø Study is a large cohort which has been the basis for numerous high-quality publications on a broad spectrum of lifestyle factors, clinical measurements and biomarkers

and associations with different disease outcomes.[130] In the present thesis the study population sample was dependent of the invited birth-cohorts selected by the Tromsø study. The power to detect associations between continuous variables is generally high. The present thesis and papers demonstrate that there was sufficient statistical power to detect odds ratios of 1.3-1.4 for psoriasis and MetS. However, lack of power may be an issue in subgroup analysis and when studying interactions.

3.5 Ethics

The Tromsø Study has undergone evaluation by the Regional Ethical Committee (REC) as well as Norwegian Data Protection Authority (NDPA) and now fulfills the requirements of a Health Registry. The study complies with the Declaration of Helsinki, the International Ethical Guidelines for Biomedical Research Involving Human Subjects, as well as the International Guidelines for Ethical Review of Epidemiological Studies.[152] The Northern Norway Regional Health Authorities have provided the grant for my research project (Medical Research Program #SFP-870-09), as well as a grant from Arne Klem's fund for Norwegian dermatologists, 2008. The project is approved by the REC as well as the NDPA as part of the Tromsø Study 2-6.

4. Main results

Paper I

Is the prevalence of psoriasis increasing? Results from a 30 year follow-up of a population-based cohort.

We observed a clear trend of increasing self-reported psoriasis prevalence among 33,387 men and women, participating up to five times in health surveys from the North Norwegian population between 1979 and 2008, from 4.8% in 1979-80 to 11.4% in 2007-08, within all investigated birth cohorts (1915-77) and age groups above age 29. There was an independent effect of time period with a 2.5 times higher overall odds for psoriasis in 2007-08 than in 1979-80, when adjusting for age and birth cohort (odds ratio, OR = 2.49; 95% confidence interval, CI: 2.08-2.99). There was no indication of increasing prevalence among those aged 20-29 from 1979 to 1995; however, these age groups were not included in the last two surveys.

Paper II

Overweight and weight gain influence psoriasis development in a population-based cohort.

The incidence proportion of psoriasis in the time period from 1994 to 2008, among 8,752 men and women with an age range of 25-69 at baseline, was 4.7% in both genders. Above a threshold of BMI 27-28 kg/m^2, the study participants displayed increasing odds of psoriasis onset in multivariable regression analysis; above versus below BMI 27 kg/m^2 both genders combined had an OR of 1.32; 95% CI: 1.06-1.64, further increasing to OR = 1.41; 95% CI: 1.12-1.79 at BMI 28 kg/m^2, with no age or gender interaction. In analysis stratified by smoking status, these results were further strengthened among non-smokers with OR = 1.62; 95% CI: 1.19-2.20, among those with BMI $\geq$ 28 kg/m^2 versus below, and even higher odds among the obese $\geq$ 30 kg/m^2; OR = 1.71, 95 % CI: 1.13-2.56. BMI and weight increase from the age of 25 was associated with higher odds of psoriasis from age 45 by up to 70-90% regardless of weight category.

Present smoking was a strong risk factor for psoriasis development in both genders combined, OR = 1.92; 95% CI: 1.56-2.37, and there was indication of an even higher association in women, OR = 2.16; 95% CI: 1.62-2.88. Although there were no significant synergistic effects between smoking and BMI, those who smoked and were overweight (BMI≥ 28 kg/m^2) had the highest odds estimates for psoriasis development, OR = 2.48; 95% CI: 1.70-3.63.

Paper III

Psoriasis and the metabolic syndrome – a population-based study of age and gender differences.

We observed that 10.8 % of the 10,521 individuals age 30-79 years who participated in the sixth Tromsø Study (T6, 2007-08) reported lifetime psoriasis of mainly mild character.

Overall 32% of those with psoriasis versus, 24% of those without the condition fulfilled the criteria of the metabolic syndrome. Psoriasis was associated with a 3.82 times higher odds of metabolic syndrome in women at age 30 (95% CI: 1.51-9.66). While the odds decreased with age, the difference in prevalence of metabolic syndrome between women with and without psoriasis remained quite stable; age 30-44 years, 21%/ 11%; 45-59 years, 27/20; 60-79 years, 37%/ 30%. In men, psoriasis was associated with an almost uniform 1.35 times higher odds of metabolic syndrome (95% CI: 1.11-1.64) in all ages. In general, the same patterns were found using both the higher and the recently proposed lower waist criteria.

Abdominal obesity was the most frequent metabolic syndrome component in women in this study. We observed a dose-response relation between psoriasis severity, indicated by treatment, in women with psoriasis, and odds of abdominal obesity measured by waistline in age-adjusted analysis (OR 1.33; 95% CI: 1.00-1.77). There was no such association in men.

5. Discussion

The overall aim of the thesis was to investigate time trends in psoriasis prevalence and exploring overweight and weight gain as potential environmental risk factors for psoriasis development. Furthermore, the association between psoriasis and the metabolic syndrome was explored, all within a population-based cohort. There are few long term population based studies exploring psoriasis, and the need for prospective cohort studies has been emphasized.[18,127] The Tromsø Study is to our knowledge the oldest running cohort for psoriasis research among men and women worldwide with high overall participation rates in repeated surveys since the 1970ies; it includes self-reported psoriasis status, information on potential confounding lifestyle factors and measured metabolic status including laboratory tests.[130] Improved knowledge about lifestyle risk factors for psoriasis is needed in order to understand the distribution of the disease and opportunities for prevention, and while many think we already have the answers to the question if psoriasis is a systemic disease independently associated with an increased burden of metabolic and cardiovascular disease, data up until today is not sufficient to draw conclusions about causality and potential targets for prevention.[18,105,126,127,153]

As a general rule caution is called for when interpreting results from individual observational studies. In order for results to be correctly interpreted it is important that the studies are repeated in different populations and performed with the correct methodology.[24] Each study is merely a small piece of a big puzzle. Basic questions to consider before drawing conclusions in research are the accuracy of outcome (in example psoriasis), predictors and other covariables used; if the associations observed are true or reflect bias, confounding or chance; and lastly if causality can be assumed. It is important to remember that an association between a predictor and an outcome may very well be statistically significant; however this does not automatically mean that the association is causal. Nor does it mean that because an association does not reach statistical significance, it cannot be causal. In many cases significance is not reached because of a too small sample size, while in other cases there is a significant association, but it has little or no biological and clinical importance.[24]

Determining causality is the key to be able to use study results for primary prevention, which is determined to modify the occurrence of the outcome of interest.[24] In order for psoriasis to debut several causal components act together, to form what Rothman calls a "sufficient cause," defined as "a set of minimal conditions and events that inevitably produce disease."[24]

The elimination of just one of these causal components may be sufficient to avoid disease. In many cases the identification of an epidemiological chain of importance to prevention precedes the discovery of the actual causal factor.[24] Guidelines for evaluation of the causality of a statistical association, the so-called "*Hill's criteria*" were originally developed as a part of the first US Surgeon General report on the health effects of smoking. Hill lists nine criteria which may strengthen the evidence that an association is causal;[154] however, apart from "temporality" the inability to satisfy many of these criteria does not justify the conclusion that the association cannot be causal.[24] The Hill's criteria set to determine whether alternative explanations like bias or confounding can be reasons for the found association, and if not, whether a cause-effect relationship can be concluded. These criteria are: "*Experimental evidence*": Randomized controlled trials are generally thought to give the best protection against bias and confounding, and are therefore at the top of the evidence pyramid. However, randomizing is often not feasible or socially acceptable. "*Temporality*": The fact that an exposure happens before an outcome does not automatically imply that the association is causal; however, if this chain of events is not present, causality can be ruled out. "*Strength of the association*": It is more difficult to explain away a strong association as bias or confounding. Associations with a relative risk above 2.0 are as a rule of thumb considered being strong. "*Dose-response/ Biological gradient*": Confounding and bias are generally thought to have less explanatory value if the outcome of interest increases or decreases steadily in tact with increased exposure to the predictor; for instance if lung cancer increases with increasing number of inhaled cigarettes or psoriasis development increases with increasing BMI. However, it is important to recognize that other biological patterns can also be present; there may be a threshold pattern with increase only after a certain threshold, or a J-shape, where small doses of the exposure have a positive health effect, while larger doses do not.[24] "*Biological plausibility*": Are there plausible biological mechanisms that can explain the association? This criterion is limited by the status of current knowledge. "*Consistency*": Consistency of results supports causality, but there are many reasons why population-based studies may end up with different results, without this implying that the found data are incorrect. Consistency could also mean that there is consistent bias or confounding in all surveys, and must thereby be used with caution. "*Coherence*": Coherence between laboratory and experimental data as well as epidemiological and clinical data increases the likelihood of causality. The cause and effect relation should not conflict with the known facts, also this limited by present knowledge. "*Specificity*": The more specific the association between a

predictor and an outcome is, the bigger the probability of a causal relationship. Lastly, "*Analogy*": The effect of similar factors must be considered.[154]

5.1 Methodological considerations

5.1.1 Validity

Validity can be separated into two components; internal validity, dealing with the degree of systematic errors in the study results or internal truthfulness; and external validity or generalizability (see also discussion of main results), dealing with the extent to which the results can be generalized to be valid in other populations.

High internal validity is a prerequisite in order to be able to draw the right conclusions in any study. An observed association between an exposure and an outcome may be real (causal or non-causal) or have three other possible explanations, which are threats to internal validity: 1) Chance (random error); 2) Bias (systematic error); and 3) Confounding.[155] All epidemiological studies wish to estimate the exposures and outcomes of interest with a minimum of error, but there will always be some level of error in any study.

Precision refers to the reproducibility or repeatability of a measurement, and is a measure of random error or sampling error, something which can never be completely avoided in epidemiological studies. Precision is statistically expressed by confidence intervals, and is dependent of a study's size/ power and design.[147] Generally, sample errors are reduced when using a larger study sample, as in the present population-based study. Bias is defined as the deviation of an estimate/ measurement from the true quantity to be estimated; in a study setting, this would lead to a systematic error.[24] Mainly, bias related to study design and procedures is categorized into two groups; selection bias and information bias. Sometimes these types of bias are intertwined, and not easily separated.[24] Some consider confounding to represent a third type of bias, but this will be handled separately here.

Performing our study within the Tromsø Study meant that all overall procedures regarding design, recruitment, data collection and data management were handled by the quality assurance and quality control procedures of the Tromsø Study; which in general holds high quality.[131] However, taking part in a large general health study limits the possibility to make extensive questionnaires and procedures, for instance in terms of skin disease, in order to minimize the total toll on attendees.

5.1.1.1 Selection bias: psoriasis, overweight and smoking

The attendance rates of the Tromsø study are still well above the often used threshold of acceptability at 60% in high-quality surveys.[131] Rates below this are thought to give a greater risk of selection bias, which is "a systematic error in a study that stems from the procedures used to select subjects and from factors that influence study participation."[155] The common element of such biases is "that the relation between exposure and disease is different for those who participate and those who do not participate in the study."[155]

Declining participation rates in health surveys are well documented.[156-158] Reasons for this are thought to be related to several aspects; invitations to several health related research projects; confusing the invitation with marketing/ advertisement; unwillingness to participate when there is no immediate benefit associated with this; general decrease in willingness to volunteer in the society; lack of trust in research due to prior experience; the informed consent leaflets are too difficult to understand, and the time burden of participation is becoming too large.[131,158] The subjects who have declined participation tend to be younger or very old.[131] The proportion of men has always been higher among non-attendees, e.g. overall attendance rates in men/women in the different surveys; Tromsø 2: 74%/ 82%; Tromsø 4: 70%/ 75%; Tromsø 6: 63%/ 68%.[130] In the last two surveys, the participation rate was higher among those who had taken part in previous surveys, than among first time invited subjects.[131] In T6 (2007-08), the participation rate was similar in all age groups among first-time attendees, except for the oldest age group. In the age groups 25-29 in T4, 30-34 in T5, and 30-44 in T6, the attendance rates were below 60%. In T6, there were relatively few persons invited and even fewer attending in the youngest age groups with attendance of 44% in men and 58% in women below age 45.[131] This gives a larger risk of selection bias and potentially reduced validity of the estimates from these age groups, in particular among men.

Non-attendees tended to be single, consistently throughout the surveys. In the last survey, 59% of attendees were married versus, 41% of non-attendees.[131] When comparing with central statistics, the educational level of attendees in T6 was somewhat higher than the general population in Tromsø and Norway.[131] A study comparing those who only returned the first questionnaire in T4, with those who returned both questionnaires, found that there was a slight increased proportion of men (12.6% versus 10.9% of women) and smokers. Differences in age, BMI, blood lipids and blood pressure were minor. This suggests that those who do not return the second questionnaire, something which is the largest source of missing on the

psoriasis questions (placed in Q2) may be slightly overrepresented in terms of smoking, but otherwise coherent with other attendees.[159] Unfortunately legal restrictions from the Norwegian Data Protection Authority have not allowed for analysis of morbidity and mortality in accordance to attendance. A study within the cohort showed that the age- and sex-adjusted total mortality for those who were invited to T4 differed between those who had attended T2-T4 (6.9/ 1,000 person-years) and those who were invited to all three surveys, but only attended T4 (11.1/ 1,000 person-years).[130] Overall, this may indicate that constant attendees may be healthier and have lower overall mortality than the general population, or that they have a health effect from attendance. The possible healthy survivor bias among the elderly who attend the survey may influence the effect estimates, and will most often lead to underestimation of the true association, when investigating associations between exposures and disease.[130]

A different selection bias problem would arise if the study population was recruited in terms of psoriasis, which often exists in studies from dermatology clinic in- or outpatient settings, because the degree of psoriasis seen here is not representative of the normal population with psoriasis. The same type of problem can develop, when persons are specifically invited to be screened for skin conditions, something which has been done to investigate psoriasis prevalence.[160,161] Another frequent approach used to assess psoriasis incidence, prevalence and related comorbidities is the utilization of health or insurance registers. Several frequently cited publications have come from the UK General Practice Research Database (UK GPRD) where approximately 7% of the UK population's diagnoses are registered from the participating general practitioners. This allows for a more truthful investigation of the burden of psoriasis in a general practice population; however study participants may represent a slightly selected group who visit their doctor with current health problems.[126]

Importantly, as psoriasis was only one of a broad panel of diseases in the Tromsø Study questionnaires, it is less likely that participation was differential by psoriasis status. Moreover, there was no publicity to recruit individuals with psoriasis prior to the surveys. A hallmark study from Sweden in the sixties showed that individuals who do not attend general health examinations are no more prone to have psoriasis.[44] However, psoriasis is more recently seen associated with both obesity and depression among others, which could potentially lead to less recruitment of individuals with psoriasis into the study. In our analyses we found that those who reported psoriasis had a lower educational level and a higher frequency of smoking in both genders in the investigated time period, and that they were also increasingly

overweight, especially in women. Both obesity as well as other unhealthy lifestyle exposures, like smoking, are linked to lower socioeconomic status and educational level.[134,162,163] Longitudinal studies have demonstrated a tendency to recruitment of healthier individuals in cohort studies.[130,131,156] It is therefore a concern that persons with psoriasis, as well as those who are obese or smokers may be slightly underrepresented in the Tromsø study cohort, which may lead to attenuation of the effect estimates in our analyses.

We reduced our sample somewhat in our analyses in order to minimize selection bias in the birth cohorts or age groups which may not be sufficiently represented. Furthermore, we performed sensitivity analyses to see if those who had missing data on psoriasis status as well as exposure data influenced the results, and no such indication was found, indicating limited bias due to missing. In conclusion, it is less likely that a large selection bias exists in the present studies (Paper I-III).

5.1.1.2 Information bias - misclassification

The design of questionnaires that correctly identify exposure and disease status may be challenging. Preferably an international well validated screening tool for psoriasis would have been used, but upon study start this did not exist. To date, there are not even international diagnostic criteria for psoriasis, which makes it more difficult to assess the disease. Information bias refers to; "a distortion of an estimate which occurs when measurement of either the exposure or the response is systematically inaccurate."[164] Measurement errors when measuring categorical variables may lead to misclassification, while measurement errors in continuous explanatory variables or covariates may lead to errors in the effect estimate.

Misclassification bias upon assessment of psoriasis

A dermatologist's skin evaluation and diagnosis is the gold standard in assessing psoriasis. The lifetime prevalence of psoriasis, which was the main measure of psoriasis in this study, is a specific subtype of period prevalence, which sets to define the proportion of the population who experienced psoriasis sometimes during their lifetime up until the time of assessment.[24] When assessing point prevalence it is easier to correctly determine who has the disease in question at that time point; however, with a chronic relapsing disease like psoriasis, this approach will most likely underestimate the true burden of the condition.

"Misclassification bias is a form of information bias where persons in the study are erroneously placed in different exposure or outcome categories. This misplacement can be

non-differential, meaning that the degree of misclassification is independent of case or control status, or it can be differential, meaning that the degree of misclassification differs between the two groups examined. In general it is said that non-differential misclassification leads to a weakening of the true association between a dichotomous exposure and an outcome, while differential misclassification can bias the association either towards or away from the null hypothesis."[24] The extent of this phenomenon can in most cases be measured through validation studies.[165] A validation study sets out to assess if a test, in this instance a questionnaire, has the ability to distinguish between those who have psoriasis and those who do not.[24] The key concepts here are; sensitivity; which is the ability of the test to correctly identify those who have the disease of interest, in this case psoriasis, and specificity; which is the ability of a test to correctly identify those who do not have the disease.[24] Ideally one could measure the degree of misclassification in each case and reclassify them, something which is very time consuming and often impossible, or use the information from a sample of the data to adjust the effect estimates on a general level.

Due to the fluctuating course of psoriasis, the validation of lifetime psoriasis through point prevalent examination or relying on medical record from a short timeframe, may lead to an underestimation of the lifetime prevalence of the disease.[36,166] Inspecting and interviewing all persons who have reported a psoriasis diagnosis over the years from 1979 to 2008 was not possible due to time and resource constraints, as well as the fact that some of the participants were no longer available for questioning. Medical records from the practices of the multitude of general practitioners in Tromsø, who attend to the majority of patients with psoriasis, were not available. Point prevalent skin inspection after the end of survey in T6 would have given an indication of the burden of psoriasis in the population of Tromsø at that time, but it would not have given a complete answer as how to determine if the persons who did not have active lesions had experienced having psoriasis at some point in their life or not; nor would it give a complete answer to what percentage of the participants were false negatives.

Self-report of psoriasis has been used in several studies,[3,21,32,34,49,167] but has rarely been validated with physical examination (discussed in Paper I-III). Generally self-reported data give a larger risk of misclassification and represent a potential weakness in study design and interpretation. Validation studies have used different approaches to assure a correct diagnosis with conflicting results. Those who have done a physical examination within short time of self-report of current symptoms or validated through patient records have found relatively acceptable sensitivity of self-report.[37,101,160] Data from the Nurses' Health Study showed that

92% of self-reported psoriasis cases were definite cases of psoriasis;[101] however a higher sensitivity of self-reported diagnosis may be expected among health care workers. Several studies have pointed out that up to 50% of psoriasis cases (generally mild) may be undiagnosed by a doctor,[34,160,168] something which could potentially attenuate the effect estimates. Due to the healthcare system being free and easily accessible for everybody in Norway the degree of undiagnosed and underreported psoriasis might be smaller in our study than in many other countries.

In order to perform a trend study, and assess the prevalence of psoriasis at different time points, we needed to use the same question to assess psoriasis for comparability. The small difference in phrasing of the question used to assess psoriasis from T2-T6 is not thought to contribute to a change in the classification of the status, but ideally all questions would be exactly the same and asked in the same order and graphical display in the questionnaire. The reproducibility of self-reported psoriasis between the first four surveys and T6 was between 84% and 91%, meaning that when persons were asked regarding their psoriasis status they consistently reported the same status in the questionnaire if they previously reported a positive psoriasis diagnosis.[24] The ability to recall prior status by repeated attendees was time dependent, and may indicate that individuals, whose disease has not been active for a while, may forget to disclose a prior positive status due to recall bias. Recall bias may lead to misclassification bias and in this case a smaller prevalence estimate in high age. Thus, the oldest birth cohorts were excluded from the study samples in order to minimize information bias in all studies.

Due to the fact that most other studies have used questions regarding doctors' or nurses'/ health personnel's diagnosis of psoriasis; in T6, the question "Have you ever been diagnosed with psoriasis by a physician?" was added for validation and comparability purposes. In 2007-08 (T6), 89.9% of female and 83.6% of male self-reported psoriasis cases reported diagnosis by a physician. A large Norwegian as well as Danish twin gene study using self-reported psoriasis data, where the Danish questionnaire asked whether the psoriasis diagnosis was given by a doctor, both found identical figures in the heritability of psoriasis, indicating a good overlap between the questions.[48,49]

According to validation studies from comparable populations, most cases of psoriasis are adequately diagnosed by trained general practitioners.[36,169,170] The rate of doctor's diagnosis of the condition in our cohort is reported to be similar to other studies from developed

societies.[161,171] Importantly, psoriasis has a strong hereditary component and its characteristic appearance is often known among family members. Prior studies have found that persons with skin disease tend to not seek medical attention,[34,37,161,171] and that there may be a gender difference in the degree that they seek consultation.[37] Men are in general known to have a higher threshold for seeking medical consultation, and reported a lower rate of physician's confirmation of psoriasis diagnosis in T6. Also in T6, a question to self-evaluation of present disease severity on a scale from one to ten was added. This question was placed in a separate section for follow-up questions in the last part of the second questionnaire (Q2), and generally had lower response rates. Among those who answered, 15.1% stated no symptoms (0), 56.8% mild (1-4), 22.5% moderate (5-7), and 5.6% stated severe symptoms (8-10). The level of self-assessed present disease severity was slightly lower than in the studies based on health databases, as could be expected,[37,117,161] and in line with the validated results from the Rotterdam cohort study (Tromsø/ Rotterdam: Mild= 72%/76%, Moderate to Severe= 28%/24%).[169] In Paper I, those with a reported doctor's diagnosis who indicated current psoriasis severity 0-1 in T6 were combined and defined as having no symptoms. Among those not reporting a doctor`s diagnosis and answering the severity questions most of the persons reported no or mild current symptoms, suggesting that they might not see their chronic relapsing skin disease as an issue in need of present treatment.

We also linked data from the 2007-08 survey (T6) with the Norwegian Prescription Database (NorPD) and found that approximately 50% of the cases reporting psoriasis had received one or more psoriasis prescriptions (median = 2) in the time interval around T6. Information on medication from NorPD was attempted used as a proxy for disease severity (see Paper III). Disregarding missing entries, misclassification psoriasis diagnosis, or that the drugs were given for other diagnoses; these data indicate that half of the psoriatic population was in remission, did not seek medical treatment, or received climate therapy, UV-treatment or other hospital based treatment in the time period. This is in line with other studies who have validated self-report of psoriasis and find that approximately 25-70% have point prevalent disease at the time of survey.[34,161,168,172]

The approximate six year time laps between the surveys in the Tromsø Study give some uncertainty as to when in the time period their psoriasis status may have changed; thereby relationships with incidence rates and duration of psoriasis disease could not be investigated (Paper II and III).

Our findings confirmed the relationships reported by others between daily smoking, higher BMI, and an increased risk of psoriasis.[1,22,25,93] This supports the validity of the self-reported psoriasis data collected in the Tromsø Study. It is unlikely that a misclassification of psoriasis explains the positive associations of psoriasis with overweight, weight gain and the metabolic syndrome in this cohort. One could expect even stronger associations with a more specific definition of psoriasis.[116,147] However, limiting the analysis to include only participants reporting a physician's diagnosis led to a slight reduction in the effect estimates for the metabolic syndrome (Paper III). This may be due to chance or reflect a detection bias in physician's diagnosis where persons with a less favorable metabolic profile consult their physician less frequently. Due to the small number of psoriasis cases without confirmed diagnosis, this could not be further evaluated.

Misclassification bias upon assessment of BMI, weight change, MetS and smoking status

All clinical measurements were performed with standardized procedures by health professionals in the Tromsø surveys, ensuring high validity, unlike many studies that have relied on self-report of weight and height. Using BMI as a tool to assess overweight and obesity has some limitations, especially in men, who have a higher muscle mass and larger bone mass. Thus, there is a risk that BMI overestimates adiposity. This may be indicated by our data, as different thresholds for men and women in regards to BMI as a risk factor for psoriasis development were suggested (Paper II). Waist circumference has proven to be a better measure of abdominal obesity, and was available for the full population sample in the 2007-08 survey (Paper III).

The degree of tracking between baseline BMI and later BMI is high in the Tromsø cohort,[173] as those who are in the higher BMI categories continue to be in the same category or increase over time. As 90% of the population increased in weight in the time period, the measured weight at the different time points was most likely representative or a slight underestimate of the past five year time period. When studying adult weight change in T4 participants, we found that in general, the largest weight gain in the population happened until middle age, after this the weight stabilized in both men and women (Paper II). Upon baseline in T4 a majority of men were already overweight; while women had the largest change in mean body weight in the time period from 1994-95 to 2007-08 (Characteristics, Paper I). Thus, the weakness in terms of interpreting the effect of BMI on incident psoriasis might be most important for women, as a prior study supported that short-time weight gain does not seem to

be the most important factor for triggering psoriasis development.[86] Furthermore, our results indicate that the biological effect of BMI in psoriasis is dependent of the reach of a biological threshold; thereby the time lapse between the surveys may not be a large concern.

Our validation study from a subsample of repeat attendees who had measured weight around age 25 and reported weight at age 25 found a strong correlation of R= 0.89, supporting the validity of this approach. The validity of recalled weight gain in adults has also been investigated in other studies, and found to be an acceptable method.[143,144] Although participants tend to slightly misreports; in two US studies females underestimated their weight by -0.8[143] to -1.4 kg,[144] while men overestimated their weight by +2.3 kg.[143] With increasing age and increasing BMI respondents tend to underestimate their own weight at age 25.[143] However, although this measure is not 100% accurate, it gives a good indication of the approximate weight at age 25.

Underreporting of smoking in epidemiologic studies is common and may constitute a validity problem, leading to biased association measures. There is a risk that persons may not be completely truthful when answering questions on known unhealthy exposures to health professionals or insurance companies/ claims. It is more likely that the listing of exposures through an unidentifiable questionnaire, will lead to more truthful results. An older Norwegian study found a strong association between self-reported smoking habits and the measure of serum thiocyanate, if the questions used for assessment were asked in a neutral setting.[136] In a recent validation of self-reported tobacco use against nicotine exposure assessed by plasma cotinine in a Norwegian cohort, the sensitivity and specificity for self-reported daily smoking, using 30 nmol/l as the cut-off concentration, were 82% and 99%, respectively.[137] Similar concordance rates in both genders have been supported by others.[174] All data in the Tromsø study were gathered in a self-administered questionnaire in a neutral setting, which supports the validity of the smoking questions. However, the degree of smoking will probably be underreported.

The level of daily smoking has been gradually reduced in Tromsø and Norway in general over the past four decades. It comprised over 50% of men and 30-35% of women in the early seventies, and was steeply reduced among men up until today, with a delayed reduction rate in women mainly from the millennium (Paper I). In the last Tromsø survey (2007-08), 19% of men and 22% of women were smokers. A stable 10% of the Norwegian population smoke occasionally over the past four decades.[175] Repeated cross-sectional analysis (Paper I) from

the Tromsø cohort shows that men have increasingly quit smoking compared to women in the time period. Persons may have given up smoking in the time-period between baseline and debut of psoriasis, something which may attenuate the effect of smoking in terms of odds of psoriasis.

An accredited laboratory was chosen to perform the laboratory tests, which were also performed within uniform procedures of collection and analysis. However, when evaluating the psoriasis−MetS association in Paper III all blood samples were taken non-fasting, which could lead to non-differential misclassification of serum lipid levels and bias the association towards the null value.

5.1.1.3 Confounding and interaction

Confounding

Confounding exists "when an association between a given exposure and an outcome is observed as a result of influence of a third variable. This factor must be causally associated with the outcome and causally or non-causally associated with the exposure."[24] In other words, there may seem to be an association between an exposure and an outcome, for instance psoriasis and the metabolic syndrome, when the reality is that this is related to the influence of a third (or more) variable(s). Confounding describes a true, but potentially misleading association between an exposure and an outcome, which can influence the interpretation of results incorrectly. In order for the confounder to have an impact on the results, it must be unequally distributed in the groups which are under comparison. Confounding can never be totally removed; however, it can be minimized through study planning and analysis methods. If possible, randomization of subjects leads to a larger chance of actually "comparing like with like." Stratification and statistical adjustment through multivariable analysis is another way of searching for other explanations for the found estimate.

Many of the traditional risk factors for psoriasis can be considered confounding factors when evaluating the relationship between psoriasis and potential comorbid conditions like the metabolic syndrome. Psoriasis has a major impact on a person's quality of life.[10,167,176] This may lead to unhealthy lifestyle choices, which in turn, increases the risk of several diseases. In the Tromsø Study detailed information on lifestyle confounders was assessed, and thereby we could adjust our effect estimates in multivariable regression models (e.g. physical activity, alcohol, smoking), and further stratify analysis to control for the effect of confounding factors

(e.g. smoking). There is also the possibility of residual confounding in any association, meaning that the confounders in question are unknown or not a part of the analysis (see also discussion of main results).

Heterogeneity of effects- Interaction

Interaction is present when "the association between a risk factor and an outcome differs in subgroups of the population,"[165] most commonly by age or gender, but also by several other potential risk factors. Statistically defined interaction exists if the product term between two exposures is significant at a p-level of 5%. This relationship between exposures was examined in all the three papers. Interaction is often dealt with by stratified presentation of the data or the introduction of multiplicative interaction terms in multivariable regression models and was explored in our data.

According to Rothman you can have a biological interaction or synergism indicating that the combined effect of two factors leads to a more or less than additive effect of each factor in itself.[147] This was something we explored further in Paper II in relations to the combined risk of overweight and smoking on psoriasis development.

5.1.2 Ethical considerations

The fact that so much information is gathered from so many individuals without too large intervention in the Tromsø Study, based on the principle of "benefice and non-maleficence," leading to multiple high-quality research publications from several research groups supports ethical research. The autonomy of the participants is respected and they are treated with dignity in all chains of the study. The information given to the study cohort has become more extensive through the years. As of T4 written consent is obtained and stored according to new regulations; while prior to this consent was given through participation. This consent can be withdrawn at all times. There are plans for follow-up of acutely deviant results which are serious or potentially life threatening from the different research groups before each survey, as well as measures to insure that persons do not receive unwanted information. The gathering and storage of biological samples and data is done according to laws and regulations, and all data are made unidentifiable before being handled over to the research groups.

5.2 Discussion of main results

5.2.1 Trends in psoriasis prevalence

Our finding of a doubling in psoriasis prevalence in a general population sample is consistent with the increased or high prevalence and incidence found by other population-based studies, [22,23,27,28,30,34,35,160] but not all.[36,177] Importantly, studies reporting trends in psoriasis occurrence are sparse and not uniform.[15,33,36] In a recent Danish health survey based study the self-reported prevalence of doctors diagnosed psoriasis was reported to be 7.1%,[23] and in line with a Norwegian study from the general population of Oslo.[22] This stands in contrast to the UK GPRD study which found a period prevalence of only 1.5% related to the total population,[36] and a similar figure from another general practice database study was recently reported from Sweden.[177] However, these database studies capture disease in all age groups from child to old age within a fairly short time frame, and may not give a total picture of the lifetime burden of psoriasis in adults. With a fluctuating disease like psoriasis there is a large chance that many chronic cases will be missed when assessing psoriasis prevalence, as individuals may not have visited their doctor in the investigated time frame. An American validation study supports that the relapsing and remitting course of psoriasis challenges the identification of prevalent cases in database studies.[166]

In the last Tromsø survey (2007-08), 11% of the population aged 30-79 years reported a present or prior history of psoriasis, which is higher than in other population-based studies in western societies;[15] but in line with recent results from Scandinavia.[22,23] In T5 (2001), the overall prevalence of psoriasis was 8.9% and the estimated doctor`s diagnosed prevalence was 7.7% which is fairly consistent with the results from Oslo Health Study (HUBRO; 2000-01), another population-based study (n= 18,770), reporting a doctor`s diagnosed prevalence rate of 8.5% in adults.[22] Interestingly, a study from 1981 using data from a telephone interview commissioned by Statistics Norway, where persons were asked to report any diseases, showed large regional differences of psoriasis within Norway with a prevalence of 1.4 % in the south and 2.7-3% in the north. This difference in disease could be related to climatic differences, as psoriasis may be more frequent closer to the earth's poles.[20,47] There are biological explanations as to why this may be so, as will be discussed further in regards to the results of Paper II. The lower prevalence reported here compared to the prevalence in the second Tromsø Study (1979-80) of 4.8% could be due to the study method, where many might not come to think of a skin condition as a "disease", fluctuations in current symptoms, as well as

variation in sampling strategies.[39] Thus, our findings of a clear gradual trend of increasing self-reported psoriasis prevalence among both genders are supported by other studies among comparable populations,[22,23,29,30,34] but also extend existing knowledge representing a unique high prevalence and increase in trends in a general population located in Northern Norway.

An interesting finding was that we observed no change in self-reported psoriasis prevalence among 20-29 year old men and women in the time period from 1979 to 1994. Similar observations were found both in Sweden in a study of 17-20-year old military recruits,[33] and in a Norwegian study of twins below age 31 years (birth cohorts 1967-79) performed over a shorter time frame.[32] These results are contrary to the results observed in North American children.[29] The fact that the prevalence in the youngest study participants, with early onset cases, has not increased may partly be explained by different immunological patterns and genetic susceptibility between individuals with early and late onset psoriasis, or be due to differences in the cumulative exposures to lifestyle risk factors.[17,178] Unfortunately the youngest cohorts were not invited to the two last surveys in 2001 and 2007-08. The increase in psoriasis prevalence among adults may be mainly related to late onset cases, which are suggested to be more influenced by environmental factors like lifestyle. However, a higher prevalence of psoriasis was also found among persons in their thirties in the last surveys, questioning if the trend may be developing also among those with earlier disease onset (Paper I).

Repeated cross-sectional studies within the same population as presented in Paper I always bear the risk that other influences in the time frame can affect both exposure and outcome estimates. Changes in diagnostic criteria over time may lead to different definitions of disease and make it difficult to evaluate time trends. However, there have been no changes in diagnostics of psoriasis over the past decades. Specific health programs determined to change behaviour, could also affect exposure or outcomes, and must be taken into account when evaluating prevalence trends. However, psoriasis has not been a disease of high interest in the Norwegian media or public, nor has it been a prioritized disease by the Norwegian health authorities. We cannot rule out that increased awareness of psoriasis among physicians and the public, as well as a general higher use of health services over the past decades have contributed to the observed time period effect. Meanwhile, the self-reported prevalence of the chronic skin disease atopic dermatitis, which has been in substantially higher focus in the study population, did not increase among adults in the Tromsø cohort in the time period from 1994; where we saw the main increase in psoriasis and supports that changes in awareness

may be less like likely to explain our results. However, one could argue that this is mainly a condition affecting children and young adults, and thereby a rise in prevalence due to increased awareness may first be detected later.

Prevalence estimates are inherently vulnerable to selection and information bias (see discussion on methodology),[179] but a stable pattern of selection or misclassification bias in repeated assessments of a prospective cohort should not influence estimates of time period effects. Our homogenous study population with high attendance rate, repeated assessments of psoriasis using almost identical methods, and strict overall study procedures strengthen the results related to changes in psoriasis. Due to the fact that the prevalence has more than doubled, increasing steadily over time in all age groups above age 29, and among all birth cohorts, supports that there has been a true increase in prevalence in the time period.

In a genetically stable population, changes in the frequency of chronic non-communicable diseases, like psoriasis, over a fairly short time frame will most likely be explained by environmental factors. When evaluating population characteristics over the surveys used to assess the time trend of psoriasis prevalence it is evident that smoking and overweight are frequent modifiable risk factors associated with psoriasis.[22,25] The difference in frequencies of lifestyle exposures between the group with self-reported psoriasis and those without the disease in each survey, is consistent with the hypothesis that changes in these exposures may influence psoriasis prevalence (see discussion main results Paper II).

These prevalence trend data represent the general population of North Norway, but may not be reproducible in countries with different genetic backgrounds, socioeconomic development and climatic conditions. The low level of non-Caucasian attendees did not allow for any sub-analysis based on ethnicity, and would limit the generalizability, should the increasing trend in psoriasis be limited to specific ethnic groups. However, recent data report doubled prevalence of psoriasis in the Chinese population above 40 years during the last decades,[35] and even though they are substantially lower than among individuals with Europid decent,[15,22,23] the increasing prevalence and incidence found on multiple continents suggests a global trend,[15,30] and generalizability of our findings to other populations.

5.2.2 Overweight, weight gain, smoking and risk of psoriasis

Our results, showing that men and women with excess weight had 32-71% higher odds of psoriasis onset, are supported by others.[25,101] Setty et al. found increasing risk of psoriasis within increasing BMI categories at baseline, from a RR of 1.40-1.48 in the overweight and obese to a RR of 2.69 in the severely obese category.[25] They also found a 20% reduced risk of psoriasis among those in the lowest WHO category.[25] This was further supported by a later study from the same cohort.[101] Upon analysis it became clear that the relationship between overweight and psoriasis was limited to a cut-off placed around BMI 27 kg/m^2 for women and 28 kg/m^2 for men, and to our knowledge this has not been explored in prior studies. This difference is likely due to the higher musculoskeletal mass in men, whereby they need higher BMI measures to indicate adipose tissue (see discussion of methodology). Overweight above BMI 28 kg/m^2 gave an indication of 40% and 45% increased odds of psoriasis in women and men respectively and no gender interaction. Upon stratification for smoking in order to further disentangle the independent effect of overweight, the results were strengthened in non-smokers overall. We did not have a sufficient number of underweight or severely obese cases to investigate this association.

Further, mainly cross-sectional and case-control, studies have also supported the relationship between overweight and psoriasis. A recent meta-analysis concluded that individuals with psoriasis have an over 50-60% increased odds of being obese compared to the general population,[97] with dose-response dependency between the severity of psoriasis and the odds of obesity.[97] A large UK study also supported that overweight and obesity both represent risk factors for psoriasis within a case-control design, reporting a 11-33% increase respectively,[28] even though, this analysis was limited due to unstandardized procedures and lacking information on major adjustment variables. A smaller Italian case-control study containing new onset psoriasis cases (within the last two years) found a graded positive association with both overweight (OR 1.6; 95% CI: 1.1-2.1) and obesity (OR 1.9; 95% CI: 1.2-2.8),[77] while a Swedish study of new onset cases (within the last year) matched with healthy controls found a 9% increased risk of psoriasis with each unit increase of BMI, and concluded that persons who were obese had a two-fold increased risk of psoriasis.[86] Psoriasis cases that are recruited to dermatological specialty clinics may be more severe than those found in the general population, and this together with further differences in study design and populations, may explain the slightly lower effect estimates found in our data.[77,86]

To our knowledge this is the first study investigating weight gain as a risk factor for psoriasis onset in men. In the female NHS cohort the multivariate RR of psoriasis in the highest weight gain category was 1.88, and there was a significant trend in the risk of psoriasis development according to adult weight gain. Our observation that weight gain from the age of 25 was associated with 70-90% higher odds of psoriasis from middle-age independent of weight category extends previous studies. In our data, belonging to the upper quartile of adult BMI/ weight gain led to a 70-90% increased risk of psoriasis compared to the first quartile among persons aged 45 years and above (*P* for trend over quartiles of BMI/ weight gain = 0.009/ 0.002. *P* for interaction between BMI/ weight gain and age = 0.03/ 0.02). Studies suggest that the different clinical phenotypes of psoriasis are genetically heterogeneous, and that there may be a difference in the genetics of plaque psoriasis of the late versus early onset type.[14,53-55] Our results suggest that overweight and weight gain may be a more important risk factor for psoriasis among late onset cases as also supported by a recent study in which patients with late onset psoriasis had a higher proportion of obesity and elevated waist circumference than the early onset group.[180] Contrary, data from the US Nurses' Health Study (NHS) found no indication of an interaction between age and overweight as a risk factor for psoriasis.[25] However, the investigated women were mainly middle-age or above and more representative of the late-onset psoriasis group. Furthermore, as the US has come further than Norway in terms of the obesity epidemic, their mean BMI may have been increased already at a younger age. Thereby, the greater effect of BMI on late onset cases could be due to the prolonged negatively influencing inflammatory environment of living with overweight/obesity, which leads to a cumulative exposure which can no longer be compensated by the individual; also it can be due to the fact that overweight over a certain threshold mainly presents later in life in our population; or it can be related to interactions with weakly predisposing genetic or epigenetic factors.

Our result related to excess weight and weight gain is supported by plausible biological mechanisms. Basic research indicates that adipocytes and activated inflammatory macrophages can play a role in both psoriasis and obesity.[97] Adipose tissue, especially in the abdominal region, is an active endocrine organ which plays a key-role in lipid and glucose metabolism, insulin mediated processes as well as inflammation and coagulation.[181] The tissue produces several hormones, adipokines, and a whole variety of pro-inflammatory cytokines important in both psoriasis as well as cardiovascular disease, among these IL-6 and TNF-α.[42] Also, obesity-related hyperinsulinemia promotes an angiogenesis state which may

also increase susceptibility to psoriasis, e.g. through VEGF (Figure 3, page 20).[42,97,182] Interestingly, insulin resistance has been reported increased also in normal weight psoriatics.[183] Psoriasis remission following bariatric surgery has been reported,[184,185] and recently a small Danish RCT found improvement of psoriasis severity after a low-energy diet.[186] Case reports of improved psoriasis immediately after gastric bypass, before any weight loss has happened, have led to the hypothesis that the effect of gastric bypass could in part be related to an increase in the release of the hormone glucagon-like peptide-1 which lowers serum glucose and is suggested to have anti-inflammatory effects.[185] Thus, it is biologically plausible that persons who are genetically disposed to develop the psoriasis phenotype may be pushed in that direction from the metabolic and inflammatory changes that comes from weight gain and weight over a certain level.

Although the proportion of smokers in most westernized populations are declining, it is still the world`s leading cause of preventable death.[187] Smoking has been identified as a predictor of increased psoriasis risk,[86,90] and in our data present smoking was associated with a 92% increased odds of psoriasis in both genders combined. A recent longitudinal North American cohort study, combining two cohorts, also found smoking to be a strong predictor of incident psoriasis, with a relative risk for current smokers between 1.8 – 2.7, and displaying a dose dependency.[93] The US study indicated a 40% higher risk in prior smokers, but with decreasing risk with time.[93] In the Tromsø study cohort median smoke stop time in prior smokers in T4 was 10-14 years. This probably explains why past smoking was not an isolated risk factor for psoriasis in this cohort. The extensive chemical cocktail of tobacco smoke contains a wide range of substances with possible effects on both the central nervous system as well as skin and immune system.[110] Chronic smoking is known to induce oxidative stress and affect both the innate and adaptive immune system as well as being correlated with the production of several proinflammatory cytokines of importance to psoriasis.[93,188-190] Nicotine can alter the immune response by interacting with dendritic cells, T-cells and keratinocytes as well as by brain-immune interaction mechanisms, which may all be of importance in psoriasis.[77,188,191,192] The genetic component of smoking behaviour in terms of potential overlaps with risk loci for psoriasis, is not yet established.[110]

Previous studies have indicated greater health risks from smoking in women than in men,[77,86,193] something which was also suggested in our data. One theory has been that smoking leads to a reduction in estrogen levels which may influence immunological diseases like psoriasis.[87,194,195] Women had higher effect estimates when investigating the effect of

tobacco on psoriasis development; OR for female and male smokers versus non-smokers = 2.16/ 1.70. Although the risk estimates for men and women showed no statistical interaction or differences in trend overall, smoking represented a risk factor for psoriasis from the lowest pack-year category in women, while this was only apparent among those within the highest pack-year category in men.

An Italian case-control study investigating the combined effects of smoking and excess weight in both genders found increased risks of psoriasis among both past and present smokers, with odds of 1.9 and 1.7 respectively, and also here a higher risk in women.[77] There was indication of a multiplicative relationship between smoking and BMI in terms of psoriasis risk, with a OR for psoriasis of 3.0 (95% CI: 1.8-5.2) among those who were ever smokers and had a BMI $\geq$ 30 kg/m^2.[77] Interestingly, the US NHS cohort showed no material change in the multivariable risk estimates upon adjustment for smoking when evaluating BMI as a predictor for psoriasis in women.[25] It is biologically plausible that the effects of adiposity and smoking may act in concert to promote systemic chronic inflammation. In order to disentangle the effects of smoking and obesity, as well as evaluate potential synergism between the risk factors, we performed several analysis stratified for smoking status and also performed Synergy-score analysis as described by Rothman, to investigate potential multiplicative effects.[150] As smokers generally have a lower BMI there was a limited number of cases who were present smokers and overweight in our cohort. There was no indication of a multiplicative risk of psoriasis among persons exposed to ever smoking and overweight. However, the combined effect of smoking and overweight gave 2.3 times increased odds of psoriasis development in men and 2.7 times higher odds in women.

It is not biologically unlikely that the relationship between psoriasis and overweight could go both ways. Especially individuals with more moderate to severe psoriasis may have a systemic inflammatory milieu which could have influence on adipose tissue. Not the least, the psychological and physiological impairment of having psoriasis can lead to unhealthier lifestyle habits like overeating and reduced physical activity, something which in term can lead to overweight and obesity. A prior cohort study indicated an increased incidence of obesity in psoriatics,[100] but the validity of this result may be questioned as long as it is not clearly stated whether the analysis was adjusted for baseline BMI.

It is possible that the effect of BMI on incident psoriasis could be confounded or modified by other lifestyle factors, something which we tried to assess and adjust for through our

multivariable regression models. A recent prospective study of female nurses found that those who consumed more than 2.3 units of alcohol per week had a 70% increased risk of developing psoriasis. When sub-analyzing for beverage type, drinking non-light beer was the only significant predictor.[85] Another study from the same cohort found that vigorous physical activity was inversely associated with the risk of incident psoriasis in women, RR 0.73.[83] We observed only minor differences between the univariable and multivariable models when adjusting for alcohol intake, recreational physical activity, and educational level which corresponds to limited confounding by these exposures.

There is always the possibility of residual confounding from factors which are either unknown or not included in the analysis. There is ongoing work to identify further genetic loci as well as environmental factors and gene-environment interactions which can explain psoriasis.[179] There may be shared genetic variants that increase the susceptibility to both obesity and psoriasis, as shown in a recent publication on a SNP in the IL12B gene.[57] However, in a meta-analysis of four psoriasis GWAS cohorts there was no differences between psoriasis cases and controls in a weighted gene risk score investigating SNPs associated with increased BMI.[111] The suggested association between psychological stress, depression and psoriasis was not explored here.[81] A large percentage of psoriasis patients feel that stressful life events can influence their disease;[77,176] however, there are few longitudinal data on this topic, and conflicting results.[196] Interestingly, a recent study from the US Nurses' health study found persons who scored highly on depressive symptoms to have a greater risk of psoriasis development.[81] More research is needed on this important topic.[78] Another possible confounder is dietary composition. Novelly high salt intake has been associated with autoimmune disease.[197,198] There is a possibility that the association between overweight and psoriasis is due to dietary intake of for instance a large amount of highly processed foods containing high concentrations of salt, which theoretically may influence both the frequency of overweight and the prevalence of psoriasis.

Moreover, recent studies have suggested that the microbiome, or collective genome of microorganism that are residing in a given niche, may play an important role in immune homeostasis; where disruptions of the natural microflora, may cause immune dysfunction or autoimmunity.[199] If increasing BMI is correlated with changes in the microbiome or infection susceptibility;[200,201] then the association between BMI and psoriasis risk may be in part due to these aspects. However, studies are limited as of today.[202] Importantly, some studies have found an association between upper respiratory infections and subsequent development of

psoriasis, as well as psoriasis exacerbation.[28,68,71,72] A study from the UK GPRD found an over doubled risk of psoriasis onset within one month of a respiratory tract infection with an unknown pathogen among individuals age 21-40, and increased risk was also seen after infectious episodes within the last year.[28] However, it is unclear if these results were adjusted for seasonality, as psoriasis and airway infections are both generally more common in winter time. Small scale studies have shown improvement of psoriasis after tonsillectomy; suggested to be related to a reduction of circulating T-cells that recognize streptococcal determinants as well as homologous skin determinants.[203] A recent publication showed that the culturing of streptococcal extract with skin cells from subjects with psoriasis led to an activation of CLA+ memory T-cells and production of Th1, Th17 and Th22 cytokines, as well as other epidermal cell mediators.[204] Intra dermal injection of the activated culture led to epidermal hyperplasia in mice, supporting that streptococcal infection may be an agent for psoriasis initiation.[204] McFadden et al have postulated that some of the genotypic as well as phenotypic changes in different immunological pathways involved in psoriasis, give protection against mortality during epidemics on invasive streptococcal infections and allow for persons to become carriers of streptococci as well as predisposing them to develop psoriasis.[68] Also, patients with psoriasis have been seen to show larger colonization rates of *Staph aureus* on both lesional and non-lesional skin,[205] and have been suggested to be carrying more toxigenic *S. aureus* strains;[206] however, data are limited. *Staphylococcus aureus* nasal colonization is a major risk factors for later infections with the bacterium.[207] A Danish twin study investigating *S. aureus* colonization determinants, found that the odds for nares colonization were increased by 73% for those reporting psoriasis.[208] However, this analysis was not adjusted for BMI or blood sugar levels; which both represent potential confounders. In our research group, we found that obesity was a clear risk factor for nasal colonization with *S. aureus*, with up to 2.6 times higher odds of colonization among the obese compared to those with normal weight.[209] Perhaps the crosstalk between microbial determinants as well as host and environmental determinant play a role in the complex puzzle that is psoriasis.

Tromsø, and large parts of Northern Norway, have subarctic climate conditions with more than five months of negligible ultraviolet radiation exposure, making inhabitants vulnerable to Vitamin D deficiency, of possible importance for skin health.[69] Climate and UV therapy are widely used to treat psoriasis, and the therapeutic effect of topical vitamin D on psoriasis is well demonstrated. Increasing BMI is inversely related to the of serum level of Vitamin D; where obese persons need higher doses of Vitamin D to obtain the same serum levels.[210] It is

possible that the obesity epidemic may be especially important in the Tromsø study cohort as Vitamin D has been inversely linked to the severity of psoriasis,[69] as well as increased risk of bacterial colonization and infections.[211-213] We found that being in the highest serum tertile of Vitamin D compared to the lowest tertile (OR 0.44, 95% CI: 0.28-0.69) led to reduced colonization of *S. aureus* in the nares of men, who also had the highest colonization rates in the Tromsø study cohort.[214] Interestingly, rotating night-shift work in US nurses also seems to lead to an increased risk of psoriasis by approximately 20%, which has been suggested to be related to reduced levels of Vitamin D through less sunlight exposure during the daytime or a disruption of the natural production of melatonin.[215] Should the interruption of the circadian rhythm due to melatonin influence psoriasis, this may be of importance in the Tromsø study cohort, which spends three months of the year in consecutively sunlight or pitch darkness.

In order to discuss causality in an association it must first be established that the risk factor precedes the debut of disease, in this case psoriasis. The longitudinal study design allows us to determine that overweight and weight gain precedes psoriasis; that it leads to an up to 70-90% increased odds of psoriasis in our cohort, and that the combined effect of smoking and being overweight leads to a high risk of psoriasis development, with 2.5 times higher odds overall for both genders combined. The relatively strong effect estimates, the dose-response relationship between gain in weight or BMI and subsequent psoriasis risk, the threshold effect observed in the BMI-psoriasis association, the biological plausibility, as well as consistency with other studies, all support that this may be a causal relationship. Overweight and obesity, as well as smoking, represent modifiable risk factors which may be targets for both primary prevention as well as supportive treatment of psoriasis in both our and comparable populations. As this relationship was present only after middle-age this could indicate that the natural history of psoriasis is changing, as there is a substantial amount of new cases developing in the middle-age and above population due to lifestyle influence.

5.2.3 Association between psoriasis and the metabolic syndrome

In the cross-sectional study in Paper III we found that young women with psoriasis had an almost four-fold increased odds of MetS compared to women without a history of psoriasis. While, these odds decreased with age, the absolute difference in prevalence of the MetS between women with and without psoriasis remained quite stable. Men with psoriasis had a uniform 35% increase in the odds of MetS compared to men without psoriasis across all ages.

These results confirm the findings from the smaller NHANES survey,[116] as well as large-scale study from the UK GPRD;[117] as they suggest that the association between psoriasis and the MetS may be strongest among women. Despite having a general practice database design, an age range from 45 to 65 years, different assessment criteria for MetS and incomplete information on potential confounders, the UK study reported almost identical overall odds as our study, and the MetS was found in 34% of individuals with psoriasis versus 26% of controls.[117] Comparably, in our population; 33-39% of participants with psoriasis versus 25-31% of those without the condition were affected depending on the used waist circumference criteria, supporting the external validity of our findings. In the NHANES study, with subjects aged 20-59 years, 40% of psoriatics versus 23% of controls fulfilled the definition of the MetS; while in our study the doubled prevalence of MetS among individuals with psoriasis was present in young women only. However, the US study population had higher waistlines compared to our study population;[116] while a Danish study, which found no difference in distribution of the MetS in persons with and without psoriasis, had a lower mean waist circumference among attendees.[216]

Several studies from multiple continents and populations have indicated that psoriasis is associated with several of the components of the MetS, as well as the full syndrome itself, giving grounds for concern that persons with psoriasis may be at higher risk of subsequent diabetes and cardiovascular disease.[5,118,121] In the UK GPRD study, several components of the syndrome; namely obesity, hypertriglyceridemia and hyperglycemia, all showed dose-response relationships with the severity of psoriasis independent of other components.[117] Although a dose-response relationship between psoriasis and the full MetS could not be investigated due to restrictions in the data; there was a dose-response relationship between psoriasis severity, indicated through oral medication use, and abdominal obesity in women in age-adjusted analysis.

To our knowledge, all but two studies[116,216] estimating the psoriasis−MetS association have been conducted in clinical settings or within samples from insurance or health care databases,[117,118,217-221] something which potentially introduces a range of biases.[126,127,169,216,222] Truly population-based data with the ability to adjust for confounding factors as well as look at age and gender interactions have been limited, and lead to challenges when attempting to generalize the findings to clinical practice.[105] To our knowledge, no prior study has evaluated the risk of MetS in psoriasis by age and gender using non-linear risk models which generally give better fit to data than traditional linear models.[151] The MetS was assessed using the new

harmonized criteria including two cut-offs for measured WC. Further strengths include the largest sample from a general population survey; including a wide age-range, high attendance, comprehensive assessment of lifestyle factors and clinical examinations using standardized and validated methods by trained health professionals, performed within a short time frame.[131]

The mechanisms contributing to the U-shaped pattern by age in the psoriasis-associated odds of MetS in women in our study are not clearly understood. Abdominal obesity, which was the most frequent MetS-component in women, is also a key initiator of insulin resistance.[223] Prior studies indicate that for increasing levels of waist circumference women exhibit more adverse metabolic disturbances than men.[224] In women 30-44 years, approximately 75% of those with psoriasis versus 45% of those without psoriasis had a WC $\geq$ 88 cm. There have been large secular changes in lifestyle in the Tromsø Study population, and younger female birth cohorts have increasingly higher BMI and waistlines compared to prior generations (Paper I).[225] This may explain some of the U-shaped association of psoriasis with the metabolic syndrome. Among the elderly the prevalence of the MetS and hypertension in particular was high; in this age group about 80% had hypertension independent of their psoriasis status. This age-related increase in metabolic components is primarily driven by other factors than psoriasis, possibly attenuating the OR estimates.[147] Furthermore, the suggested higher cardiovascular mortality among individuals with psoriasis,[7,8,12] could produce lower effect estimates in the older age groups, due to a healthy survivor bias. In men the odds of MetS in psoriatics were almost uniform; however, here blood pressure was already increased from middle-age, and triglycerides decreased with age, possibly contributing to more stable odds ratios (Paper III).

Several potential pathophysiological mechanisms may link psoriasis with the metabolic syndrome.[42] The chronic skin inflammation with a Th-1 and Th-17 shift, leads to an increased production of cytokines like TNF-alfa and IL-6; which not only promote epidermal hyperplasia, but also antagonize insulin signaling, effect adipokine expression and mediate insulin resistance and obesity.[42,226] Conversely, the hyperinsulinemic state in the MetS could potentially promote psoriasis susceptibility or severity through increased chronic inflammation as well as increased angiogenesis.[33,215] Insulin-resistance has been seen to block keratinocyte differentiation, and may contribute in the pathogenesis of both psoriasis as well as metabolic and cardiovascular disease.[14,227,228] Furthermore, pleiotropic genetic loci (e.g. PSORS2-4, CDKAL1, ApoE4) suggest that there may be a common genetic susceptibility between psoriasis and the MetS.[226] Although women with psoriasis displayed a particularly unfavorable metabolic profile in our study; both genders had substantially elevated hs-CRP

indicating low-grade systemic inflammation, despite reporting mild or no present symptoms. It is plausible that psoriasis serves as a marker of a common genetic susceptibility bridging the association between psoriasis and systemic manifestations such as the MetS given the right environmental conditions, as supported by recent genetic and epigenetic studies.[19,111,112,229]

Our study extends present knowledge of the psoriasis−MetS relationship in comparisons with others by its thorough adjustment of important lifestyle factors.[125,126] However, factors which have not been evaluated in this study, including genetic predisposition, infections, diet and mental health, may lead to residual confounding of the association (see discussion of main results Paper II). The impact of Psoriasis arthritis on risk of MetS is also something which we could not assess, as data were lacking on this important comorbid condition. Recent data from psoriasis and PsA patients in a clinical setting support that those who have PsA may have even higher risks of MetS and cardiovascular disease than persons who are only affected from psoriasis.[105,230] Furthermore, several drugs given for psoriasis are known to induce weight-gain or affect the blood-lipid profile. Due to the low number of persons on systemic drugs in this study this was not further investigated. However, including statins to our multivariable model did not influence the results.

In order to evaluate causality, a longitudinal relationship between psoriasis and the MetS needs to be established; something which is not possible within a cross-sectional study design. Presently, it is not known if psoriasis is a driving factor behind the MetS or if the MetS leads to a debut and/or worsening of psoriasis.[121] Overweight influenced psoriasis development in our cohort (Paper II), and this could indicate that metabolic disturbances precede psoriasis; however, studies show that persons with psoriasis are more prone to develop diabetes and hypertension, independent of traditional risk factors like obesity.[231] The strong association in younger women, the indication of a dose-response relationship between psoriasis severity and having a high waistline in women, and the consistent results also after adjustment for lifestyle confounders; all support a true relationship between psoriasis and the MetS. Interestingly, some suggest that psoriasis should be treated aggressively in order to prevent escalation of severity as well as secondary comorbid disease; however the data supporting this view are very sparse.[232-236] If the reason for the comorbid conditions associated with psoriasis, lies in shared genetics or shared risk factors, than the aggressive treatment of psoriasis per se will not necessarily lead to a large influence on comorbidity. Should the comorbid conditions be related to elevated systemic inflammation, from substrates produced in the psoriasis plaques;

it seems a bit odd that persons with very mild or inactive disease, like the majority of persons in our study cohort, should show such an increase in the MetS, which we know to be a predictor of both diabetes and cardiovascular disease. More research is needed to disentangle this complex relationship (Figure 3, page 20).[105]

Targeted screening for metabolic and cardiovascular disease risk factors for psoriasis patients, especially in more severe cases, has already been suggested by several expert groups.[227,237-239] In order to recommend a secondary prevention measure, and identify persons with psoriasis, also of mild subtypes, as high risk subjects; there must be an either causal or unbiased statistical association between psoriasis and the MetS.[24] This means that even if the causal component behind the increased MetS in psoriasis is not clearly identified; the quality of our data, which is also supported by data from comparable populations,[116,117] suggest that the psoriasis seen on the skin surface may be a warning sign that a person has a higher risk of MetS and thereby subsequent diabetes and cardiovascular disease.

6. Main conclusions

The present population based cohort study among men and women, focusing on psoriasis time trends as well as risk factors for disease development throughout 30 years, supports a high and increased prevalence of this chronic skin disease. Moreover, the observed overweight epidemic represents a possible environmental risk factor in relation to the observed increase, and leads to further concern as a high burden of MetS is seen especially among young women with psoriasis. Specifically:

- There was a more than a doubled risk of reporting psoriasis in the sixth Tromsø Study (2007-08) compared to the second study in 1979-80, with a lifetime prevalence of up to 11%. This increase in prevalence could not be explained by specific birth cohort effects or population ageing, and this suggests that environmental factors play a role in psoriasis development in adults above age 29. Although changes in disease awareness may explain some of the reported increase, it seems likely that this time trend may partly be explained by lifestyle changes.
- Our findings support the results of others that overweight, weight gain and smoking represent modifiable risk factors that may be targets for primary prevention of psoriasis. Above a threshold BMI of 27-28 kg/m^2 both genders combined displayed increasing odds of psoriasis development, and adult weight-gain was associated with up till 70-90% increased risk of developing psoriasis from middle-age independent of weight category. No synergistic effects were found between psoriasis and smoking, however overweight smokers displayed the highest risk of psoriasis development with up to 2.3 and 2.7 increased odds in men and women respectively.
- The odds of having the MetS were substantially increased among individuals with psoriasis in the Tromsø study cohort, where 32% of those with psoriasis versus 24% of those without the condition fulfilled the criteria of the MetS. Young women displayed four times increased odds of having the MetS in multivariable analysis; while in psoriatic men there was a uniform 35% increased odds of MetS compared to men without the condition. Abdominal obesity was the most frequent MetS component in women in this study, and we observed a dose-response relation between psoriasis severity and odds of higher waistline in age-adjusted analysis.

7. Implications of study findings and further research

Psoriasis is a highly prevalent disease in a lifetime perspective; affecting approximately 1 out of 10 adults in the Tromsø population. Despite that participants reported lifetime diagnosis in our recent study, approximately 5% of attendees in the last Tromsø study had received a prescription for psoriasis within close proximity to the survey (2006-09), indicating high period prevalence of psoriasis, and the demand of considerable resources from the health care system in region North. While the total self-reported lifetime prevalence of psoriasis is highest in Scandinavia, doubled figures are also reported on multiple continents, suggesting a global trend, and generalizability of our results to other populations. Due to the impact of psoriasis on quality of life, as well as all the comorbidities associated with the condition, this could have an effect on public health worldwide.

Identification of environmental agents or mechanisms which may trigger psoriasis development, not the least giving the possibility to give targeted recommendations for prevention will be of importance for this large patient group, as well as benefit in the reduction of costs for society. The observed association between excess weight, weight gain and smoking on psoriasis onset may be explained by plausible biological mechanisms and is in line with results from others, making overweight and smoking possible preventive target in terms of psoriasis development. Considering the global obesity trend and high number of smokers, this finding is important also for other populations.

The substantially increased prevalence of the MetS among persons with psoriasis in a general population setting, with mainly mild disease, supports the priorly suggested screening of individuals with psoriasis for the metabolic syndrome from a relatively early age, in order to reduce the risk of diabetes and cardiovascular outcomes in this patient group. However, more studies investigating the causal mechanisms behind this association and potential benefit from screening are needed.

In further studies it will be interesting to explore the associations between overweight/ obesity and incident psoriasis within validated, more strict case definitions of psoriasis and within different phenotypes of psoriasis, as well as gaining detailed information on debut and severity, including data on potential PsA diagnosis. The prolonged follow-up period will allow for other analysis methods, better assessment of possible interactions due to increasing power, as well as repeated data from the cohort. As the degree of smoking is declining and

obesity is on the rise in the Troms Study cohort, it will be valuable to repeat these analyses in further studies to see if this influences the prevalence of psoriasis. Comparing data with other national and international cohorts will also be of essence, in order to validate findings and gain further information on the epidemiology of psoriasis.

To date, epidemiological analyses have been limited by established cut-offs for obesity and related biomarkers, which does not give a sufficient picture of the complex interplay between psoriasis and the total pool of metabolites, known as the metabolome.[240] We wish to further investigate the relationship between psoriasis, metabolic risk factors and cardiovascular disease using a novel high throughput method quantifying the total pool of metabolites, "the metabolome." Novel methods like metabolomics which take into account both genetic and environmental influence, may also give insight into the biological mechanisms responsible for the interplay between the metabolic state and psoriasis.[241] Characteristic combinations of assessed biomarkers could lead to pathway specific identification and risk assessments in patient groups, like psoriatics, even on an individual level.[240]

Over the years several cross-sectional and case-control studies have found an increased risk of cardiovascular risk factors as well as myocardial infarction and stroke among individuals with mainly moderate to severe psoriasis.[105,242,243] Nearly all studies to date were performed in patient or register populations without the possibility to adequately control for possible confounding factors, as well as being subject to several possible biases. Thus, the causality of the association between psoriasis and cardiovascular disease is still a matter of debate.[7,126,127,153,169,244] There seems to be a consensus that psoriasis patients with moderate to severe disease have more lifestyle-related cardiovascular risk factors, but there is still disagreement as to if psoriasis in itself represents an independent risk factor for cardiovascular disease.[6,7,127,244,245] Studies investigating whether the traditional Framingham risk criteria apply equally to psoriasis patients compared to the general population, indicate that these do not adequately assess the cardiovascular disease risk in persons with psoriasis.[245,246] Interestingly, the newly presented psoriasis cohort study from Rotterdam showed no increase in atherosclerosis or cardiovascular events among individuals with mostly mild psoriasis;[169] however, this cohort was limited due to a small sample size and selected age span of attendees. Recent meta-analyses have also pointed out discrepancies between truly population-based and register or clinic based results.[105,129]

Our research on the association between psoriasis and the MetS shows that there may be age and gender dependencies in the distribution of risk factors related to metabolic and cardiovascular disease risk among persons with psoriasis, as also supported by others.[116,117] The increased prevalence of MetS, as well as high fraction of smokers, among individuals with psoriasis suggests that more cardiovascular events can be expected in this patient group. The Tromsø Study includes in addition to self-reported psoriasis status and information on potential confounding lifestyle factors; measured metabolic and cardiovascular status through carotid ultrasound, end-point registry for cardiovascular outcomes, as well as biological samples for molecular analysis including DNA analysis. All of these data represent a unique resource for population-based research into the association between psoriasis and cardiovascular disease.

Furthermore, the suggested interplay between the host and the microbiome is an interesting new pathway for exploration. The microbiome of healthy human skin shows great diversity, and microbiota compositions of psoriasis plaques indicate differences from unaffected skin.[202] Changes in the gut or skin microbiota are hypothesized to predispose or influence psoriasis in genetically susceptible individuals.[247] A small RCT investigating the role of oral probiotics in systemic inflammatory disease found systemic effects of intervention, which supports that the immune modulatory effects of the microbiota in humans are not limited to the mucosa surface, but may also lead to systemic effects.[248] The Tromsø Staph and Skin Study research group performs interdisciplinary research and plans to explore this association, including the influence of latitude related factors, in future studies.

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Paper I

Paper II

Paper III

Appendix I

Questionnaire 1 & 2, Tromsø Study 2

A

Yes | No

Do you have, or have you had:

- A heart attack? 33
- Angina pectoris (heart cramp)? 34
- Any other heart disease? 35
- Hardened arteries in the legs? 36
- A cerebral stroke? 37
- Diabetes? 38

Are you being treated for:

- High blood pressure? 39

Do you use:

- Nitroglycerine? 40

B

Yes | No

Do you have get or discomfort in the chest when:

- Walking up hills or stairs, or walking fast on level ground? 41
- Walking at normal pace at level ground? . . . 42

If you get pain or discomfort in the chest when walking, do you usually:

1. Stop? 43
2. Slow down? .....
3. Carry on at the same pace? .....

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

1. Within 10 minutes? 44
2. After more than 10 minutes? .....

Do you get pain in the calf while:

- Walking? 45
- Resting? 46

If you get pain in the calf, then:

- Does the pain increase when you walk faster or uphill? 47
- Does the pain disappear when you stop? 48

Do you usually have:

- Cough in the morning? 49
- Phlegm chest in the morning? 50

C

Yes

Exercise and physical exertion in leisure time.
If your activity varies much, for example between summer and winter, then give an average.
The question refers only to the last twelve months:

Tick "Yes" beside the description that fits best:

1. Reading, watching TV, or other sedentary Activity? 51
2. Walking, cycling, or other forms of exercise at least 4 hours a week? .....
   (include walking or cycling to place of work, Sunday walk/stroll, etc.)
3. Participation in recreational sports, heavy gardening, etc.? .....
   (note: duration of activity at least 4 hours a week)
4. Participation in hard training or sports competitions, regularly several times a week?

D

Yes | No

Do you smoke daily at present? 52

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

Do you smoke cigarettes daily? 53
(hand-rolled or factory made)

If you do not smoke cigarettes at present, then:

Have you previously smoked cigarettes daily? 54

If "Yes", how long is it since you stopped:

1. Less than 3 months? 55
2. 3 months to 1 year? .....
3. 1 to 5 years? .....
4. More than 5 years? .....

For those who smoke or have smoked previously:

How many years altogether have you smoked daily? 56-57
No. of years

How many cigarettes do you smoke, or did you, smoke daily? Give number of cigarettes per day 61
(hand-rolled or factory made)
No. of cigarettes

Do you smoke tobacco products other than cigarettes daily?

- Cigars or cigarillos? 62
- A pipe? 63

If you smoke a pipe, how many packs of tobacco (50 grams) do you smoke per week?
Give the average number of packs per week. 64
No. of tobacco packs

E

Yes | No

Do you usually work shifts or at nights? 67

Can you usually come home from work:

- Every day? 68
- Every weekend? 69
- Are there periods during which your working days are longer than usual? 70
  (e.g. fishing season, harvest)

During the last year, have you had:

Tick "Yes" beside description that fits best

1. Mostly sedentary work? 71
   (e.g. office work, watchmaker, light manual work)
2. Work that requires a lot of walking .....
   (e.g. shop assistant, light industrial work, teaching)
3. Work that requires a lot of walking and lifting?
   (e.g. postman, heavy industrial work, construction)
4. Heavy manual labour? .....
   (e.g. forestry, heavy farm-work, heavy construction)

During the last 12 months, have you had to move for work reasons? 72

Is housekeeping your main occupation? 73

Have you within the last 12 months received unemployment benefit? 74

Are you at present on sick leave, or receiving rehabilitation allowance? 75

Do you receive a complete or partial disability pension?

F

Yes | No | Don't know

Have one or more of your parents or sisters or brothers had a heart attack (heart wound) or angina pectoris (heart cramp)? 77

Are two or more of your grandparents of Finnish origin? 78

Are two or more of your grandparents of Sami origin? 79

LABEL

TR - II

ADDITIONAL QUESTIONS FOR PERSONS ATTENDING THE MASS X-RAY EXAMINATION IN TROMSØ

Together with the invitation to attend you received a questionnaire from the National Mass Radiography Service. You delivered this questionnaire at the examination.

Cardiovascular diseases are, however, a complex group of diseases. The causes are still partly unknown. In Tromsø we are therefore trying to obtain a more complete description of factors which may be of importance for the course of these diseases, such as diet, psychological pressure ("stress"), social conditions, and occurrence of disease in relatives. We hope you will take the trouble to complete this questionnaire as well, an return it to the Tromsø Board of Health in the enclosed envelope.

All information in connection with the mass x-ray examination will be treated as strictly confidential.

I YOUR OWN DIET

1. What type of bread do you usually eat?
Tick the most appropriate box.

	YES
White bread *(e.g. French bread)*	1 ☐
Ordinary bread (light texture)	2 ☐
Whole meal (brown) bread	3 ☐
Home-made (brown) bread	4 ☐

2. What type of butter of margarine do you usually eat?
Tick the most appropriate box.

	YES
Butter	1 ☐
Ordinary margarine	2 ☐
Plant margarine	3 ☐
Soft margarine spread	4 ☐

3. How many slices of bread do you usually eat **daily**?
Tick the most appropriate box.

	YES
Less than two slices	1 ☐
2-6 slices	2 ☐
7-12 slices	3 ☐
13 or more slices	4 ☐

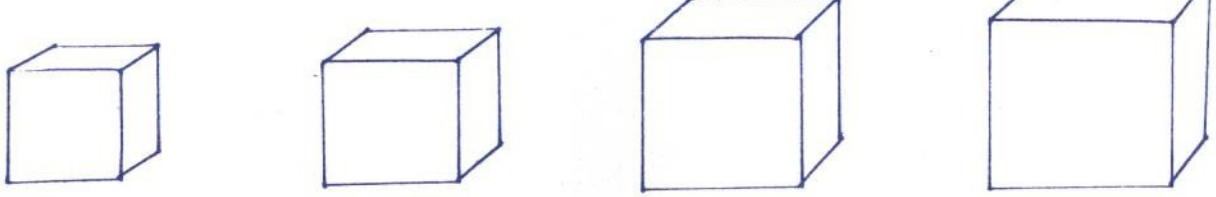
4. What type of milk do you usually drink?
Tick the most appropriate box.

	YES
Do not drink milk	1 ☐
Full cream milk: ordinary type or curdled	2 ☐
Skimmed milk: ordinary type or curdled	3 ☐
Mixture of full cream and skimmed milk	4 ☐

5. The drawings below show cubes of butter of margarine (actual size).
Tick the box above the cube which best resembles the amount you spread on a slice of bread.
If in doubt, try buttering a slice.

Do not use butter or margarine ☐

1. ☐ 2. ☐ 3. ☐ 4. ☐



6. How many glasses/cups of milk do you usually drink daily?
Tick the most appropriate box.

	YES
Do not drink milk, or drink less than 1 glass/cup	1
1-2 glasses/cups	2
3-4 glasses/cups	3
5 or more glasses/cups	4

7. How many cups of coffee do you usually drink daily?
Tick the most appropriate box.

	YES
Do not drink coffee, or drink less than 1 cup	1
1-4 cups	2
5-8 cups	3
9 or more cups	4

8. Are you a teetotaller?

	YES	No

If "No",

— How often do you usually drink beer?
Tick the most appropriate box.

	YES
Never or just a few times a year	1
Once or twice a month	2
About once a week	3
2-3 times a week	4
More or less daily	5

— How often do you usually drink wine?
Tick the most appropriate box.

	YES
Never or just a few times a year	1
Once or twice a month	2
About once a week	3
2-3 times a week	4
More or less daily	5

— How often do you usually drink spirits?
Tick the most appropriate box.

	YES
Never or just a few times a year	1
Once or twice a month	2
About once a week	3
2-3 times a week	4
More or less daily	5

9. Approximately how often during the last 12 months have you drunk so much wine, beer or spirits that you got drunk?
Tick the most appropriate box.

	YES
Have never been drunk, or have not been drunk during the last year	1
A few times during the last year	2
Once or twice a month	3
Once or twice a week	4
3 or more times a week	5

10. How often does your main meal consist of fish or fish dishes?
Tick the most appropriate box.

	YES
Less than once a week	1
Once or twice a week	2
3-4 times a week	3
5-6 times a week	4
7 times a week	5

11. How often do you eat fruit or vegetables?
Tick the most appropriate box.

	YES
Never eat fruit or vegetables	1
A few time a year	2
Once or twice a month	3
About once a week	4
2-3 times a week	5
More or less daily	6

12. How many times a month do you eat boiled or fried sausages, meat balls, other processed meat, etc.?
Tick the most appropriate box.

	YES
Never or less than once a month	1
Once or twice a month	2
3-4 times a month (up to once a week)	3
5-8 times a month (up to twice a week)	4
More than 8 times a month (more than twice a week)	5

13. Have you made any changes in your diet during the last 5 years as regards the following food items?
Tick each item in the appropriate box.

	As before	More now	Less now
Ordinary margarine or butter			
Skimmed milk			
Lean meat			
Full cream milk			
Soya margarine (soft)			
Fatty meat			

II OWN ILLNESSES PAST AND PRESENT

14. Have you ever had?

	YES	No
Sudden paralysis or numbness on one side of your face or body, in your hand or foot		
Sudden loss of ability to speak		
Sudden loss of eye sight, complete or partial, or sudden onset of double vision		

15. Have you had a peptic ulcer? | | |
Do you often have a gnawing pain in the upper part of your stomach? | | |
Do you suffer much from heartburn or regurgitation of gastric juices? | | |
Do you suffer much from wind and rumbling in your stomach? | | |
Do you often get cramps in your stomach? | | |
Have you ever had your large intestine x-rayed? | | |
Have you ever had gallstones? | | |

16. Have you had kidney stones or stones in the urinary tract? | | |
If yes, how many times? | no. of times | |
and, when did you have the last attack? | Year | |

17. Have you ever had cancer? | | |
If yes, in what year was the disease discovered? | Year | |

18. Do you have, or have had you the skin disease psoriasis? | | |

19. Have you had allergy-induced eczema on your hands during the last 12 months? | | |

20. Have you been on sick leave, or been unable to work due to allergic eczema on your hands at any time during the past 3 years? | | |

21. Have you ever had arthritis? (chronic rheumatoid arthritis) | | |

22. Have you suffered from back pain during the past 12 months lasting for more than 4 weeks? | | |
If yes, did the back pain improve if you exercised? | | |

23. Have you suffered from morning stiffness in your back lasting more than 30 minutes? | | |

24. Have you suffered from pains lasting more than 3 months, in the joints listed below during the last 3 years? | | |
Knees | | |
Elbows | | |
Innermost finger joints | | |
Other joints | | |
If yes, did you suffer from stiff joints in the mornings lasting more than 30 minutes? | | |

25. Have you had any infectious disease during the past 14 days? (influenza, common cold, vomiting, diarrhoea, etc.) | | |

26. Have you taken iron tablets during the past 14 days? | | |

27. How often do you take painkillers such as Globoid, Novid, Dispril, Albyl, etc.? Tick the most appropriate box.

	YES	No
1-3 times a week 1		
1-3 times a month 2		
Seldom or never 3		
Have you used such painkillers during the last 14 days?		

28. Have you changed the amount of physical exercise you take in leisure time during the last five years? Tick the most appropriate box.

	YES
As before 1	
More than before 2	
Less than before 3	

III ILLNESS IN PARENTS AND SIBLINGS

29. Have any of these relatives had:

	mother	father	sister	brother
Cerebral stroke or brain haemorrhage				
Diabetes				
Arthritis (chronic rheumatoid arthritis)				
Cancer				
Kidney stones or stone in urinary tract				
Psoriasis				
Peptic ulcer				
None of the above mentioned illnesses				

IV SOCIAL CONDITIONS AND PSYCHOLOGICAL PRESSURE ("STRESS")

30. How many years of education have you had? (including primary and secondary schools) — no. of years

31. How was your family's financial situation when you were growing up? Tick the most appropriate box.

	YES
Very good 1	
Good 2	
Poor 3	
Very poor 4	

32. Do you suffer from sleeplessness? If yes, at what time of the year do you suffer from sleeplessness? Tick the most appropriate box.

	YES	No
No particular time 1		
Especially during the polar night 2		
Especially during the midnight sun season 3		
Especially in spring and autumn 4		
What form does your sleeplessness take?		
Difficult to fall asleep at night? 1		
Wake up a lot during the night? 2		
Wake up very early in the morning? ... 3		

33. Have you had difficulty sleeping in the past couple of weeks? Tick the most appropriate box.

	YES
Not at all 1	
No more than usual 2	
Rather more than usual 3	
Much more than usual 4	

34. Have you felt unhappy and depressed during the last couple of weeks? Tick the most appropriate box.

	YES
Not at all	
No more than usual 2	
Rather more than usual 3	
Much more than usual 4	

35. Have you felt unable to cope with your difficulties during the last couple of weeks? Tick the most appropriate box.

	YES
Not at all 1	
No more than usual 2	
Rather more than usual 3	
Much more than usual 4	

Appendix II

Questionnaire 1 & 2, Tromsø Study 3

THE TROMSØ HEALTH SURVEY

(Applies only to the person to whom the letter is addressed.)

The health survey is coming now to your district.

You find the time and place for attendance below.

You will find an orientation on the survey in the enclosed brochure.

We would like you to fill in the form on the back and take it with you to the survey.

We ask those possibly not attending to report their absence in the attached absence report.

Yours sincerely

MUNICIPAL HEALTH AUTHORITY OF TROMSØ
COUNTY DOCTOR OF TROMS UNIVERSITY OF TROMSØ
NATIONAL HEALTH SCREENING SERVICE

Birth date | Personal number | Municipality | Circuit number

Meeting place | Gender | First letter of last name | Day and date | Time

HEIGHT ⌊⌊⌊ WEIGHT ⌊⌊⌊⌊ ANM 70 ⌊	M ⌊ P ⌊ Ø ⌊ KODE 75 ⌊⌊	AVVIK ⌊ ARM ⌊⌊ MAN ⌊ APP.NR. ⌊⌊⌊ TSM 82 ⌊
MEASUREMENT 1	**MEASUREMENT 2**	**MEASUREMENT 3**
MAR ⌊⌊⌊ 85 S ⌊⌊⌊ 88	MAR ⌊⌊⌊ 91 S ⌊⌊⌊ 94	MAR ⌊⌊⌊ 97 S ⌊⌊⌊ 100
HR ⌊⌊⌊ 103 D ⌊⌊⌊ 106	HR ⌊⌊⌊ 109 D ⌊⌊⌊ 112	HR ⌊⌊⌊ 115 D ⌊⌊⌊ 118

A FAMILY

Have one or more of your parents or siblings had a heart attack (heart wound) or angina pectoris (heart cramp)? 12

Yes | No | Don't know

B OWN ILLNESSES

Do you have, or have you had:

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

Yes | No

Are you being treated for:

High blood pressure? 17

Do you use:

Nitroglycerine? 18

C SYMPTOMS

Do you get pain or discomfort in the chest when:

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

Yes | No

If you get pain or discomfort in the chest when walking, do you usually:

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

1 2 3

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

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

1 2

Do you usually have:

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

Yes | No

D EXERCISE

Exercise and physical exertion in leisure time. If your activity varies much, for example between summer and winter, then give an average. The question refers only to the last year:

Tick the most appropriate box.

Reading, watching TV, or other sedentary activity? 25

1

Walking, cycling or other forms of exercise at least 4 hours a week? .....
(include walking or cycling to work, Sunday walk/stroll, etc.)

2

Participation in recreational sports, heavy gardening, etc.? .....
(note: duration of activity at least 4 hours a week)

3

Participation in hard training or sports competitions, regularly several times a week? ...

4

E SALT/ FAT

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

Tick the most appropriate box.

Never or less than once a month 26
Once a week or less .....
Twice a week or less .....
More than twice a week.....

1 2 3 4

How often do you add extra salt to your dinner?

Tick the most appropriate box.

Rarely or never 27
Sometimes or often .....
Always or nearly always .....

1 2 3

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

Tick the most appropriate box.

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

1 2 3 4 5

What type of cooking fat do you normally use in your household?

Tick the most appropriate box.

Butter or hard margarine 29
Soft (soya) margarine or oil .....
Butter/ margarine mixtures .....

1 2 3

F SMOKING

Do you smoke daily at present? 30

Yes | No

If the answer is "YES", then:

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

If you do not smoke cigarettes at present, then:

Have you previously smoked cigarettes daily? ... 32

If you answered "Yes", how long is it since you stopped:

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

1 2 3 4

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

How many years altogether have you smoked daily? 34

Year

How many cigarettes do you smoke or did you smoke daily? .....
Give number of cigarettes per day 36
(hand-rolled + factory made)

Cigarettes

Do you smoke anything else other than cigarettes daily?

Cigars or cigarillos/cheroots? 40
A pipe? 41

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

Give the average number of packs per week 42

Tobacco packets

G COFFEE

How many cups of coffee do you usually drink daily?

Tick the most appropriate box.

Do not drink coffee, or less than one cup 45
1 -4 cups .....
5 -8 cups .....
9 or more cups .....

1 2 3 4

What type of coffee do you usually drink daily?

Coarsely ground coffee for brewing (boiled) 46
Finely ground filter coffee 47
Instant coffee 48
Caffeine free coffee 49
Do not drink coffee 50

H EMPLOYMENT

Have you within the last 12 months received unemployment benefit? 51

Yes | No

Are you at present on sick leave, or receiving rehabilitation benefit? 52

Do you receive a complete or partial disability pension? 53

Do you usually work shifts or at night? 54

During the last year, have you had:

Tick the most appropriate box.

Mostly sedentary work? 55
(e.g. office work, watchmaker, light manual work)

1

Work that requires a lot of walking? .....
(e.g. shop assistant, light industrial work, teaching)

2

Work that requires a lot of walking and lifting? ...
(e.g. postman, heavy industrial work, construction)

3

Heavy manual labour? .....
(e.g. forestry, heavy farm-work, heavy construction)

4

Yes | No

Is house-keeping your main occupation? ... 56

I FOLLOW-UP EXAMINATION

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

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

Write the doctor's name here? →

..... 58

No particular doctor 61

Don't write here

ADDITIONAL QUESTIONS TO THE TROMSØ HEALTH SURVEY 1986-87.

Cardiovascular heart and circulatory diseases, on which the surveys of the 1974 and 1979-80 focused, are a very varied category of diseases whose causes are still partly unknown. In Tromsø we are therefore trying to obtain a more complete description of factors which may be important for the course of these diseases, such as diet, psychological pressure, "stress", social conditions and the occurrence of disease in relatives. Such a description is also important in the search of factors that contribute to cancer, a group of diseases which also we try to combat in the coming years.

When you were called in, you received a questionnaire which you handed in at the survey. The present questionnaire asks for further information about your health and includes questions on various diseases and physical and psychological complaints. We have included questions on pregnancy, birth and menstruation.

In addition, we are interested in obtaining information on the public use of medical health services in order to find out how to improve the health service.

We hope that you will take the trouble to fill in yet another questionnaire and return it to "Tromsø Board of Health" in the enclosed envelope. All information will be treated with strict confidentiality If you have any comments regarding the survey, you may write them down in the space provided on the last page of the questionnaire.

Yours sincerely

Tromsø Board of Health

Department of medicine
University of Tromsø

GENERAL STATE OF HEALTH

How is your health?
Tick the box where "Yes" is appropriate.

		Yes
Very bad	12	☐ 1
Bad		☐ 2
Neither good nor bad, "middling"		☐ 3
Good		☐ 4
Excellent		☐ 5

ILLNESSES

Do you have, or have you had:
Tick "Yes" or "No" for each question.

		Yes	No
The skin disease psoriasis	13	☐	☐
Asthma	14	☐	☐
Allergic eczema	15	☐	☐
Hay fever	16	☐	☐
Chronic bronchitis	17	☐	☐
Gastric ulcer	18	☐	☐
Duodenal ulcer	19	☐	☐
Your appendix removed	20	☐	☐
An operation for a stomach ulcer	21	☐	☐
Chronic rheumatoid arthritis	22	☐	☐
Cancer	23	☐	☐
Epilepsy	24	☐	☐
Migraine	25	☐	☐

INFECTIONS

		Number / Yes	No
How many times in the last 6 months have you had infections like a cold, influenza (flu) diarrhoea/vomiting, or similar illnesses?	26	☐	
Have you had one of these infections in the past 14 days?	27	☐	☐

ILLNESSES IN PARENTS OR SIBLINGS

Tick for the relatives who have or have ever had any of the following illnesses:

		mother	father	brother	Sister
Cerebral stroke or brain haemorrhage	28	☐	☐	☐	☐
Diabetes	32	☐	☐	☐	☐
Rheumatoid arthritis	36	☐	☐	☐	☐
Cancer	40	☐	☐	☐	☐
Psoriasis	44	☐	☐	☐	☐
Gastric or duodenal ulcer	48	☐	☐	☐	☐
Asthma	52	☐	☐	☐	☐

		Yes	No
Tick if none of the relatives have or have had any of those illnesses	56	☐	☐

MEDICINES

		Yes	No
Have you during the last year used tablets/sprays or had injections for asthma or allergies?	60	☐	☐

Have you used any of the following medicines in the past 14 days?

		Yes	No
Painkillers	61	☐	☐
Antipyretic drugs (to reduce fever)	62	☐	☐
Eczema ointment	63	☐	☐
Blood pressure medicines	64	☐	☐
Heart medicines	65	☐	☐
Sleeping pills	66	☐	☐
Nerve tablets	67	☐	☐
Migraine drugs	68	☐	☐
Epilepsy drugs	69	☐	☐
Other medicines	70	☐	☐

CONTACT DUE TO OWN HEALTH OR ILLNESS

How many visits have you made during the past year due to your own health or illness?

Number of visits

- To a GP (general practitioner) ..... 71 ☐
- To a specialist (not hospital) ..... 72 ☐
- Emergency GP ..... 85 ☐
- Medical officer at work ..... 87 ☐
- Physiotherapist ..... 89 ☐
- Chiropractor ..... 81 ☐
- Alternative practitioner (homoeopath, foot zone therapist, etc.) .. 83 ☐
- Hospital outpatient department ..... 85 ☐

Number of hospital admissions in the past year . 87 ☐

DIET

How many slices of bread do you usually eat daily?
Tick the box where "Yes" is appropriate.

Yes

- Less than 2 slices ..... 88 ☐ 1
- 2 - 4 slices ..... ☐ 2
- 5 – 6 slices ..... ☐ 3
- 7 – 12 slices ..... ☐ 4
- 13 or more slices ..... ☐ 5

What type of milk do you usually drink?
Tick the box where "Yes" is appropriate.

Yes

- Do not drink milk ..... 89 ☐ 1
- Full cream milk (ordinary or curdled) ..... ☐ 2
- Semi-skimmed milk ..... ☐ 3
- Skimmed milk (ordinary or curdled) ..... ☐ 4

How many glasses/cups of milk do you usually drink daily?

Yes

- Less than 1 glass/cup ..... 90 ☐ 1
- 1 – 2 glasses/cups ..... ☐ 2
- 3 – 4 glasses/cups ..... ☐ 3
- 5 or more glasses/cups ..... ☐ 4

FISH

How often do you eat cod/pollock or other lean fish for dinner or in a sandwich?
Tick the box where "Yes" is appropriate.

Yes

- Less than once a week ..... 91 ☐ 1
- Once a week ..... ☐ 2
- Twice a week ..... ☐ 3
- 3 or more times a week ..... ☐ 4

How often do you eat fatty fish such as herring, halibut, red fish, mackerel, salmon or trout for dinner or in a sandwich?
Tick the box where "Yes" is appropriate.

Yes

- Less than once a week ..... 92 ☐ 1
- Once a week ..... ☐ 2
- Twice a week ..... ☐ 3
- 3 or more times a week ..... ☐ 4

Do you take cod liver oil regularly?
Tick the box where "Yes" is appropriate.

Yes

- No ..... 93 ☐ 1
- During polar night ..... ☐ 2
- All year ..... ☐ 3

BREAKFAST

Yes No

Do you usually eat breakfast daily? ..... 94 ☐ ☐

DINNER

How often do you eat meat for dinner?
Tick the box where "Yes" is appropriate.

Yes

- Less than once a week ..... 95 ☐ 1
- Once or twice a week ..... ☐ 2
- 3 – 4 times a week ..... ☐ 3
- 5 or more times a week ..... ☐ 4

How often do you use fat like butter, margarine, mayonnaise, etc. with your dinner?
Tick the box where "Yes" is appropriate.

Yes

- Less than once a week ..... 96 ☐ 1
- Once or twice a week ..... ☐ 2
- 3 – 4 times a week ..... ☐ 3
- 5 or more times a week ..... ☐ 4

Yes No

Do you usually eat vegetables with your dinner? ..... 97 ☐ ☐

FRUIT

How often do you usually eat fruit?
Tick the box where "Yes" is appropriate.

Yes

- Less than once a week ..... 98 ☐ 1
- About once a week ..... ☐ 2
- 2 – 3 times a week ..... ☐ 3
- 4 – 5 times a week ..... ☐ 4
- More or less ..... ☐ 5

ALCOHOL

Yes No

Are you a teetotaller? ☐ ☐

If not,
- How often do you usually drink beer?
Tick the box where "Yes" is appropriate.

Yes

- Never or just a few times a year ..... 100 ☐ 1
- 1 – 2 times a month ..... ☐ 2
- About once a week ..... ☐ 3
- 2 – 3 times a week ..... ☐ 4
- More or less daily ..... ☐ 5

How often do you usually drink wine?
Tick the box where "Yes" is appropriate.

Yes

- Never or just a few times a year ..... 101 ☐ 1
- 1 – 2 times a month ..... ☐ 2
- About once a week ..... ☐ 3
- 2 – 3 times a week ..... ☐ 4
- More or less daily ..... ☐ 5

- How often do you usually drink spirits?
Tick the box where "Yes" is appropriate.

Yes

- Never or just a few times a year ..... 102 ☐ 1
- 1 – 2 times a month ..... ☐ 2
- About once a week ..... ☐ 3
- 2 – 3 times a week ..... ☐ 4
- More or less daily ..... ☐ 5

Approximately how often have you during the last year consumed alcohol corresponding to at least 5 small bottles of beer, a bottle of wine, or 1/4 bottle of spirits?
Tick the box where "Yes" is appropriate.

Yes

- Not at all the past year ..... 103 ☐ 1
- A few times ..... ☐ 2
- Once or twice a month ..... ☐ 3
- 3 or more times a week ..... ☐ 4

PHYSICAL ACTIVITY

How often do you take part in physical activity lasting at least 20 minutes, which makes you perspire or become breathless?
Tick the box where "Yes" is appropriate.

		Yes
Rarely or never	104	☐ 1
Weekly		☐ 2
Several times a week		☐ 3
Daily		☐ 4

If you usually take part in this type of activity at least weekly, how much time do you spend exercising?
Tick the box where "Yes" is appropriate.

		Yes
Less than 30 minutes a week	105	☐ 1
Between 30 minutes and 1 hour a week		☐ 2
Between 1 and 2 hours a week		☐ 3
More than 2 hours a week		☐ 4

CHANGE IN DIETARY HABITS AND OTHER HABITS

Have you changed any of the following habits during the last 5 years: (Tick once for each question)

		Now use more	As before	Less
Dietary fat	106	☐	☐	☐
Soya margarine or oil	107	☐	☐	☐
Skimmed or low fat milk	108	☐	☐	☐
Coffee intake	109	☐	☐	☐
Alcohol intake	110	☐	☐	☐
Physical activity	111	☐	☐	☐

MARRIAGE / PARTNER

		Yes	No
Are you married or partner	112	☐	☐

How old were you when you first married or Moved in with a partner? 113 ☐ years

HOUSEHOLD

How many people live in your household? 115 ☐ Number

		Yes	No
Is anyone in your household 10 years or younger?	117	☐	☐
Does anyone in your household need special care/assistance – other than the children?	118	☐	☐

SCHOOLING

How many years education have you had? (including primary and secondary schools) 119 ☐ years

EMPLOYMENT

Have you had paid work the entire past year?
Tick the box where "Yes" is appropriate.

		Yes
Full-time work	121	☐ 1
Part-time work		☐ 2
Unpaid work		☐ 3

How much house work do you normally do yourself?
Tick the box where "Yes" is appropriate.

All or almost all	122	☐ 1
At least half		☐ 2
More than quarter		☐ 3
Less than quarter		☐ 4

BACK AND JOINTS CONDITIONS

		Yes	No
During this last year have you suffered from back pain that has lasted longer than 4 weeks?	123	☐	☐
If yes, does the pain improve when you move around?	124	☐	☐
Have you suffered from morning stiffness in your back lasting more than 30 minutes?	125	☐	☐

During the past 3 years have you suffered from pain in any of the following joints lasting more than 30 minutes?

		Yes	No
Knees	126	☐	☐
Elbows	127	☐	☐
Innermost finger joints	128	☐	☐
Other joints	129	☐	☐

		Yes	No
If yes, have you suffered from stiff joints in the morning lasting more than 30 minutes?	130	☐	☐

NECK, HEAD AND SHOULDER COMPLAINTS

How often do you suffer from headache?
Tick the box where "Yes" is appropriate.

		Yes
Rarely of never	131	☐ 1
Once or more a month		☐ 2
Once or more a week		☐ 3
Daily		☐ 4

How often do you suffer pain in the neck or shoulder?
Tick the box where "Yes" is appropriate.

		Yes
Rarely of never	132	☐ 1
Once or more a month		☐ 2
Once or more a week		☐ 3
Daily		☐ 4

Do the pains in your head, neck or shoulder reduce your ability to work?
Tick the box where "Yes" is appropriate.

		Yes
Little or no effect	133	☐ 1
To some degree		☐ 2
To a large degree		☐ 3
Cannot do ordinary work		☐ 4

		Yes	No
Have your back, shoulder, and/or neck ever been x-rayed?	134	☐	☐

SLEEPLESSNESS/ LOSS OF CONSCIOUSNESS

		Yes	No
Have you ever suffered from sleeplessness?	135	☐	☐

If yes, what time of the year does it affect you most? Tick the box where "Yes" is appropriate.

		Yes
No particular time	136	☐ 1
Especially during the polar night		☐ 2
Especially during the midnight sun season		☐ 3
Especially in spring and autumn		☐ 4

		Yes	No
Have you at any time during the last 12 months suffered from tiredness that has affected your work performance?	137	☐	☐
Have you suffered from sudden loss of consciousness in the past year?	138	☐	☐
Have you noticed sudden changes in your pulse rate of heartbeat in the past year?	139	☐	☐

REACTION TO PROBLEMS

If you have major personal problems, do you expect to get help and support from your spouse or family? ..... 140 — Yes ☐ No ☐

In the last year, have you for a long time felt a need to seek help with personal problems, without doing so? ..... 141 — Yes ☐ No ☐

During the past 2 weeks have you felt unable to cope with your problems?
Tick the box where "Yes" is appropriate.
- Seldom or never ..... 142 — Yes ☐ 1
- Sometimes ..... ☐ 2
- Often ..... ☐ 3
- Nearly always ..... ☐ 4

During the past 2 weeks have you felt unhappy or depressed?
Tick the box where "Yes" is appropriate.
- Seldom or never ..... 143 — Yes ☐ 1
- Sometimes ..... ☐ 2
- Often ..... ☐ 3
- Nearly always ..... ☐ 4

Do you ever feel lonely?
Tick the box where "Yes" is appropriate.
- Very often ..... 144 — Yes ☐ 1
- Sometimes ..... ☐ 2
- Rarely or never ..... ☐ 3

THE REMAINING SECTION OF THE QUESTIONNAIRE APPLIES TO WOMEN ONLY

MENSTRUATION

How old were you when you started menstruating? ..... 145 — ☐ years

When did your last period start? ..... 147 — day / month / year

How many days usually pass from the first day of one period to the first day of your next period (the time lapsed between the start of two periods) ..... 153 — ☐ days

Do/ did you menstruate regularly? ..... 155 — Yes ☐ No ☐

Do you usually take painkillers during menstruation? ..... 156 — Yes ☐ No ☐

PRE-MENSTRUAL TENSION

Do you have any of the following complaints before your period:
- Are you depressed or irritable?
Tick the box where "Yes" is appropriate.
  - Hardly at all ..... 157 — Yes ☐ 1
  - Noticeably ..... ☐ 2
  - Very much so ..... ☐ 3
- Are your breasts painful?
Tick the box where "Yes" is appropriate.
  - Hardly at all ..... 158 — Yes ☐ 1
  - Noticeably ..... ☐ 2
  - Very much so ..... ☐ 3
- Do you have swollen hands/feet, put on weight, or feel bloated?
Tick the box where "Yes" is appropriate.
  - Hardly at all ..... 159 — Yes ☐ 1
  - Noticeably ..... ☐ 2
  - Very much so ..... ☐ 3

Do the complaints disappear when you get your period? ..... 160 — Yes ☐ No ☐

For these complaints, do you use?
- diuretics? ..... 161 — Yes ☐ No ☐
- other medications? ..... 162 — ☐ ☐

PREGNANY

How many children have given birth to? .... 163 — number ☐

How old were you when you got pregnant for the first time? ..... 164 — ☐ years

CONTRACEPTION

Do you use or have you ever used oral contraceptive pills or an intrauterine device? ..... 166 — Yes ☐ No ☐

If yes, for how many years altogether have you used:
- The pill? ..... 167 — ☐ years
- An intrauterine device? ..... 169 — ☐ years

How old were you when you started using:
- The pill? ..... 171 — ☐ years
- An intrauterine device? ..... 173 — ☐ years

If you have stopped taking the pill, did 6 months or more pass without menstruating without you being pregnant? 175 — Yes ☐ No ☐

Did you have to stop taking the pill due to high blood pressure? ..... 176 — Yes ☐ No ☐

CERVICAL SMEAR TEST

How many times have you had a cervical smear test in the last 3 years? ..... 177 — Number of tests ☐

How many years is it since you had your last cervical smear test? ..... 178 — ☐ years

Your comments: 179

Thank you for the help! Remember to post the questionnaire today!

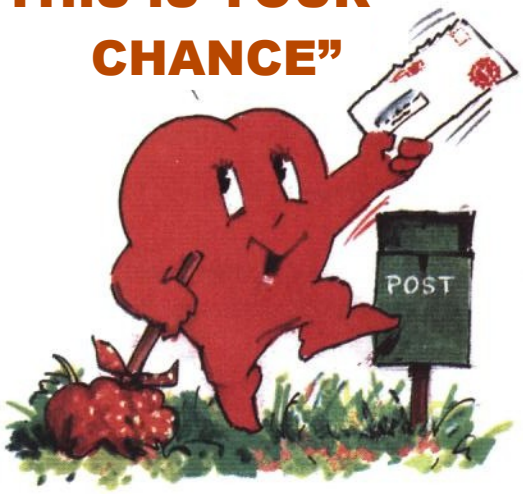
The Tromsø survey 1986-1987

Appendix III

Questionnaire 1 & 2, Tromsø Study 4

HEALTH SURVEY
Invitation

"THIS IS YOUR CHANCE"



Date of birth **Social security No.** **Municipality** **Electoral ward No.**

Welcome to the Tromsø Health Survey!

The Health Survey is coming to Tromsø. This leaflet will tell you when and where. You will also find information about the survey in the enclosed brochure.

We would like you to fill in the form overleaf and take it with you to the examination.

The more people take part in the survey, the more valuable its results will be. We hope, therefore, that you will be able to come. Attend even if you feel healthy, if you are currently receiving medical treatment, or if you have had your cholesterol and blood pressure measured recently.

Yours sincerely,
Municipal Health Authorities
Faculty of Medicine - University of Tromsø
National Health Screening Service

"THIS IS A REAL OPPORTUNITY- TAKE IT!"

YOUR OWN HEALTH

What is your current state of health? *Tick one box only.*

Poor	12	1
Not so good		2
Good		3
Very good		4

Do you have, or have you had:

		Yes	No	Age first time
A heart attack	13			years
Angina pectoris (heart cramp)	16			years
A cerebral stroke/ brain haemorrhage	19			years
Asthma	22			years
Diabetes	25			years

Do you use blood pressure lowering drugs?

Currently	28	1
Previously, but not now		2
Never used		3

Have you during the last year suffered from pains and/or stiffness in muscles and joints that have lasted continuously for at least 3 months? 29 Yes / No

Have you in the last two weeks felt:

		No	A little	A lot	Very much
Nervous or worried?	30				
Anxious?	31				
Confident and calm?	32				
Irritable?	33				
Happy and optimistic?	34				
Down/depressed?	35				
Lonely?	36				
		1	2	3	4

SMOKING

Did any of the adults at home smoke while you were growing up? 37 Yes / No

Do you currently, or did you previously, live together with daily smokers after your 20th birthday? 38 Yes / No

If "YES", for how many years in all? 39 ____ Years

How many hours a day do you normally spend in smoke-filled rooms? 41 ____ Hours

Put 0 if you do not spend time in smoke-filled rooms.

Do you yourself smoke:

		Yes	No
Cigarettes daily?	43		
Cigars/ cigarillos daily?	44		
A pipe daily?	45		

If you previously smoked daily, how long is it since you quit? 46 ____ Years

If you currently smoke, or have smoked previously:

How many cigarettes do you or did you usually smoke per day? 48 ____ cigarettes

How old were you when you began daily smoking? 52 ____ Age years

How many years in all have you smoked daily? 54 ____ Years

EXERCISE

How has your physical activity in leisure time been during this last year? *Think of your weekly average for the year.*

Time spent going to work counts as leisure time.

		Hours per week: None	Less than 1	1-2	3 or more
Light activity *(not sweating/out of breath)*	56				
Hard activity *(sweating/ out of breath)*	57				
		1	2	3	4

COFFEE

How many cups of coffee do you drink daily?

Put 0 if you do not drink coffee daily.

Coarsely ground coffee for brewing 58 ____ Cups

Other coffee 60 ____ Cups

ALCOHOL

Are you a teetotaller? 62 Yes / No

How many times a month do you normally drink alcohol? *Do not count low-alcohol beer.*

Put 0 if less than once a month. 63 ____ Times

How many glasses of beer, wine or spirits do you normally drink in a fortnight? 65

Do not count low-alcohol beer.

Put 0 if less than once a month.

Beer	Wine	Spirits
Glasses	Glasses	Glasses

FAT

What type of margarine or butter do you usually use on bread? *Tick one box only.*

Don't use butter/margarine	71	1
Butter		2
Hard margarine		3
Soft margarine		4
Butter/margarine mixtures		5
Light margarine		6

EDUCATION/WORK

What is the highest level of education you have completed?

7-10 years primary/secondary school, modern secondary school	72	1
Technical school, middle school, vocational school, 1-2 years senior high school		2
High school diploma (3-4 years)		3
College/university, less than 4 years		4
College/university, 4 or more years		5

What is your current work situation?

Paid work	73	
Full-time housework	74	
Education, military service	75	
Unemployed, on leave without payment	76	

How many hours of paid work do you have per week? 77 ____ No. of hours

Do you receive any of the following benefits?

Sickness benefit (sick leave)	79	
Rehabilitation benefit	80	
Disability pension	81	
Old-age pension	82	
Social welfare benefit	83	
Unemployment benefit	84	

ILLNESS IN THE FAMILY

Have one or more of your parents or siblings had a heart attack or had angina (heart cramp)? 85

Yes	No	Don't know

The Tromsø Health Survey

The main aim of the Tromsø Study is to improve our knowledge about cardiovascular diseases in order to aid prevention. The survey is also intended to improve our knowledge of cancer and other general conditions, such as allergies, muscle pains and mental conditions. We would therefore like you to answer some questions about factors that may be relevant for your risk of getting these and other illnesses.

This form is a part of the Health Survey, which has been approved by the Norwegian Data Inspectorate and the Regional Board of Research Ethics. The answers will only be used for research purposes and will be treated in strict confidence. The information you give us may later be stored along with information from other public health registers in accordance with the rules laid down by the Data Inspectorate and the Regional Board of Research Ethics.

If you are in doubt about what to answer, tick the box that you feel fits best.

The completed form should be sent to us in the enclosed pre-paid envelope.

Thank you in advance for helping us.

Yours sincerely,

Faculty of Medicine
University of Tromsø

National Health Screening Service

If you do not wish to answer the questionnaire, tick the box below and return the form. Then you will not receive reminders.

I do not wish to answer the questionnaire ..... 17 ☐

Day Month Year

Date for filling in this form:..... 18 ...../...../.....

CHILDHOOD/YOUTH

In which Norwegian municipality did you live at the age of 1 year?

..... 24 - 28

If you did not live in Norway, give country of residence instead of municipality.

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

- Very good ..... 29 ☐
- Good ..... ☐
- Difficult ..... ☐
- Very difficult ..... ☐

How many of the first three years of your life

- did you live in a town/city? ..... 30 ____years
- did your family have a cat or dog in the home? ..... 31 ____years

How many of the first 15 years of your life

- did you live in a town/city? ..... 32 ____years
- did your family have a cat or dog in the home? ..... 34 ____years

HOME

Who do you live with?

Tick once for each item and give the number .		Yes	No	Number
Spouse/partner	36	☐	☐	
Other people over 18 years	37	☐	☐	_____
People under 18 years	40	☐	☐	_____

How many of the children attend day care/kindergarten? .... 43 _____

What type of house do you live in?

- Villa/detached house ..... 45 ☐ 1
- Farm ..... ☐ 2
- Flat /apartment ..... ☐ 3
- Terraced /semi-detached house ..... ☐ 4
- Other ..... ☐ 5

How big is your house? ..... 46 _____ m^2

Approximately what year was your house built? ..... 49 _____

		Yes	No
Has your house been insulated after 1970?	53	☐	☐
Do you live on the lower ground floor/basement?	54	☐	☐
If "Yes", is the floor laid on concrete?	55	☐	☐

What is the main source of heat in your home?

- Electric heating ..... 56 ☐
- Wood-burning stove ..... ☐
- Central heating system using:
  - Paraffin ..... ☐
  - Electricity ..... ☐

		Yes	No
Do you have fitted carpets in the living room?	60	☐	☐
Is there a cat in your home?	61	☐	☐
Is there a dog in your home?	62	☐	☐

WORK

If you have paid or unpaid work, how would you describe your work?

- Mostly sedentary work? ..... 63 ☐ 1
  (e.g. office work, mounting)
- Work that requires a lot of walking? ..... ☐ 2
  (e.g. shop assistant, light industrial work, teaching)
- Work that requires a lot of walking and lifting? ..... ☐ 3
  (e.g. postman, nursing, construction)
- Heavy manual work? ..... ☐ 4
  (e.g. forestry, heavy farm-work, heavy construction)

Can you decide yourself how your work should be organised?

- No, not at all ..... 64 ☐ 1
- To a small extent ..... ☐ 2
- Yes, to a large extent ..... ☐ 3
- Yes, I decide myself ..... ☐ 4

		Yes	No
Are you on call, do you work shifts or nights?	65	☐	☐

Do you do any of the following jobs (full- or part-time)?

Tick one box only for each item.		Yes	No
Driver	66	☐	☐
Farmer		☐	☐
Fisherman		☐	☐

YOUR OWN ILLNESSES

Have you ever had:
Tick one box only for each item. Give your age at the time.
*If you have had the condition several times, how old were you **last** time?*

	Yes	No	Age
Hip fracture 69	❑	❑	_____
Wrist/forearm fracture 72	❑	❑	_____
Whiplash 75	❑	❑	_____
Injury requiring hospital admission 78	❑	❑	_____
Gastric ulcer 81	❑	❑	_____
Duodenal ulcer 84	❑	❑	_____
Gastric/duodenal ulcer surgery 87	❑	❑	_____
Neck surgery 90	❑	❑	_____

Have you you ever had, or do you still have:
Tick one box only for each item.

	Yes	No
Cancer 93	❑	❑
Epilepsy	❑	❑
Migraine	❑	❑
Chronic bronchitis	❑	❑
Psoriasis	❑	❑
Osteoporosis 98	❑	❑
Fibromyalgia/fibrositis/chronic pain syndrome	❑	❑
Psychological problems for which you have sought help	❑	❑
Thyroid disease	❑	❑
Liver disease	❑	❑
Kidney disease 103	❑	❑
Appendectomy	❑	❑
Allergy and hypersensitivity:		
Atopic eczema (e.g. childhood eczema)	❑	❑
Hand eczema	❑	❑
Hay fever	❑	❑
Food allergy 108	❑	❑
Other hypersensitivity (not allergy)	❑	❑

How many times have you had a cold, influenza (flu), vomiting/diarrhoea, or similar in the last six months? ____ times

	Yes	No
Have you had this in the last 14 days? 112	❑	❑

ILLNESS IN THE FAMILY

Tick for the relatives who have or have ever had any of the following diseases:
Tick "None" if none of your relatives have had the disease.

	Mother	Father	Brother	Sister	Child	None
Cerebral stroke or brain haemorrhage 113	❑	❑	❑	❑	❑	❑
Heart attack before age 60 119	❑	❑	❑	❑	❑	❑
Cancer 125	❑	❑	❑	❑	❑	❑
Asthma 131	❑	❑	❑	❑	❑	❑
Gastric/duodenal ulcer 137	❑	❑	❑	❑	❑	❑
Osteoporosis 143	❑	❑	❑	❑	❑	❑
Psychological problems 149	❑	❑	❑	❑	❑	❑
Allergy 155	❑	❑	❑	❑	❑	❑
Diabetes 161	❑	❑	❑	❑	❑	❑
– age when they got diabetes 167	___	___	___	___	___	

SYMPTOMS

	Yes	No
Do you cough about daily for some periods of the year? ..177	❑	❑
If "Yes":		
Is your cough productive ? 178	❑	❑
Have you had this kind of cough for as long as 3 months in each of the last two years? 179	❑	❑
Have you had episodes of wheezing in your chest? ..180	❑	❑
If "Yes", has this occurred:		
Tick one box only for each item.		
At night 181	❑	❑
In connection with respiratory infections	❑	❑
In connection with physical exertion	❑	❑
In connection with very cold weather	❑	❑
Have you noticed sudden changes in your pulse or heart rhythm in the last year? 185	❑	❑

How often do you suffer from sleeplessness?

Never, or just a few times a year 186	❑ 1
1-2 times a month	❑ 2
Approximately once a week	❑ 3
More than once a week	❑ 4

If you suffer from sleeplessness, what time of the year does it affect you most?

No particular time of year 187	❑ 1
Especially during the polar night	❑ 2
Especially during the midnight sun season	❑ 3
Especially in spring and autumn	❑ 4

	Yes	No
Have you in the last year suffered from sleeplessness to the extent that it has affected your ability to work? ..188	❑	❑

How often do you suffer from headaches?

Rarely or never 189	❑ 1
Once or more a month	❑ 2
Once or more a week	❑ 3
Daily	❑ 4

Does the thought of getting a serious illness ever worry you?

Not at all 190	❑ 1
Only a little	❑ 2
Some	❑ 3
Very much	❑ 4

USE OF HEALTH SERVICES

How many visits have you made during the past year due to your own health or illness:
*Tick **0** if you have **not** had such contact*

	Number of times the past year
To a general practitioner (GP)/Emergency GP 191	_____
To a psychologist or psychiatrist	_____
To an other medical specialist (not at a hospital)	_____
To a hospital out-patient clinic 197	_____
Admitted to a hospital	_____
To a medical officer at work	_____
To a physiotherapist 203	_____
To a chiropractor	_____
To an acupuncturist	_____
To a dentist 209	_____
To an alternative practitioner (homoeopath, foot zone therapist, etc.)	_____
To a healer, faith healer, clairvoyant	_____

MEDICATION AND DIETARY SUPPLEMENTS

Have you for any length of time in the past year used any of the following medicines or dietary supplements daily or almost daily? Indicate how many months you have used them.
*Put **0** for items you have **not** used.*

Medicines

Painkillers	215	_____ months
Sleeping pills		_____ months
Tranquillizers		_____ months
Antidepressants	221	_____ months
Allergy drugs		_____ months
Asthma drugs		_____ months

Dietary supplements

Iron tablets	227	_____ months
Calcium tablets or bonemeal		_____ months
Vitamin D supplements		_____ months
Other vitamin supplements	233	_____ months
Cod liver oil or fish oil capsules		_____ months

Have you in the last 14 days used the following medicines or dietary supplements?
*Tick **one** box only for **each** item.*

		Yes	No
Medicines			
Painkillers	237	❑	❑
Antipyretic drugs (to reduce fever)		❑	❑
Migraine drugs		❑	❑
Eczema cream/ointment		❑	❑
Heart medicines (not blood pressure)		❑	❑
Cholesterol lowering drugs		❑	❑
Sleeping pills		❑	❑
Tranquillizers		❑	❑
Antidepressants		❑	❑
Other drugs for nervous conditions		❑	❑
Antacids	247	❑	❑
Gastric ulcer drugs		❑	❑
Insulin		❑	❑
Diabetes tablets		❑	❑
Drugs for hypothyroidism (Thyroxine)		❑	❑
Cortisone tablets	252	❑	❑
Other medicine(s)		❑	❑
Dietary supplements			
Iron tablets		❑	❑
Calcium tablets or bonemeal		❑	❑
Vitamin D supplements		❑	❑
Other vitamin supplements	257	❑	❑
Cod liver oil or fish oil capsules		❑	❑

FRIENDS

How many good friends do you have whom you can talk confidentially with and who give you help when you need it? 259 _____ good friends
Do not count people you live with, but do include other relatives!

How many of these good friends do you have contact with at least once a month? ..... 261 _____

	Yes	No
Do you feel you have enough good friends? 263	❑	❑

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

Never, or just a few times a year	264	❑ 1
1-2 times a month		❑ 2
Approximately once a week		❑ 3
More than once a week		❑ 4

FOOD HABITS

If you use butter or margarine on your bread, how many slices does a small catering portion normally cover? By this, we mean the portion packs served on planes, in cafés, etc. (10-12g)

A catering portion is enough for about ..... 265 _____ slices

What kind of fat is normally used in **cooking** (not on the bread) in your home?

Butter	266	❑
Hard margarine		❑
Soft margarine		❑
Butter/margarine blend		❑
Oils	270	❑

What kind of bread (bought or home-made) do you usually eat?
Tick one or two boxes!

	White bread	Light textured	Ordinary brown	Coarse brown	Crisp bread
The bread I eat is most similar to:	❑ 271	❑	❑	❑	❑ 275

How much (in **number** of glasses, cups, potatoes or slices) do you usually eat or drink **daily** of the following foodstuffs?
*Tick one box for **each** foodstuff.*

	0	Less than 1	1-2	3-4	5-6	More than 6
Full milk (ordinary or curdled) (glasses) 276	❑	❑	❑	❑	❑	❑
Semi-skimmed milk (ordinary or curdled) (glasses)	❑	❑	❑	❑	❑	❑
Skimmed milk (ordinary or curdled) (glasses)	❑	❑	❑	❑	❑	❑
Tea (cups)	❑	❑	❑	❑	❑	❑
Orange juice (glasses)	❑	❑	❑	❑	❑	❑
Potatoes 281	❑	❑	❑	❑	❑	❑
Slices of bread in total (incl. crisp-bread)	❑	❑	❑	❑	❑	❑
Slices of bread with						
- fish (e.g. mackerel in tomato sauce)	❑	❑	❑	❑	❑	❑
- lean meat (e.g. ham)	❑	❑	❑	❑	❑	❑
- fat meat (e.g. salami)	❑	❑	❑	❑	❑	❑
- cheese *(e.g. Gouda/ Norvegia)* 286	❑	❑	❑	❑	❑	❑
- brown cheese	❑	❑	❑	❑	❑	❑
- smoked cod caviare	❑	❑	❑	❑	❑	❑
- jam and other sweet spreads	❑ 1	❑ 2	❑ 3	❑ 4	❑ 5	❑ 6

How many **times per week** do you normally eat the following foodstuffs?
*Tick a box for **all** foodstuffs listed.*

	Never	Less than 1	1	2-3	4-5	almost daily
Yoghurt 290	❑	❑	❑	❑	❑	❑
Boiled or fried egg	❑	❑	❑	❑	❑	❑
Breakfast cereal/ oat meal, etc.	❑	❑	❑	❑	❑	❑
Dinner with						
- unprocessed meat	❑	❑	❑	❑	❑	❑
- sausage/meatloaf/ meatballs	❑	❑	❑	❑	❑	❑
- fatty fish (e.g. salmon/redfish) 295	❑	❑	❑	❑	❑	❑
- lean fish (e.g. cod)	❑	❑	❑	❑	❑	❑
- fishballs/fishpudding/fishcakes	❑	❑	❑	❑	❑	❑
- vegetables	❑	❑	❑	❑	❑	❑
Mayonnaise, remoulade	❑	❑	❑	❑	❑	❑
Carrots 300	❑	❑	❑	❑	❑	❑
Cauliflower/cabbage/ broccoli	❑	❑	❑	❑	❑	❑
Apples/pears	❑	❑	❑	❑	❑	❑
Oranges, mandarins	❑	❑	❑	❑	❑	❑
Sweetened soft drinks	❑	❑	❑	❑	❑	❑
Sugar-free ("Light") soft drinks	❑	❑	❑	❑	❑	❑
Chocolate	❑	❑	❑	❑	❑	❑
Waffles, cakes, etc. 307	❑ 1	❑ 2	❑ 3	❑ 4	❑ 5	❑ 6

ALCOHOL

How often do you usually drink	beer?	wine?	spirits?
Never, or just a few times a year	❑	❑	❑ 1
1-2 times a month	❑	❑	❑ 2
About once a week	❑	❑	❑ 3
2-3 times a week	❑	❑	❑ 4
More or less daily	❑	❑	❑ 5
	308		310

Approximately how often during the last year have you consumed alcohol corresponding to at least 5 small bottles of beer, a bottle of wine, or 1/4 bottle of spirits?

- Not at all the last year ..... ❑ 1
- A few times ..... ❑ 2
- 1-2 times a month ..... ❑ 3
- 1-2 times a week ..... ❑ 4
- 3 or more times a week ..... ❑ 5

For approximately how many years has your alcohol consumption been as you described above? ..... 312 ____years

WEIGHT REDUCTION

About how many times have you deliberately tried to lose weight? Write **0** if you never have.

- before age 20 ..... 314 _____ times
- later ..... 316 _____ times

If you have lost weight deliberately, about how many kilos have you ever lost at the most?

- before age 20 ..... 318 _____ kg
- later ..... 320 _____ kg

What weight would you be satisfied with (your "ideal weight")? ..... 322 _____ kg

URINARY INCONTINENCE

How often do you suffer from urinary incontinence?

- Never ..... 325 ❑ 1
- Not more than once a month ..... ❑ 2
- Two or more times a month ..... ❑ 3
- Once a week or more ..... ❑ 4

Your comments:

TO BE ANSWERED BY WOMEN ONLY

MENSTRUATION

How old were you when you started menstruating? ..... 326 _____years

If you no longer menstruate, how old were you when you stopped menstruating? ..... 328 _____years

Apart from pregnancy and after giving birth, have you ever stopped having menstruation for 6 months or more? ..... 330 Yes ❑ No ❑

If "Yes", how many times? ..... 331 _____ times

If you still menstruate or are pregnant:

What date did your last menstruation period begin? 333 day/month/year ___/___/___

Do you usually use painkillers to relieve period pains? ..... 339 Yes ❑ No ❑

PREGNANCY

How many children have you given birth to? ..... 340 _____ children

Are you pregnant at the moment? ..... 342 Yes ❑ No ❑ Don't know ❑

Have you during pregnancy had high blood pressure and/or proteinuria? ..... 343 Yes ❑ No ❑

If "Yes", during which pregnancy?

	Pregnancy First	Later
High blood pressure 344	❑	❑
Proteinuria 346	❑	❑

If you have given birth, fill in for each child the year of birth and approximately how many months you breastfed the child.

Child	Year of birth:	Number of months breastfed:
1	348 _____	_____
2	_____	_____
3	356 _____	_____
4	_____	_____
5	364 _____	_____
6	_____	_____

CONTRACEPTION AND ESTROGEN

Do you use, or have you ever used:	Now	Before	Never
Oral contraceptive pills (incl. minipill) ... 372	❑	❑	❑
Hormonal intrauterine device	❑	❑	❑
Estrogen (tablets or patches) 374	❑	❑	❑
Estrogen (cream or suppositories)	❑	❑	❑
	1	2	3

If you use oral contraceptive pills, hormonal intrauterine device, or estrogen, what brand do you currently use?

376 .....

If you use or have ever used oral contraceptive pills:

Age when you started to take the pill? ..... 380 _____years

How many years in total have you taken the pill? ..... 382 _____years

If you have given birth, how many years did you take the pill before your first delivery? ..... 384 _____years

If you have stopped taking the pill:

Age when you stopped? ..... 386 _____years

Thank you for the help! Remember to mail the form today!

The Tromsø Health Survey

Tromsø Health Survey
for the over 70s

The main aim of the Tromsø Study is to improve our knowledge about cardiovascular diseases in order to aid prevention. The survey is also intended to improve our knowledge of cancer and other general conditions, such as allergies, muscle pains and mental conditions. Finally, the survey should give knowledge about the older part of the population. We would therefore like you to answer the questions below.

This form is a part of the Health Survey, which has been approved by the Norwegian Data Inspectorate and the Regional Board of Research Ethics. The answers will only be used for research purposes and will be treated in strict confidence. The information you give us may later be stored along with information from other public health registers in accordance with the rules laid down by the Data Inspectorate and the Regional Board of Research Ethics.

If you are in doubt about what to answer, tick the box that you feel fits best.

The completed form should be sent to us in the enclosed pre-paid envelope.

Thank you in advance for helping us.

Yours sincerely,

Faculty of Medicine
University of Tromsø

National Health
Screening Service

If you do not wish to answer the questionnaire, tick the box below and return the form. Then you will not receive reminders.

I do not wish to answer the questionnaire .....17 ❑

Day Month Year

Date for filling in this form: .....18 ...../...../.....

CHILDHOOD/YOUTH

In which Norwegian municipality did you live at the age of 1year?

.....24 -28

If you did not live in Norway, give country instead of municipality

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

- Very good .....29 ❑ 1
- Good ..... ❑ 2
- Difficult ..... ❑ 3
- Very difficult ..... ❑ 4

How old were your parents when they died?

- Mother .....30 _____Years
- Father .....32 _____Years

HOME

Who do you live with?
Tick once for each item and give the number.

	Yes	No	Number
Spouse/partner 34	❑	❑	
Other people over 18 years 35	❑	❑	_____
People under 18 years 38	❑	❑	_____

What type of house do you live in?

- Villa/ detached house .....41 ❑ 1
- Farm ..... ❑ 2
- Flat/apartment ..... ❑ 3
- Terraced /semi-detached house ..... ❑ 4
- Other ..... ❑ 5

How long have you lived in your present home? .....42 _____years

	Yes	No
Is your home adapted to your needs? 44	❑	❑
If "No", do you have problems with:		
Living space 45	❑	❑
Variable temperature, too cold/too warm 46	❑	❑
Stairs 47	❑	❑
Toilet 48	❑	❑
Bath/shower 49	❑	❑
Maintenance 50	❑	❑
Other (please specify) 51	❑	❑

Would you like to move into a retirement home? ...52 ❑ ❑

PREVIOUS WORK AND FINANCIAL SITUATION

How will you describe the type of work you had for the last 5-10 years before you retired?

- Mostly sedentary work? .....53 ❑ 1
  (e.g. office work, mounting)
- Work that requires a lot of walking? ..... ❑ 2
  (e.g. shop assistant, housewife, teaching)
- Work that requires a lot of walking and lifting? ..... ❑ 3
  (e.g. postman, nurse, construction)
- Heavy manual work ..... ❑ 4
  (e.g. forestry, heavy farm-work, heavy construction)

Did you do any of the following jobs (full-time or part-time)?
Tick one box only for each item.

	Yes	No
Driver 54	❑	❑
Farmer 55	❑	❑
Fisherman 56	❑	❑

How old were you when you retired? .....57 _____Years

What kind of pension do you have?

- Basic state pension .....59 ❑
- An additional pension .....60 ❑

How is your current financial situation?

- Very good .....61 ❑ 1
- Good ..... ❑ 2
- Difficult ..... ❑ 3
- Very difficult ..... ❑ 4

HEALTH AND ILLNESS

Has your state of health changed in the last year?

- Yes, it has got worse .....62 ❑ 1
- No, unchanged ..... ❑ 2
- Yes, it has got better ..... ❑ 3

How do you feel your health is now compared to others of your age?

- Much worse .....63 ❑ 1
- A little worse ..... ❑ 2
- About the same ..... ❑ 3
- A little better ..... ❑ 4
- Much better ..... ❑ 5

YOUR OWN ILLNESSES

Have you ever had:
Tick one box only for each item. Give your age at the time. If you have had the condition several times, how old were you last time?

	Yes	No	Age
Hip fracture 64	❑	❑	_____
Wrist /forearm fracture 67	❑	❑	_____
Whiplash 70	❑	❑	_____
Injury requiring hospital admission 73	❑	❑	_____
Gastric ulcer 76	❑	❑	_____
Duodenal ulcer 79	❑	❑	_____
Gastric/duodenal ulcer surgery 82	❑	❑	_____
Neck surgery 85	❑	❑	_____

Have you ever had, or do you have:
Tick one box only for each item.

	Yes	No
Cancer 88	❑	❑
Epilepsy	❑	❑
Migraine	❑	❑
Parkinson's disease	❑	❑
Chronic bronchitis	❑	❑
Psoriasis 93	❑	❑
Osteoporosis	❑	❑
Fibromyalgia/fibrositis/chronic pain syndrome	❑	❑
Psychological problems for which you have sought help	❑	❑
Thyroid disease	❑	❑
Liver disease 98	❑	❑
Recurrent urinary incontinence	❑	❑
Glaucoma	❑	❑
Cataract	❑	❑
Arthrosis (osteoarthritis)	❑	❑
Rheumatoid arthritis 103	❑	❑
Kidney stones	❑	❑
Appendectomy	❑	❑
Allergy and hypersensitivity		
Atopic eczema (e.g. childhood eczema)	❑	❑
Hand eczema	❑	❑
Hey fever 108	❑	❑
Food allergy	❑	❑
Other hypersensitivity (not allergy)	❑	❑

How many times have you had a common cold, influenza (flu), diarrhoea/vomiting or similar in the last 6 months? 111 _____ times

	Yes	No
Have you had this in the last 14 days? 113	❑	❑

ILLNESS IN THE FAMILY

Tick for the relatives who have or have ever had any of the following diseases:
Tick "None" if none of your relatives have had the disease.

	Mother	Father	Brother	Sister	Child	None
Cerebral stroke or brain haemorrhage 114	❑	❑	❑	❑	❑	❑
Heart attack before age 60 120	❑	❑	❑	❑	❑	❑
Cancer 126	❑	❑	❑	❑	❑	❑
Hypertension 132	❑	❑	❑	❑	❑	❑
Asthma 138	❑	❑	❑	❑	❑	❑
Osteoporosis 144	❑	❑	❑	❑	❑	❑
Arthrosis (osteoarthritis) 150	❑	❑	❑	❑	❑	❑
Psychological problems 156	❑	❑	❑	❑	❑	❑
Dementia 162	❑	❑	❑	❑	❑	❑
Diabetes 168	❑	❑	❑	❑	❑	❑
- age when they got diabetes 174	__	__	__	__	__	

SYMPTOMS

	Yes	No
Do you cough about daily for some periods of the year? 184	❑	❑
If "Yes":		
Is your cough productive? 185	❑	❑
Have you had this kind of cough for as long as 3 months in each of the last two years? 186	❑	❑
Have you had episodes with wheezing in your chest?187	❑	❑
If "Yes", has this occurred:		
Tick one box only for each item.		
At night 188	❑	❑
In connection with respiratory infections	❑	❑
In connection with physical exertion	❑	❑
In connection with very cold weather 191	❑	❑
Have you noticed sudden changes in your pulse or heart rhythm in the last year? 192	❑	❑
Have you lost weight in the last year? 193	❑	❑
If "Yes":		
How many kilograms? 194	_____ kg	

How often do you suffer from sleeplessness?

- Never, or just a few times a year .....196 ❑ 1
- 1-2 times a month ..... ❑ 2
- Approximately once a week ..... ❑ 3
- More than once a week ..... ❑ 4

If you suffer from sleeplessness, what time of the year does it affect you most?

- No particular time of year .....197 ❑ 1
- Especially during the polar night ..... ❑ 2
- Especially during the midnight sun season ..... ❑ 3
- Especially in spring and autumn ..... ❑ 4

	Yes	No
Do you usually take a nap during the day? 198	❑	❑
Do you feel that you usually get enough sleep?	❑	❑

Do you suffer from:	No	A little	A lot
Dizziness 200	❑	❑	❑
Poor memory	❑	❑	❑
Lack of energy	❑	❑	❑
Constipation 203	❑	❑	❑

Does the thought of getting a serious illness ever worry you?

- Not at all ..... 204 ☐
- Only a little ..... ☐
- Some ..... ☐
- Very much ..... ☐

BODILY FUNCTIONS

Can you manage the following everyday activities on your own without help from others?	Yes	With some help	No
Walking indoors on one level 205	☐	☐	☐
Walking up/down stairs	☐	☐	☐
Walking outdoors	☐	☐	☐
Walking approx. 500 metres	☐	☐	☐
Going to the toilet	☐	☐	☐
Washing yourself 210	☐	☐	☐
Taking a bath/shower	☐	☐	☐
Dressing and undressing	☐	☐	☐
Getting in and out of bed	☐	☐	☐
Eating	☐	☐	☐
Cooking 215	☐	☐	☐
Doing light housework *(e.g. washing up)*	☐	☐	☐
Doing heavier housework *(e.g. cleaning floor)* ..	☐	☐	☐
Go shopping	☐	☐	☐
Take the bus	☐	☐	☐

	Yes	With difficulty	No
Can you hear normal speech (if necessary with hearing aid)? 220	☐	☐	☐
Can you read (if necessary with glasses)? 221	☐	☐	☐

Are you dependent on any of the following aids? ?

	Yes	No
Walking stick 222	☐	☐
Crutches	☐	☐
Walking frame/zimmer frame	☐	☐
Wheelchair	☐	☐
Hearing aid	☐	☐
Safety alarm device..... 227	☐	☐

USE OF HEALTH SERVICES

How many visits have you made during the past year due to vour own health or illness:
Put 0 if you have not had such contact

	Number of times the past year
To a general practitioner (GP)/emergency GP 228	
To a psychologist or psychiatrist	
To an other medical specialist (not at a hospital)	
To a hospital out-patient clinic 234	
Admitted to a hospital	
To a physiotherapist	
To a chiropractor 240	
To a acupuncturist	
To a dentist	
To a chiropodist 246	
To an alternative practitioner (homoeopath, foot zone therapist, etc.)	
To a healer, faith healer, clairvoyant	

Do you have home aid?	Yes	No
Private 252	☐	☐
Municipal	☐	☐

Do you receive home nursing care? ..... ☐ ☐

Are you pleased with the health care and home assistance services in the municipality?

	Yes	No	Don't know
Assigned family GP 255	☐	☐	☐
Home nursing care	☐	☐	☐
Home assistance services	☐	☐	☐

Do you feel confident that you will receive health care and home assistance services if you need it?

- Confident ..... 258 ☐ 1
- Not confident ..... ☐ 2
- Very unsure ..... ☐ 3
- Don't know ..... ☐ 4

MEDICATION AND DIETARY SUPPLEMENTS

Have you for any length of time in the last year used any of the following medicines or dietary supplements daily or almost daily? Indicate how many months you have used them.
Put 0 for items you have not used.

Medicines:

- Painkillers ..... 259 _____months
- Sleeping pills ..... _____months
- Tranquillizers ..... _____months
- Antidepressants ..... 265 _____months
- Allergy drugs ..... _____months
- Asthma drugs ..... _____months
- Heart medicines (not blood pressure) ..... 271 _____months
- Insulin ..... _____months
- Diabetes tablets ..... _____months
- Drugs for hypothyroidism (Thyroxine) ..... 277 _____months
- Cortisone tablets ..... _____months
- Remedies for constipation ..... _____months

Dietary supplements:

- Iron tablets ..... 283 _____months
- Vitamin D supplements ..... _____months
- Other vitamin supplements ..... _____months
- Calcium tablets or bone meal ..... 289 _____months
- Cod liver oil or fish oil capsules ..... _____months

FAMILY AND FRIENDS

Do you have close relatives who can give you help and support when you need it? 293	Yes	No
	☐	☐
If "Yes", who can give you help?		
Spouse/partner 294	☐	
Children	☐	
Others	☐	

How many good friends do you have whom you can talk confidentially with and who give you help when you need it? ..... 297 ____ good friends

Do not count people you live with, but do include other relatives!

	Yes	No
Do you feel you have enough good friends?..... 299	☐	☐

Do you feel that you belong to a community (group of people) who can depend on each other and who feel committed to each other (e.g. a political party, religious group, relatives, neighbours, work place, or organisation)?

- Strong sense of belonging ..... 300 ☐ 1
- Some sense of belonging ..... ☐ 2
- Not sure ..... ☐ 3
- Little or no sense of belonging ..... ☐ 4

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

- Never, or just a few times a year ..... 301 ☐ 1
- 1-2 times a month ..... ☐ 2
- Approximately once a week ..... ☐ 3
- More than once a week ..... ☐ 4

FOOD HABITS

Number

How many meals a day do you normally eat (dinner and bread meals)? ..... 302 _____

How many times a week do you eat warm dinner? ..... 304 _____

What kind of bread (bought or home-made) do you usually eat?

Tick one or two boxes.

	White Bread	Light textured	Ordinary brown	Coarse brown	Crisp bread
The bread type is most similar to:	☐ 306	☐	☐	☐	☐ 310

What kind of fat is normally used in *cooking* (not on the bread) in your home?

- Butter ..... 311 ☐
- Hard margarine ..... ☐
- Soft margarine ..... ☐
- Butter/margarine blend ..... ☐
- Oils ..... 315 ☐

How much (in number of glasses, cups, potatoes or slices) do you usually eat/drink daily the following foodstuffs?

Tick one box for each foodstuff.

	None	Less than 1	1-2	3 or more
Milk of all types (glasses) 316	☐	☐	☐	☐
Orange juice (glasses)	☐	☐	☐	☐
Potatoes	☐	☐	☐	☐
Slices of bread in total (incl. crispbread)	☐	☐	☐	☐
Slices of bread with				
– fish (e.g. mackerel in tomato sauce)	☐	☐	☐	☐
– cheese *(e.g. Gouda/Norvegia)*	☐	☐	☐	☐
– smoked cod caviare 322	☐ 1	☐ 2	☐ 3	☐ 4

How many times per week do you normally eat the following foodstuffs?

Tick for all foodstuffs listed.

	Never	Less than 1	1	2 or more
Yoghurt 323	☐	☐	☐	☐
Boiled or fried egg	☐	☐	☐	☐
Breakfast cereal/oatmeal, etc.	☐	☐	☐	☐
Dinner with				
– unprocessed meat	☐	☐	☐	☐
– fatty fish (e.g. salmon/red-fish)	☐	☐	☐	☐
– lean fish (e.g. cod) 328	☐	☐	☐	☐
– vegetables (fresh or cooked)	☐	☐	☐	☐
Carrots (fresh or cooked)	☐	☐	☐	☐
Cauliflower/cabbage/broccoli	☐	☐	☐	☐
Apples/pears	☐	☐	☐	☐
Oranges, mandarins, etc. 333	☐ 1	☐ 2	☐ 3	☐ 4

WELL BEING

How content do you generally feel with growing old?

- Good ..... 334 ☐ 1
- Quite good ..... ☐ 2
- Up and down ..... ☐ 3
- Bad ..... ☐ 4

What is your view of the future?

- Bright ..... 335 ☐ 1
- Not too bad ..... ☐ 2
- Quite worried ..... ☐ 3
- Dark ..... ☐ 4

TO BE ANSWERED BY WOMEN ONLY

MENSTRUATION

How old were you when you started menstruating? ..... 336 _____ years

How old were you when you stopped menstruating? ..... 338 _____ years

PREGNANCY

How many children have you given birth to? ..... 340 _____ Children

If you have given birth, fill in for each child the year of birth and approximately how many months you breastfed the child. If you have given birth to more than 6 children, note their birth year and number of months you breastfed at the space provided below for comments.

Child	Year of birth:	Number of months breastfed:
1	342 _____	_____
2	346 _____	_____
3	_____	_____
4	_____	_____
5	358 _____	_____
6	_____	_____

Have you during pregnancy had high blood pressure and/or proteinuria? ..... 366 Yes ☐ No ☐

If "Yes", during which pregnancy?	Pregnancy First	Later
High blood pressure 367	☐	☐
Proteinuria 369	☐	☐

ESTROGEN

Do you use, or have you ever used estrogen:

	Now	Previously	Never
Tablets or patches 371	☐	☐	☐
Cream or suppositories 372	☐	☐	☐

If you use estrogen, what brand do you currently use?

..... 373

Your comments:

Thank you for the help! Remember to mail the form today!

Tromsø Health Survey

Appendix IV

Questionnaire 1 & 2, Tromsø Study 5

Health survey

Personal Invitation

Don't write here

5.3 (Municipality) (County) (Country)

9.3 (Business) 9.4 (Occupation) 14.7 (Mark)

1. YOUR OWN HEALTH

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

Poor ☐ 1 | Not so good ☐ 2 | Good ☐ 3 | Very good ☐ 4

1.2 Do you have, or have you had?:

	Yes	No	Age first time
Asthma	☐	☐	
Hay fever	☐	☐	
Chronic bronchitis/emphysema	☐	☐	
Diabetes	☐	☐	
Osteoporosis	☐	☐	
Fibromyalgia/chronic pain syndrome	☐	☐	
Psychological problems for which you have sought help	☐	☐	
A heart attack	☐	☐	
Angina pectoris (heart cramp)	☐	☐	
Cerebral stroke/brain haemorrhage	☐	☐	

1.3 Have you noticed attacks of sudden changes in your pulse or heart rhythm in the last year? Yes ☐ No ☐

1.4 Do you get pain or discomfort in the chest when:
Walking up hills, stairs or walking fast on level ground? Yes ☐ No ☐

1.5 If you get such pain, do you usually:

Stop? ☐ 1 | Slow down? ☐ 2 | Carry on at the same pace? ☐ 3

1.6 If you stop, does the pain disappear within 10 minutes? Yes ☐ No ☐

1.7 Can such pain occur even if you are at rest? Yes ☐ No ☐

2. MUSCULAR AND SKELETAL COMPLAINTS

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

	No complaint	Some complaint	Severe complaint	Duration: Up to 2 weeks	Duration: 2 weeks or more
Neck/shoulders	☐	☐	☐	☐	☐
Arms, hands	☐	☐	☐	☐	☐
Upper part of your back...	☐	☐	☐	☐	☐
Lumbar region	☐	☐	☐	☐	☐
Hips, legs, feet	☐	☐	☐	☐	☐
Other places	☐	☐	☐	☐	☐
	1	2	3	1	2

2.2 Have you ever had:

	Yes	No	Age last time
Fracture in the wrist/forearm	☐	☐	
Hip fracture?	☐	☐	

3. OTHER COMPLAINTS

3.1 Below is a list of various problems. Have you experienced any of this during the last week (including today)?
(Tick once for each complaint)

	No complaint	Little complaint	Pretty much	Very much
Sudden fear without reason	☐	☐	☐	☐
Felt afraid or anxious	☐	☐	☐	☐
Faintness or dizziness	☐	☐	☐	☐
Felt tense or upset	☐	☐	☐	☐
Tend to blame yourself	☐	☐	☐	☐
Sleeping problems	☐	☐	☐	☐
Depressed, sad	☐	☐	☐	☐
Feeling of being useless, worthless	☐	☐	☐	☐
Feeling that everything is a struggle	☐	☐	☐	☐
Feeling of hopelessness with regard to the future	☐	☐	☐	☐
	1	2	3	4

4. USE OF HEALTH SERVICES

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

	None	1-3 times	4 or more
General practitioner (GP)	☐	☐	☐
Medical officer at work	☐	☐	☐
Psychologist or psychiatrist *(private or out-patient clinic)*	☐	☐	☐
Other specialist *(private or out-patient clinic)*	☐	☐	☐
Emergency GP *(private or public)*	☐	☐	☐
Hospital admission	☐	☐	☐
Home nursing care	☐	☐	☐
Physiotherapist	☐	☐	☐
Chiropractor	☐	☐	☐
Dentist	☐	☐	☐
Alternative practitioner	☐	☐	☐

5. CHILDHOOD/YOUTH AND AFFILIATION

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

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

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

Same municipality .... ☐ 1

Another municipality in the county ..... ☐ 2 Which one: _____

Another county in Norway ☐ 3 Which one: _____

Outside Norway ..... ☐ 4 Country:: _____

5.4 Have you moved within the last five years?

No ☐ 1 | Yes, one time ☐ 2 | Yes, more than once ☐ 3

6. BODY WEIGHT

6.1 Estimate your body weight when you were 25 years old: ☐☐☐ kg

7. FOOD AND BEVERAGES

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

	Rarely /never	1-3 times /month	1-3 times /week	4-6 times /week	1-2 times /day	3 times or more /day
Fruit, berries	☐	☐	☐	☐	☐	☐
Cheese *(all types)*	☐	☐	☐	☐	☐	☐
Potatoes	☐	☐	☐	☐	☐	☐
Boiled vegetables	☐	☐	☐	☐	☐	☐
Fresh vegetables/salad	☐	☐	☐	☐	☐	☐
Fatty fish *(e.g. salmon, trout, mackerel, herring)*	☐	☐	☐	☐	☐	☐
	1	2	3	4	5	6

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

	Don't use	Butter	Hard margarine	Soft/light margarine	Oils	Other
On bread	☐	☐	☐	☐	☐	☐
For cooking	☐	☐	☐	☐	☐	☐
	1	2	3	4	5	6

7.3 Do you use the following dietary supplements:

	Yes, daily	Sometimes	No
Cod liver oil, fish oil capsules	☐	☐	☐
Vitamins and/or mineral supplements?	☐	☐	☐

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

	Rarely /never	1-6 glasses /week	1 glass /day	2-3 glasses /day	4 glasses or more /day
Full milk, full-fat curdled milk, yoghurt	☐	☐	☐	☐	☐
Semi-skimmed milk, semi-skimmed curdled milk,low-fat yoghurt	☐	☐	☐	☐	☐
Skimmed milk, skimmed curdled milk	☐	☐	☐	☐	☐
Extra semi-skimmed milk	☐	☐	☐	☐	☐
Juice	☐	☐	☐	☐	☐
Water	☐	☐	☐	☐	☐
Mineral water (e.g. Farris, Ramløsa etc)	☐	☐	☐	☐	☐
Cola-containing soft drink	☐	☐	☐	☐	☐
Other soda/soft drink	☐	☐	☐	☐	☐
	1	2	3	4	5

7.5 Do you usually drink soft drink: with sugar ☐ 1 without sugar ☐ 2

7.6 How many cups of coffee and tea do you drink daily? *Number of cups*
(Put 0 for the types you don't drink daily)

Filtered coffee ..... ☐☐

Boiled coffee/coarsely ground coffee for brewing ..... ☐☐

Other type of coffee ..... ☐☐

Tea ..... ☐☐

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

Never consumed alcohol ☐ 1	Have not consumed alcohol last year ☐ 2	A few times last year ☐ 3	About 1 time a month ☐ 4
2-3 times per month ☐ 5	About1 time a week ☐ 6	2-3 times a week ☐ 7	4-7 times a week ☐ 8

To those who have consumed the last year:

7.8 When you drink alcohol, how many glasses or drinks do you normally drink? *number* ☐☐

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

7.10 When you drink, do you normally drink: *(Tick one or more)*

Beer ☐ Wine ☐ Spirits ☐

8. SMOKING

8.1 How many hours a day do you normally spend in smoke-filled rooms? *Number of total hours* ☐☐

	Yes	No
8.2 Did any of the adults smoke at home while you were growing up?	☐	☐
8.3 Do you currently, or did you previously live together with a daily smoker after your 20th birthday?	☐	☐

	Yes, now	Yes, previously	Never
8.4 Do you/did you smoke daily?	☐	☐	☐

If NEVER: Go to question 9 : (EDUCATION AND WORK)

8.5 If you smoke daily now, do you smoke:	Yes	No
Cigarettes?	☐	☐
Cigars/cigarillos?	☐	☐
A pipe?	☐	☐

8.6 If you previously smoked daily, how long is it since you quit? *Number of years* ☐☐

8.7 If you currently smoke, or have smoked previously:

How many cigarettes do you or did you normally smoke per day? *Number of cigarettes* ☐☐

How old were you when you began daily smoking? *Age in years* ☐☐

How many years in all have you smoked daily? *Number of years* ☐☐

9. EDUCATION AND WORK

9.1 How many years of education have you completed? *Number of years* ☐☐
(Include all the years you have attended school or studied)

9.2 Do you currently have paid work?

Yes, full-time ☐ 1 Yes, part-time ☐ 2 No ☐ 3

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

Business: _____
If retired, enter the former business and occupation. Also applies to 9.4

9.4 Which occupation/title have or had you at this workplace? *(e.g. Secretary, teacher, industrial worker, nurse, carpenter, manager, salesman, driver, etc.)*

Occupation: _____

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

Self-employed ☐ Employee ☐ Family member ☐

	Yes	No
9.6 Do you believe that you are in danger of losing your current work or income within the next two years?	☐	☐

9.7 Do you receive any of the following benefits?	Yes	No
Sickness benefit (are on sick leave)	☐	☐
Old age pension, early retirement (AFP) or survivor pension	☐	☐
Rehabilitation/reintegration benefit	☐	☐
Disability pension (full or partial)	☐	☐
Unemployment benefits during unemployment	☐	☐
Social welfare benefits	☐	☐
Transition benefit for single parents	☐	☐

10. EXERCISE AND PHYSICAL ACTIVITY

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

	Hours per week: None	Less than 1	1-2	3 or more
Light activity *(not sweating/out of breath)...*	☐	☐	☐	☐
Hard physical activity *(sweating/out of breath).....*	☐ 1	☐ 2	☐ 3	☐ 4

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

Reading, watching TV or other sedentary activity? ..... ☐ 1

Walking, cycling or other forms of exercise at least 4 hours a week? ..... ☐ 2
(Include walking or cycling to work, Sunday walk/stroll,etc.)

Participation in recreational sports, heavy gardening, etc.? ☐ 3
(Note: duration of activity at least 4 hours a week)

Participation in hard training or sports competitions, regularly several times a week? ..... ☐ 4

11. FAMILY AND FRIENDS

11.1 Do you live with:

	Yes	No
Spouse/partner?.....	☐	☐

11.2 How many good friends do you have? *Number of friends* ☐☐

Count the ones you can talk confidentially with and who can give you help when you need it. Do not count people you live with, but do include other relatives.

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

Great interest	Some interest	Little interest	No interest	Uncertain
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

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

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

Yes, a lot	Yes, some	Yes, a little	No	Never tried
☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

12. ILLNESS IN THE FAMILY

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

	Yes	No	Don't know
	☐	☐	☐

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

	Mother	Father	Brother	Sister	Child	None of these
Cerebral stroke or brain haemorrhage	☐	☐	☐	☐	☐	☐
Heart attack before age of 60 years	☐	☐	☐	☐	☐	☐
Asthma.....	☐	☐	☐	☐	☐	☐
Cancer	☐	☐	☐	☐	☐	☐
Diabetes	☐	☐	☐	☐	☐	☐

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

Don't know, not applicable	Mother's age	Father's age	Brother's age	Sister's age	Child's age
☐	☐☐	☐☐	☐☐	☐☐	☐☐

13. USE OF MEDICINES

With medicines, we mean drugs purchased at pharmacies. Supplements and vitamins are not considered here.

13.1 Do you use:

	Now	Previously, but not now	Never used
Blood pressure lowering drugs	☐	☐	☐
Cholesterol-lowering drugs	☐	☐	☐

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

	Not used in the last 4 weeks	Less than every week	Every week but not daily	Daily
Painkillers non-prescription	☐	☐	☐	☐
Painkillers on prescription	☐	☐	☐	☐
Sleeping pills	☐	☐	☐	☐
Tranquillizers	☐	☐	☐	☐
Antidepressants	☐	☐	☐	☐
Other prescription medicines ...	☐ 1	☐ 2	☐ 3	☐ 4

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

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

Name of the medicine: *(one name per line)*	Reason for use of the medicine	How long have you used the medicine: Up to 1 year	1 year or more
		☐	☐
		☐	☐
		☐	☐
		☐	☐
		☐	☐
		☐	☐
		☐	☐

If there is not enough space here, you may continue on a separate sheet that you attach

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

14.1 How old were you when you started menstruating? *Age in years* ☐☐

14.2 If you no longer menstruating, how old were you when you stopped menstruating? *Age in years* ☐☐

14.3 Are you pregnant at the moment?

Yes	No	Uncertain	Above fertile age
☐ 1	☐ 2	☐ 3	☐ 4

14.4 How many children have you given birth to? *Number of children* ☐☐

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

	Now	Before, but not now	Never
Oral contraceptive pills/mini pill/ contraceptive injection	☐	☐	☐
Hormonal intrauterine device (IUD) *(not ordinary IUD)*..	☐	☐	☐
Estrogen *(tablets or patches)*	☐	☐	☐
Estrogen *(cream or suppositories)*	☐	☐	☐

14.6 If you use/have used prescription estrogen:
How long have you used it? *Number of years* ☐☐

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

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E

Health survey

Personal invitation

Do not write here:

E13 (Municipality) (County) (Country) E15 (Mark)

E1. YOUR OWN HEALTH

What is your current state of health? *(Tick only once)*

Poor ☐ 1 | Not so good ☐ 2 | Good ☐ 3 | Very good ☐ 4

Do you have, or have you had?:

	Yes	No	Age first time
Asthma	☐	☐	☐☐
Chronic bronchitis/emphysema	☐	☐	☐☐
Diabetes	☐	☐	☐☐
Osteoporosis	☐	☐	☐☐
Fibromyalgia/chronic pain syndrome	☐	☐	☐☐
Psychological problems for which you have sought help	☐	☐	☐☐
A heart attack	☐	☐	☐☐
Angina pectoris (heart cramp)	☐	☐	☐☐
Cerebral stroke/brain haemorrhage	☐	☐	☐☐

Do you get pain or discomfort in the chest when:

	Yes	No
Walking up hills, stairs, or walking fast on level ground?	☐	☐

If you get such pain, do you usually:

Stop? ☐ 1 | Slow down? ☐ 2 | Carry on at the same pace? ☐ 3

	Yes	No
If you stop, does the pain disappear within 10 minutes?	☐	☐
Can such pain occur even if you are at rest?	☐	☐

E2. ILLNESS IN THE FAMILY

Have one or more of your parents or siblings had:

	Yes	No	Don't know
A heart attack (heart wounds) or angina pectoris (heart cramp)	☐	☐	☐

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

	Mother	Father	Brother	Sister	Child	None of these
Cerebral stroke or brain haemorrhage	☐	☐	☐	☐	☐	☐
Heart attack before age of 60 years	☐	☐	☐	☐	☐	☐
Asthma	☐	☐	☐	☐	☐	☐
Cancer	☐	☐	☐	☐	☐	☐
Diabetes	☐	☐	☐	☐	☐	☐

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

Don't know, not applicable	Mother's age	Father's age	Brother's age	Sister's age	Child's age
☐	☐☐	☐☐	☐☐	☐☐	☐☐

E3. COMPLAINTS

Below is a list of various problems.
Have you experienced any of this during the last week (including today)?
(Tick once for each line)

	No complaint	Little complaint	Pretty much	Very much
Sudden fear without reason	☐	☐	☐	☐
Felt afraid or anxious	☐	☐	☐	☐
Faintness or dizziness	☐	☐	☐	☐
Felt tense or upset	☐	☐	☐	☐
Tend to blame yourself	☐	☐	☐	☐
Sleeping problems	☐	☐	☐	☐
Depressed, sad	☐	☐	☐	☐
Feeling of being useless, worthless	☐	☐	☐	☐
Feeling that everything is a struggle	☐	☐	☐	☐
Feeling of hopelessness with regard to the future.	☐ 1	☐ 2	☐ 3	☐ 4

E4. TEETH, MUSCLE AND SKELETON

How many teeth have you lost/extracted? *Number of teeth* ☐☐
(disregard milk-teeth and wisdom teeth)

Have you been bothered by pain and/or stiffness in muscles and joints during the last 4 weeks?

	No complaint	Little complaint	Severe complaint
Neck / shoulders	☐	☐	☐
Arms, hands	☐	☐	☐
Upper part of the back	☐	☐	☐
Lumbar regions	☐	☐	☐
Hips, legs, feet	☐	☐	☐
Other places	☐	☐	☐

Have you ever had:

	Yes	No	Age last time
Fracture in wrist/forearm?	☐	☐	☐☐
Hip fracture?	☐	☐	☐☐

Have you fallen down during the last year? *(Tick once only)*

No ☐ 1 | Yes, 1-2 times ☐ 2 | Yes, more than 2 times ☐ 3

E5. EXERCISE AND PHYSICAL ACTIVITY

How has your physical activity been during this last year?
Think of a weekly average for the year.
Answer both questions.

	Hours per week: None	Less than 1	1-2	3 or more
Light activity *(not sweating/out of breath)*	☐	☐	☐	☐
Hard physical activity *(sweating/out of breath)*	☐ 1	☐ 2	☐ 3	☐ 4

E6. BODY WEIGHT

Estimate your body weight when you were 25 years old: ☐☐☐ **kg.**

E7. EDUCATION

How many years of education have you completed? *Number of years*

(include all the years you have attended school or studied)

E8. FOOD AND BEVERAGES

How often do you usually eat these foods?
(Tick once for each line)

	Rarely /never	1-3 times /month	1-3 times /week	4-6 times /week	1-2 times /day	3 times or more /day
Fruit, berries	☐	☐	☐	☐	☐	☐
Cheese (all types)	☐	☐	☐	☐	☐	☐
Potatoes	☐	☐	☐	☐	☐	☐
Boiled vegetables	☐	☐	☐	☐	☐	☐
Fresh vegetables/salad	☐	☐	☐	☐	☐	☐
Fat fish (e.g. salmon, trout, mackerel, herring)	☐	☐	☐	☐	☐	☐
	1	2	3	4	5	6

Do you use dietary supplements:

	Yes, daily	Sometimes	No
Cod liver oil, fish oil capsules	☐	☐	☐
Vitamins and/or mineral supplements	☐	☐	☐

How much of the following do you usually drink?
(Tick once for each line)

	Rarely /never	1-6 glasses /week	1 glass /day	2-3 glasses /day	4 glasses or more /day
Full milk, full-fat curdled milk, yoghurt	☐	☐	☐	☐	☐
Semi-skimmed milk, semi-skimmed curdled milk, low-fat yoghurt	☐	☐	☐	☐	☐
Skimmed milk, skimmed curdled milk	☐	☐	☐	☐	☐
Extra semi-skimmed milk	☐	☐	☐	☐	☐
Juice	☐	☐	☐	☐	☐
Water	☐	☐	☐	☐	☐
Soft drink, mineral water	☐	☐	☐	☐	☐
	1	2	3	4	5

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

Filtered coffee

Boiled coffee/coarsely ground coffee for brewing

Other type of coffee

Tea

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

Never consumed alcohol ☐ 1	Have not consumed alcohol last year ☐ 2	A few times last year ☐ 3	About 1 time a month ☐ 4
2-3 times per month ☐ 5	About 1 time a week ☐ 6	2-3 times a week ☐ 7	4-7 times a week ☐ 8

To those who have consumed the last year:

When you drink alcohol, how many glasses or drinks do you normally drink? *Number*

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

E9. SMOKING

How many hours a day do you normally spend in smoke-filled rooms? *Number of total hours*

Did any of the adults smoke at home while you were growing up? ☐ Yes ☐ No

Do you currently, or did you previously live together with a daily smoker after your 20th birthday? ☐ Yes ☐ No

Do you/did you smoke daily? ☐ Yes, now ☐ Yes, previously ☐ Never

If you have NEVER smoked daily;
Go to question E11 (BODILY FUNCTIONS AND SAFETY)

If you smoke daily now, do you smoke:

	Yes	No
Cigarettes?	☐	☐
Cigars/cigarillos?	☐	☐
A pipe?	☐	☐

If you previously smoked daily, how long is it since you quit? *Number of years*

If you currently smoke, or have smoked previously:

How many cigarettes do you or did you normally smoke per day? *Number of cigarettes*

How old were you when you began daily smoking? *Age in years*

How many years in all have you smoked daily? *Number of years*

E10. BODILY FUNCTIONS AND SAFETY

Would you feel safe by walking alone in the evening in the area where you live?

Yes	A little unsafe	Very unsafe
☐ 1 2 3	☐	☐

When it comes to mobility, sight and hearing, can you:
(Tick once for each line)

	Without problems	With some problems	With great problems	No
Take a 5 minute walk in fairly high pace?	☐	☐	☐	☐
Read ordinary text in newspaper, if necessary with glasses?	☐	☐	☐	☐
Hear what is said in a normal conversation?	☐	☐	☐	☐
	1	2	3	4

Do you because of chronic health problems have difficulties with: *(Tick once for each line)*

	No difficulties	Some difficulties	Great difficulties
Move around in your home?	☐	☐	☐
Get out of your home by yourself?	☐	☐	☐
Participate in organization or other leisure time activities?	☐	☐	☐
Use public transport?	☐	☐	☐
Perform necessary daily shopping?	☐	☐	☐

E11. USE OF HEALTH SERVICES

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

	None	1-3 times	4 or more
A general practitioner (GP)	☐	☐	☐
Specialist *(private or out-patient clinic)*	☐	☐	☐
Emergency GP *(private or public)*.....	☐	☐	☐
Hospital admission	☐	☐	☐
Home nursing care	☐	☐	☐
Physiotherapist	☐	☐	☐
Chiropractor	☐	☐	☐
Municipal home care	☐	☐	☐
Dentist	☐	☐	☐
Alternative practitioner	☐	☐	☐

Are you confident that you will receive health care and home assistance if you need it?

YES ☐ 1 NO ☐ 2 Don't know ☐ 3

E12. FAMILY AND FRIENDS

Do you live: At home? ☐ 1 In an institution/shared apartment? ☐ 2

Do you live with:

	YES	NO
Spouse/ partner?.....	☐	☐
Other people?	☐	☐

How many good friends do you have?
Count the ones you can talk confidentially with and who can give you help when you need it. Do not count people you live with, but do include your children and other relatives.....

Number of friends ☐☐

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

Great interest ☐ 1 Some interest ☐ 2 Little interest ☐ 3 No interest ☐ 4 Uncertain ☐ 5

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

Number ☐☐

E13. CHILDHOOD/YOUTH AND AFFILIATION

How long altogether have you lived in the county? ☐☐ years

How long altogether have you lived in the municipality? ☐☐ years

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

Same municipality..... ☐ 1

Another municipality in the county..... ☐ 2 Which one:_____

Another county in Norway ☐ 3 Which one:_____

Outside Norway ..... ☐ 4 Country: _____

Have you moved during the last five years?

No ☐ 1 Yes, once ☐ 2 Yes, more than once ☐ 3

E14. USE OF MEDICINES

With medicines, we mean drugs purchased at pharmacies. Supplements and vitamins are not considered here

Do you use?
(Tick once for each line)

	Now	previously, but not now	Never used
Blood pressure lowering drugs	☐	☐	☐
Cholesterol-lowering drugs	☐	☐	☐
Drugs for osteoporosis	☐	☐	☐
Insulin.....	☐	☐	☐
Tablets for diabetes	☐	☐	☐

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

	Not used in the last 4 weeks	Less than every week	Every week, but not daily	Daily
Painkillers non-prescription.....	☐	☐	☐	☐
Painkillers on prescription	☐	☐	☐	☐
Sleeping pills.....	☐	☐	☐	☐
Tranquillizers	☐	☐	☐	☐
Antidepressants	☐	☐	☐	☐
Other prescription medicines	☐	☐	☐	☐
	1	2	3	4

State the name of the medicines you are using now and the reason you are taking the medicines (disease or symptom):
(Tick for each duration you have used the medicine)

Name of the medicine: (one name per line):	Reason for use of the medicine:	How long have you used the medicine: Up to 1 year	How long have you used the medicine: One year or more
		☐	☐
		☐	☐
		☐	☐
		☐	☐
		☐	☐
		☐	☐
		☐	☐

If there is not enough space here, you may continue on a separate sheet that you attach.

E15. THE REST OF THE FORM IS TO BE ANSWERED BY WOMEN ONLY

How old were you when you started menstruating? *Age in years* ☐☐

How old were you when you stopped menstruating? *Age in years* ☐☐

How many children have you given birth to? *Number of children* ☐☐

Do you use, or have you ever used estrogen? *Total number of years*

	Never	Previously	Now	
Tablets or patches	☐	☐	☐	☐☐
Cream or suppositories	☐	☐	☐	☐☐

If you use estrogen, which brand you use now?

_____

Have you ever used contraceptives pills? ..... Yes ☐ No ☐

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Label

Additional questions to the health survey in Troms and Finnmark 2001-2002

The main aim of the Tromsø Study is to improve our knowledge about cardiovascular diseases in order to aid prevention. The study is also intended to improve our knowledge of cancer and other general conditions, such as allergies, muscle pains and mental conditions. We would therefore like you to answer some questions about factors that may be relevant for your risk of getting these and other illnesses. This form is part of the Health Survey, which has been approved by the Norwegian Data Inspectorate and the Regional Board of Research Ethics. The answers will only be used for research purposes and will be treated strictly confidential.

The information you give us may later be linked with information from other public health registers in accordance with the rules laid down by the Data Inspectorate and the Regional Board of Research Ethics.

If you are unsure about what to answer, tick the box that you feel fits best.

The completed form should be sent to us in the enclosed prepaid envelope. Thank you in advance for helping us.

Yours sincerely

Department of Community Medicine
University of Tromsø

National Health Screening Service

If you do not wish to answer the questionnaire, tick the box below and return the form. Then you will not receive reminders.

I do not wish to answer the questionnaire ☐

Date of completion:

Day ☐☐ Month ☐☐ Year ☐☐☐☐

T1. NEIGHBORHOOD AND HOME

1.1 In which municipality did you live at the age of 1 year? *(If you have not lived in Norway, state country of residence instead of the municipality)*

_____

1.2 What type of house do you live in? *(Tick only once)*

- Detached house/villa ☐ 1
- Farm ☐ 2
- Flat/apartment ☐ 3
- Terraced/semi-detached house ☐ 4
- Institution/care home ☐ 5
- Other ☐ 6

1.3 How big is your house? ☐☐☐ m^2 *(gross)*

1.4 Are you bothered by: *(Tick once for each line)*

	No complaint	Little complaint	Severe complaint
Moisture, drought or coldness in your home	☐	☐	☐
Other forms of bad indoor climate	☐	☐	☐
Traffic noise (cars or aircraft)	☐	☐	☐
Other noise (industrial, construction, etc.)	☐	☐	☐
Neighbour noise	☐	☐	☐
Drinking water quality	☐	☐	☐
Air pollution from traffic	☐	☐	☐
Air pollution from wood/oil heating, factory etc.	☐	☐	☐

1.5 What home language did your grandparents have? *(Tick for one or more alternatives)*

	Norwegian	Sami	Kven/ Finnish	Other language
Mother's mother	☐	☐	☐	☐
Mother's father	☐	☐	☐	☐
Father's mother	☐	☐	☐	☐
Father's father	☐	☐	☐	☐

T1. NEIGHBORHOOD AND HOME (cont.)

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

Norwegian ☐ Sami ☐ Kven/ Finnish ☐ Other ☐

1.7 Do you feel that you have enough good friends? Yes ☐ No ☐

1.8 How often do you normally take part in organised gatherings, e.g. sewing circles, sports clubs, political meetings or other associations? *(Tick only once)*

- Never, or just a few times a year ☐ 1
- 1-3 times a month ☐ 2
- Approximately once a week ☐ 3
- More than once a week ☐ 4

T2. PAID AND UNPAID WORK

2.1 If you have paid or unpaid work, how would you describe your work? *(Tick only once)*

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

2.2 Can you decide yourself how your work (paid or unpaid) should be organised? *(Tick only once)*

- No, not at all ☐ 1
- To a small extent ☐ 2
- Yes, to a large extent ☐ 3
- Yes, I decide myself ☐ 4

2.3 Are you on call, do you work shifts or nights? Yes ☐ No ☐

T3. TOBACCO

3.1 Do you smoke?

Yes, daily ☐ 1 | Yes, sometimes ☐ 2 | No, never ☐ 3

If "Yes, sometimes"

What do you smoke?

☐ Cigarettes ☐ Pipe ☐ Cigar/cigarillos

3.2 Have you used or do you use snuff daily?

Yes, now ☐ | Yes, previously ☐ | Never ☐

If YES:

How many years altogether have you used snuff? ☐☐ years

T4. ALCOHOL

4.1 Are you a teetotaller? ..... Yes ☐ No ☐

4.2 How many times a month do you normally drink alcohol? ..... ☐☐ *Number of times*

(Do not count low-alcohol beer. Put 0 if less than once a month)

4.3 How many glasses of beer, wine or spirits do you normally drink in a fortnight?

Beer ☐☐ Wine ☐☐ Spirits ☐☐

(Do not count low-alcohol beer. Put 0 if you do not drink alcohol)

4.4 For approximately how many years has your alcohol consumption been at the same level you described above? ☐☐ years

4.5 Have you, in one or more periods in the last 5 years consumed so much alcohol that it has inhibited your work or social life?

Yes, at work ☐ 1 | Yes, socially ☐ 2 | Yes, both at work and social life ☐ 3 | No, never ☐ 4

T5. FOOD AND DIETARY SUPPLEMENTS

5.1 Do you usually eat breakfast every day? ... Yes ☐ No ☐

5.2 How many times a week do you eat a warm dinner? ..... ☐ *times*

5.3 How important is it for you to have a healthy diet?

Very ☐ 1 | Somewhat ☐ 2 | Little ☐ 3 | Not ☐ 4

5.4 Do you use the following dietary supplements?

	Yes, daily	sometimes	No
Iron tablets	☐	☐	☐
Calcium tablets or bonemeal	☐	☐	☐
Vitamin D supplements	☐	☐	☐
Cod liver oil	☐	☐	☐

T6. BODY WEIGHT

6.1 Do you currently try to change your body weight?

No ☐ 1 | Yes, I try to gain weight ☐ 2 | Yes, I try to lose weight ☐ 3

6.2 What weight would you be satisfied with (your "ideal weight")? ..... ☐☐☐ kg

T7. ILLNESSES AND INJURIES

7.1 Have you ever had:

Tick once for each question. Also give the age at the time. If you have had the condition several times, how old were you the last time

	Yes	No	Age last time
Severe injury requiring hospital admission	☐	☐	☐☐ years
Ankle fracture	☐	☐	☐☐ years
Peptic ulcer	☐	☐	☐☐ years
Peptic ulcer surgery	☐	☐	☐☐ years
Neck surgery	☐	☐	☐☐ years
Prostate surgery	☐	☐	☐☐ years

7.2 Do you have, or have you ever had:

(Tick once for each question)

	Yes	No
Cancer	☐	☐
Psoriasis.....	☐	☐
Thyroid disease	☐	☐
Glaucoma	☐	☐
Cataract	☐	☐
Osteoarthritis (arthrosis).....	☐	☐
Bent fingers	☐	☐
Skin contractions in your palms	☐	☐
Kidney stone	☐	☐
Appendectomy.....	☐	☐
Hernia surgery	☐	☐
Surgery/treatment for urine incontinence	☐	☐
Epilepsy.....	☐	☐
Poliomyelitis (polio)	☐	☐
Parkinson's disease.....	☐	☐
Migraine.....	☐	☐
Leg ulcer	☐	☐
Allergy and hypersensitivity:	Yes	No
Atopic eczema (e.g. childhood eczema)	☐	☐
Hand eczema.....	☐	☐
Food allergy	☐	☐
Other hypersensitivity (not allergy).....	☐	☐

7.3 Have you had common cold, influenza, gastroenteritis, etc. during the last 14 days? Yes ☐ No ☐

7.4 Have you during the last 3 weeks had common cold, influenza, bronchitis, pneumonia, sinusitis, or other respiratory infection? ..... Yes ☐ No ☐

7.5 Have you ever had bronchitis or pneumonia? ..... Yes ☐ No ☐

7.6 Have you during the last 2 years had bronchitis or pneumonia? *(Tick only once)*

No ☐ 1 | 1-2 times ☐ 2 | More than 2 times ☐ 3

T8. SYMPTOMS

8.1 Have you in the last two weeks felt:
(Tick once for each question)

	No	A Little	A lot	Very much
Nervous or worried	☐	☐	☐	☐
Bothered by anxiety	☐	☐	☐	☐
Confident and calm	☐	☐	☐	☐
Irritable	☐	☐	☐	☐
Happy and optimistic	☐	☐	☐	☐
Down/depressed	☐	☐	☐	☐
Lonely	☐	☐	☐	☐
	1	2	3	4

8.2 Do you cough about daily for periods of the year? Yes ☐ No ☐

If YES:
Is your cough productive? ☐ ☐

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

8.3 Have you had episodes with wheezing in the chest? ☐ ☐

If YES:
Has this occurred: *(Tick once for each question)*

	Yes	No
At night	☐	☐
In connection with respiratory infections	☐	☐
In connection with physical exertion	☐	☐
In connection with very cold weather	☐	☐

8.4 Do you get pain in the calf while walking Yes ☐ No ☐

If YES:
How long can you go before you notice the pain? ☐☐☐ *meter*

8.5 Do you get short-winded in the following situations?
(Tick once for each question)

	Yes	No
While walking fast on level ground or slight up hills	☐	☐
While walking calmly on level ground	☐	☐
While washing or dressing yourself	☐	☐
While resting	☐	☐

8.6 Do you have to stop because of short-windedness while walking in your own pace on level ground? Yes ☐ No ☐

8.7 Have you during the last year suffered from pain and/or stiffness in muscles and joints that have lasted continuously for at least 3 months? Yes ☐ No ☐

If YES:
Has the complaint reduced your leisure time activity? Yes ☐ No ☐

For how long has the complaint endured in total?

approx. ☐☐ years and ☐☐ months

Has the complaint reduced your ability to work during the last year? *(Also applies to domestic workers and pensioners (Tick once)*

No/insignificantly	To some extend	Significantly reduced	Do not know
☐ 1	☐ 2	☐ 3	☐ 4

Have you been on sick leave due to these complaints during the last year? Yes ☐ No ☐ Do not work ☐

T8. SYMPTOMS (continue)

8.8 How often do you suffer from sleeplessness?
(Tick only once)

Never, or just a few times a year	☐ 1
1-3 times a month	☐ 2
Approximately once a week	☐ 3
More than once a week	☐ 4

8.9 If you suffer from sleeplessness monthly or more frequently, what time of the year does it affect you most?

No particular time of the year	☐ 1
Especially during the polar night	☐ 2
Especially during the midnight sun season	☐ 3
Especially in spring and autumn	☐ 4

8.10 Have you in the last year suffered from sleeplessness to the extend that it has affected your ability to work ? Yes ☐ No ☐

8.11 Do you usually sleep during the day? ☐ ☐

8.12 How often do you suffer from urinary incontinence?

Never	☐ 1
Not more than once a month	☐ 2
Two or more times a month	☐ 3
Once a week or more	☐ 4

8.13 Are you able to walk down 10 steps without holding on to something (e.g. a handrail) Yes ☐ No ☐

8.14 Do you use glasses? ☐ ☐

8.15 Do you use a hearing aid? ☐ ☐

8.16 How is your memory?
(Tick once for each question)

	Yes	No
Do you forget what you just have heard or read?	☐	☐
Do you forget where you have placed things?	☐	☐
Is it more difficult to remember now than earlier?	☐	☐
Do you more often write memos now than earlier?	☐	☐

If "YES" on one of these questions; **Is this a problem in your daily life?** Yes ☐ No ☐

T9. MEDICINES

9.1 Do you use, or have you used any of the following medicines:

	Now	Previously, but not now	Age when used 1st time	Never used
Drugs for osteoporosis	☐	☐	☐☐ years	☐
Tablets for diabetes	☐	☐	☐☐ years	☐
Drugs for hypothyroidism (thyroxine)	☐	☐	☐☐ years	☐

9.2 Do you use any medicines which you take as injections? Yes ☐ No ☐

If YES:
Give the name of the medicines (for injection):
(one name per line)

_____

_____

T10. ILLNESS IN THE FAMILY

10.1 Tick for the relatives who have or have ever had any of the diseases: *(Tick for each line)*

	Mother	Father	Brother	Sister	Child	None of these
Heart attack (heart wound)	☐	☐	☐	☐	☐	☐
Angina pectoris (heart cramp)	☐	☐	☐	☐	☐	☐
High blood pressure	☐	☐	☐	☐	☐	☐
Aneurysm.....	☐	☐	☐	☐	☐	☐
Gastric/duodenal ulcer	☐	☐	☐	☐	☐	☐
Hip fracture	☐	☐	☐	☐	☐	☐
Psychological problems ..	☐	☐	☐	☐	☐	☐
Allergy	☐	☐	☐	☐	☐	☐
Osteoarthritis (arthrosis) ..	☐	☐	☐	☐	☐	☐
Dementia	☐	☐	☐	☐	☐	☐

10.2 How many siblings and children do you have?

	Brothers	Sisters	Children
Number	☐☐	☐☐	☐☐

10.3 Do you usually do extra caring work because of illness etc. in your close family?

Yes, daily/almost daily ☐ 1 Yes, sometimes ☐ 2 No ☐ 3

10.4 Do you/your family receive home aid or home nursing care?..... Yes ☐ No ☐

	Yes	No	Age at death
10.5 Is your mother alive?	☐	☐	☐☐☐ years
10.6 Is your father alive?	☐	☐	☐☐☐ years

T11. MOBILE TELEPHONE

11.1 Do you have (own, rent, etc.) a mobile telephone?

Yes, always ☐ 1 Yes, sometimes ☐ 2 No ☐ 3

If Yes:

What do you use your mobile telephone for, and how often do you use it? *(Tick once for each line)*

	Number of times per day				
	30 or more	10-29	2-9	1 or less	Never
Conversations..	☐	☐	☐	☐	☐
Text messaging	☐	☐	☐	☐	☐
	12345				

T12. THE REST IS TO BE ANSWERED BY WOMEN ONLY

12.1 If you have given birth, fill in each child's birth year and how many months you breastfed after delivery.
(If you did not breastfeed, write 0)

Child:	Birth year:	Number of months breastfed:
1st child	☐☐☐☐	☐☐
2nd child	☐☐☐☐	☐☐
3rd child	☐☐☐☐	☐☐
4th child	☐☐☐☐	☐☐
5th child	☐☐☐☐	☐☐
6th child	☐☐☐☐	☐☐

(If more children, use additional sheet)

T12. THE REST IS TO BE ANSWERED BY WOMEN ONLY

12.2 If you still have menstrate or are pregnant:
What date did your last menstruation start?

Day ☐☐ Month ☐☐ Year ☐☐☐☐

12.3 If you no longer menstruate; why did your periods stop? *(Tick once)*

It stopped by itself ..... ☐ 1
Uterus surgery ..... ☐ 2
Surgically removed both ovaries ..... ☐ 3
Other reason (e.g. radiation, chemotherapy) ... ☐ 4

12.4 Do you use or have you used prescribed estrogen (tablets or patches)?..... Yes ☐ No ☐

If YES:
How old were you when you started taking estrogen ? ..... ☐☐ years

If you stopped using estrogen,
How old were you when you stopped taking estrogen?..... ☐☐ years

12.5 Do you use or have you used oral contraceptive pills?..... Yes ☐ No ☐

If YES:
How old were you when you started taking the pill?..... ☐☐ years

How many years in total have you taken the pills?.... *Number of years* ☐☐

If you have given birth:
How many years did you take the pill before your first delivery?... *Number of years* ☐☐

If you stopped taking the pill:
How old were you when you stopped?.... ☐☐ years

12.6 Apart from pregnancy and after giving birth, have you ever stopped having menstruation for 6 months or more? Yes ☐ No ☐

If YES:
How many times?..... ☐☐ times

12.7 How is your current menstruation status?

I have not had menstruation in the last year ☐ 1
I have regular menstruation ..... ☐ 2
I have irregular menstruation ..... ☐ 3

12.8 When you were 25-29 years old, how many days usually passed between the start of two periods?

Minimum ☐☐ days Maximum ☐☐ days Do not know ☐

The periods were of approximately equal length every time?..... Yes ☐ No ☐

How many days did a typical menstrual bleeding period last?... ☐☐ days

Thank you for the help!
Remember to mail the form today!

IE 050000-1046-1 - 25.000 - Beyer Hecos 02.01

Appendix V

Questionnaire 1 & 2, Tromsø Study 6

The Tromsø Study

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

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HEALTH AND DISEASES

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

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

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

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

3 **Do you have, or have you had?**

	Yes	No	Age first time
A heart attack	☐	☐	
Angina pectoris *(heart cramp)*	☐	☐	
Cerebral stroke/brain hemorrhage	☐	☐	
Atrial fibrillation	☐	☐	
High blood pressure	☐	☐	
Osteoporosis	☐	☐	
Asthma	☐	☐	
Chronic bronchitis/Emphysema/COPD	☐	☐	
Diabetes	☐	☐	
Psychological problems *(for which you have sought help)*	☐	☐	
Hypothyroidism	☐	☐	
Kidney disease, *not including urinary tract infection (UTI)*	☐	☐	
Migraine	☐	☐	

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

- ☐ Yes ☐ No

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

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

6 **Below you find a list of various problems. Have you experienced any of this during the last week (including today)?** (Tick once for each complaint)

	No complaint	Little complaint	Pretty much	Very much
Sudden fear without reason	☐	☐	☐	☐
Felt afraid or anxious	☐	☐	☐	☐
Faintness or dizziness	☐	☐	☐	☐
Felt tense or upset	☐	☐	☐	☐
Tend to blame yourself	☐	☐	☐	☐
Sleeping problems	☐	☐	☐	☐
Depressed, sad	☐	☐	☐	☐
Feeling of being useless, worthless	☐	☐	☐	☐
Feeling that everything is a struggle	☐	☐	☐	☐
Feeling of hopelessness with regard to the future	☐	☐	☐	☐

USE OF HEALTH SERVICES

7 **Have you during the last 12 months visited:** If YES; how many times?

	Yes	No	No. of times
General practitioner (GP)	☐	☐	
Psychiatrist/psychologist	☐	☐	
Medical specialist outside hospital *(other than general practitioner/psychiatrist)*	☐	☐	
Physiotherapist	☐	☐	
Chiropractor	☐	☐	
Alternative practitioner *(homeopath, acupuncturist, foot zone therapist, herbal medicine practitioner, laying on hands practitioner, healer, clairvoyant, etc.)*	☐	☐	
Dentist/dental service	☐	☐	

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

	Yes	No	No. of times
Admitted to a hospital	☐	☐	
Had consultation in a hospital without admission;			
At psychiatric out-patient clinic	☐	☐	
At another out-patient clinic	☐	☐	

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

- ☐ Yes ☐ No

USE OF MEDICINES

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

	Never used	Now	Earlier	Age first time
Blood pressure lowering drugs	☐	☐	☐	
Cholesterol lowering drugs	☐	☐	☐	
Drugs for heart disease	☐	☐	☐	
Diuretics	☐	☐	☐	
Drugs for osteoporosis	☐	☐	☐	
Insulin	☐	☐	☐	
Tablets for diabetes	☐	☐	☐	
The drugs for hypothyroidism Thyroxine/levaxin	☐	☐	☐	

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

	Not used in the last 4 weeks	Less than every week	Every week, but not daily	Daily
Painkillers on prescription	☐	☐	☐	☐
Painkillers non-prescription	☐	☐	☐	☐
Sleeping pills	☐	☐	☐	☐
Tranquillizers	☐	☐	☐	☐
Antidepressants	☐	☐	☐	☐

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

_____

_____

_____

_____

_____

_____

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

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

FAMILY AND FRIENDS

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

	Yes	No	Number
Spouse/partner	☐	☐	
Other people older than 18 years	☐	☐	
People younger than 18 years	☐	☐	

14 **Tick for the relatives who have or have had**

	Parents	Children	Siblings
A heart attack	☐	☐	☐
A heart attack before age of 60	☐	☐	☐
Angina pectoris *(heart cramp)*	☐	☐	☐
Cerebral stroke/brain haemorrhage	☐	☐	☐
Osteoporosis	☐	☐	☐
Gastric/duodenal ulcers	☐	☐	☐
Asthma	☐	☐	☐
Diabetes	☐	☐	☐
Dementia	☐	☐	☐
Psychological problems	☐	☐	☐
Substance abuse	☐	☐	☐

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

☐ Yes ☐ No

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

☐ Yes ☐ No

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

☐ Never, or just a few times a year

☐ 1-2 times a month

☐ Approximately once a week

☐ More than once a week

WORK, SOCIAL SECURITY AND INCOME

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

☐ Primary/secondary school, modern secondary school

☐ Technical school, vocational school, 1-2 years senior high school

☐ High school diploma

☐ College/university less than 4 years

☐ College/university 4 years or more

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

☐ Full time work ☐ Housekeeping

☐ Part time work ☐ Retired/benefit recipient

☐ Unemployed ☐ Student/military service

20 **Do you receive any of the following benefits?**

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

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

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

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

☐ Yes ☐ No

PHYSICAL ACTIVITY

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

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

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

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

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

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

26 **How hard do you exercise on average?**

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

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

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

ALCOHOL AND TOBACCO

28 **How often do you drink alcohol?**

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

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

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

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

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

31 **Do you smoke sometimes, but not daily?**

☐ Yes ☐ No

32 **Do you/did you smoke daily?**

- ☐ Yes, now
- ☐ Yes, previously
- ☐ Never

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

Number of years ☐☐

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

Number of cigarettes ☐☐

35 **How old were you when you began daily smoking?**

Age in years ☐☐

36 **How many years in all have you smoked daily?**

Number of years ☐☐

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

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

DIET

38 **Do you usually eat breakfast every day?**

☐ Yes ☐ No

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

Number of units ☐☐

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

Number ☐☐

41 **How often do you usually eat these foods?**
(Tick once for each line)

	0-1 times/ mth	2-3 times/ mth	1-3 times/ week	4-6 times/ week	1-2 times/ day
Potatoes	☐	☐	☐	☐	☐
Pasta/rice	☐	☐	☐	☐	☐
Meat *(not processed)*	☐	☐	☐	☐	☐
Processed meat *(sausages, hamburger, etc.)*	☐	☐	☐	☐	☐
Fruits, vegetables, berries	☐	☐	☐	☐	☐
Lean fish	☐	☐	☐	☐	☐
Fatty fish *(e.g. salmon, trout, mackerel, herring, halibut, redfish)*	☐	☐	☐	☐	☐

42 **How much do you usually drink the following?**
(Tick once for each line)

	Rarely/ never	1-6 glasses /week	1 glass /day	2-3 glasses /day	4 or more glasses /day
Milk, curdled milk, yoghurt	☐	☐	☐	☐	☐
Juice	☐	☐	☐	☐	☐
Soft drinks with sugar	☐	☐	☐	☐	☐

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

	Number of cups
Filtered coffee	☐☐
Boiled coffee (coarsely ground coffee for brewing)	☐☐
Other types of coffee	☐☐
Tea	☐☐

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

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

45 **Do you use the following nutritional supplements?**

	Daily	Sometimes	No
Cod liver oil or fish oil capsules	☐	☐	☐
Omega 3 capsules *(fish oil, seal oil)*	☐	☐	☐
Calcium tablets	☐	☐	☐

QUESTIONS FOR WOMEN

46 **Are you pregnant at the moment?**

☐ Yes ☐ No ☐ Uncertain

47 **How many children have you given birth to?**

Number ☐☐

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

Child	Birth year	Birth weight in grams	Months of breastfeeding
1	☐☐☐☐	☐☐☐☐	☐☐
2	☐☐☐☐	☐☐☐☐	☐☐
3	☐☐☐☐	☐☐☐☐	☐☐
4	☐☐☐☐	☐☐☐☐	☐☐
5	☐☐☐☐	☐☐☐☐	☐☐
6	☐☐☐☐	☐☐☐☐	☐☐

49 **Have you during pregnancy had high blood pressure?**

☐ Yes ☐ No

50 **If yes, during which pregnancy?**

☐ The first ☐ Second or later

51 **Have you during pregnancy had proteinuria?**

☐ Yes ☐ No

52 **If yes, during which pregnancy?**

☐ The first ☐ Second or later

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

☐ Yes ☐ No

54 **If yes, which child?**

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

55 **How old were you when you started menstruating?**

Age ☐☐

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

Oral contraceptives, hormonal intrautrine or similar ☐ Yes ☐ No

Hormone treatment for menopausal problems ☐ Yes ☐ No

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

Tromsø 6

- part of The Tromsø Study

FILL OUT THE FORM IN THIS WAY:

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

☒ Correct

☑ Wrong

☒ Wrong

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

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

7 4 Correct

7 4 Wrong

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

1. DESCRIPTION OF YOUR HEALTH STATUS

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

1.01 **Mobility**

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

1.02 **Self-care**

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

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

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

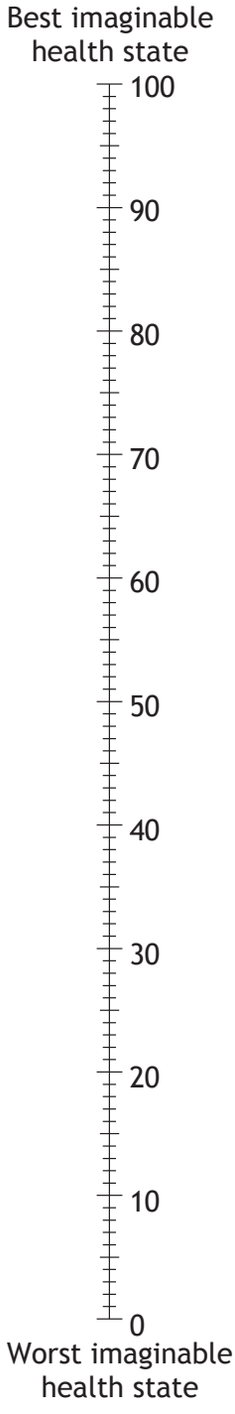
1.04 **Pain and discomfort**

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

1.05 **Anxiety and depression**

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

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



2. CHILDHOOD/YOUTH AND AFFILIATION

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

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

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

- ☐ Very good
- ☐ Good
- ☐ Difficult
- ☐ Very difficult

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

- ☐ Very important
- ☐ Somewhat important
- ☐ Not important

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

- ☐ Norwegian
- ☐ Sami
- ☐ Kven/Finnish
- ☐ Another

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

Number of siblings ..... ☐☐

Number of children ..... ☐☐

2.06 **Is your mother alive?**

☐ Yes ☐ No

If NO: her age when she died ..... ☐☐

Is your father alive?

☐ Yes ☐ No

If NO: his age when he died ..... ☐☐

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

	Mother	Father	Spouse/ partner
7-10 years primary/secondary school, modern secondary school	☐	☐	☐
Technical school, vocational school, 1-2 years senior high school	☐	☐	☐
High school diploma	☐	☐	☐
College or university (less than 4 years)	☐	☐	☐
College or university (4 years or more)	☐	☐	☐

3. WELL BEING AND LIVING CONDITIONS

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

	Completely disagree 1	2	3	4	5	6	7 Completely agree
In most ways my life is close to my ideal	☐	☐	☐	☐	☐	☐	☐
My life conditions are excellent	☐	☐	☐	☐	☐	☐	☐
I am satisfied with my life	☐	☐	☐	☐	☐	☐	☐
I have a positive view of my future health	☐	☐	☐	☐	☐	☐	☐
By living healthy, I can prevent serious diseases	☐	☐	☐	☐	☐	☐	☐

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

	Completely disagree 1	2	3	4	5	6	7 Completely agree
My work is tiring, physically or mentally	☐	☐	☐	☐	☐	☐	☐
I have sufficient influence on when and how my work should be done	☐	☐	☐	☐	☐	☐	☐
I am being bullied or harassed at work	☐	☐	☐	☐	☐	☐	☐
I am being treated fairly at work	☐	☐	☐	☐	☐	☐	☐

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

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

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

	No	Yes, as a child	Yes, as adult	Yes, last year
Been tormented, or threatened with violence	☐	☐	☐	☐
Been beaten, kicked at or victim of other types of violence	☐	☐	☐	☐
Someone in your close family have used alcohol or drugs in such a way that it has caused you worry	☐	☐	☐	☐

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

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

4. ILLNESS AND WORRIES

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

☐ Yes ☐ No

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

	Yes	No
Been to a general practitioner	☐	☐
Been to a medical specialist	☐	☐
Been to emergency department	☐	☐
Been admitted to a hospital	☐	☐
Been to an alternative practitioner *(chiropractor, homeopath or similar)*	☐	☐

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

☐ Yes ☐ No

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

	Yes	No
When you walk rapidly on level ground or up a moderate slope	☐	☐
When you walk calmly on level ground	☐	☐
While you are washing or dressing	☐	☐
At rest	☐	☐

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

☐ Yes ☐ No

If YES: Is the cough usually productive?

☐ Yes ☐ No

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

☐ Yes ☐ No

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

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

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

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

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

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

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

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

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

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

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

	Yes	No
Do you think that your memory has declined?	☐	☐
Do you often forget where you have placed your things?	☐	☐
Do you have difficulties finding common words in a conversation?	☐	☐
Have you problems performing daily tasks you used to master?	☐	☐
Have you been examined for memory problems?	☐	☐

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

☐ Yes ☐ No

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

	No complaint	Little complaint	Severe complaint
Neck, shoulders	☐	☐	☐
Arms, hands	☐	☐	☐
Upper part of the back	☐	☐	☐
The lumbar region	☐	☐	☐
Hips, leg, feet	☐	☐	☐
Other places	☐	☐	☐

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

	No complaint	Little complaint	Severe complaint
Neck, shoulders	☐	☐	☐
Arms, hands	☐	☐	☐
Upper part of the back	☐	☐	☐
The lumbar region	☐	☐	☐
Hips, leg, feet	☐	☐	☐
Other places	☐	☐	☐

4.12 **Have you ever had:**

	Yes	No	Age last time
Fracture in the wrist/forearm?	☐	☐	☐☐
Hip fracture?	☐	☐	☐☐

4.13 **Have you been diagnosed with arthrosis by a physician?**
☐ Yes ☐ No

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

	Never	Some	Much
Nickel allergy	☐	☐	☐
Pollen allergy	☐	☐	☐
Other allergies	☐	☐	☐

4.15 **Have you ever experienced infertility for more than 1 year?**
☐ Yes ☐ No

If Yes: was it due to:

	Yes	No	Do not know
A condition concerning you?	☐	☐	☐
A condition concerning your partner?	☐	☐	☐

4.16 **To which degree have you had the following complaints during the last <u>12 months</u>?**

	Never	Some	Much
Nausea	☐	☐	☐
Heartburn/regurgitation	☐	☐	☐
Diarrhoea	☐	☐	☐
Constipation	☐	☐	☐
Alternating diarrhoea and constipation	☐	☐	☐
Bloated stomach	☐	☐	☐
Abdominal pain	☐	☐	☐

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

	Yes	No
Was it located in your upper stomach?	☐	☐
Were you bothered as often as once a week or more during the last 3 months?	☐	☐
Do you feel symptoms relief after bowel movement?	☐	☐
Are the symptoms related to more frequent or rare bowel movements than normally?	☐	☐
Are the symptoms related to more loose or hard stool than normally?	☐	☐
Do the symptoms appear after a meal?	☐	☐

4.18 **Have you ever had:**

	Yes	No	Age last time
Gastric ulcer	☐	☐	☐☐
Duodenal ulcer	☐	☐	☐☐
Ulcer surgery	☐	☐	☐☐

4.19 **For women: Have you ever had a miscarriage?**
☐ Yes ☐ No ☐ Do not know
If Yes: number of times ☐☐

4.20 **For men: Have your partner ever had a miscarriage?**
☐ Yes ☐ No ☐ Do not know
If Yes: number of times ☐☐

4.21 **Is your diet gluten-free?**
☐ Yes ☐ No ☐ Do not know

4.22 **Have you been diagnosed with Dermatitis Herpetiformis (DH)?**
☐ Yes ☐ No ☐ Do not know

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

☐ Yes ☐ No ☐ Do not know

4.24 **Do you have your natural teeth?**

☐ Yes ☐ No

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

☐ 0 ☐ 1-5 ☐ 6-10 ☐ 10+

4.26 **Have you been suffering from headache <u>the last year</u>?**

☐ Yes ☐ No

If No: go to section 5, food habits

4.27 **What kind of headache are you suffering from?**

☐ Migraine ☐ Other headache

4.28 **How many days <u>per month</u> do you suffer from headache?**

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

4.29 **Is the headache attacks <u>usually</u>:** (tick once for each line)

	Yes	No
Pounding/pulsatory pain	☐	☐
Pressing/tightening pain	☐	☐
Unilateral pain *(right or left)*	☐	☐

4.30 **What is the normal intensity of your headache attacks?**

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

4.31 **What is the normal duration of the headache attacks?**

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

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

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

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

	Yes	No
Visual disturbances? *(flickering, blurred vision, flashes of light)*	☐	☐
Unilateral numbness in your face or hand?	☐	☐
Aggravated pain by moderate physical activity?	☐	☐
Nausea and/or vomiting?	☐	☐

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

Number of days ☐☐

5. FOOD HABITS

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

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

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

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

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

Number ☐☐

5.04 **Do you take vitamins and/or mineral supplements?**

☐ Yes, daily ☐ Sometimes ☐ Never

5.05 **How often do you eat?**

	Never	1-3 times per month	1-3 times per week	4-6 times per week	1-2 times per day	3 times per day or more
Dark chocolate	☐	☐	☐	☐	☐	☐
Light chocolate/milk chocolate	☐	☐	☐	☐	☐	☐
Chocolate cake	☐	☐	☐	☐	☐	☐
Other sweets	☐	☐	☐	☐	☐	☐

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

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

¼	½	1	1 ½	2	More than 2
☐	☐	☐	☐	☐	☐

5.07 **How often do you drink cocoa/hot chocolate?**

Never	1-3 times per month	1-3 times per week	4-6 times per week	1-2 times per day	3 times per day or more
☐	☐	☐	☐	☐	☐

6. ALCOHOL

6.01 **How often have you in the last year:**	Never	Less than monthly	Monthly	Weekly	Daily or almost daily
Not been able to stop drinking alcohol when you have started?	☐	☐	☐	☐	☐
Failed to do what was normally expected of you because of drinking?	☐	☐	☐	☐	☐
Needed a drink in the morning to get yourself going after a heavy drinking session?	☐	☐	☐	☐	☐
Had feeling of guilt or remorse after drinking?	☐	☐	☐	☐	☐
Not been unable to remember what happened the night before because of your drinking?	☐	☐	☐	☐	☐

	Never	Yes, but not in the last year	Yes, during the last year
6.02 **Have you or someone else been injured because of your drinking?**	☐	☐	☐
Has a relative, friend, physician, or other health care workers been concerned about your drinking or suggested you to cut down?	☐	☐	☐

7. WEIGHT

7.01 **Have you involuntary lost weight during the last 6 months?**

☐ Yes ☐ No

If Yes: how many kilograms? ..... ☐☐

7.02 **Estimate your body weight when you were 25 years old:**

Number of kilograms ..... ☐☐☐

7.03 **Are you satisfied with your present body weight?**

☐ Yes ☐ No

7.04 **What weight would you be satisfied with (your "ideal" weight)?**

Number of kilograms ..... ☐☐☐

8. SOLVENTS

8.01 **How many hours per week, do you do the following leisure- or professional activities:**

Automobile repair/paint, ceramic work, painting/varnishing/solvents, hair dressing, glazier, electrician. (Put 0 if you do not engage in such leisure or professional activities)

Number of hours per week on average ☐☐

8.02 **Do you use hair color preparations**

☐ Yes ☐ No

If Yes: How many times per year? .. ☐☐

9. USE OF HEALTH SERVICES

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

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

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

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

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

☐ Yes ☐ No

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

☐ Yes ☐ No

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

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

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

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

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

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

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

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

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

- ☐ Not relevant
- ☐ No problem
- ☐ Some problem
- ☐ Major problem

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

- ☐ Not relevant
- ☐ No problem
- ☐ Some problem
- ☐ Major problem

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

- ☐ Not relevant
- ☐ Very difficult
- ☐ Some difficulties
- ☐ Easy
- ☐ Very easy

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

☐ Yes ☐ No

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

0 1 2 3 4 5 6 7 8 9 10

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

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

0 1 2 3 4 5 6 7 8 9 10

☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐ ☐

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

☐ Yes ☐ No

9.13 **Have you, during the <u>last 12 months</u>, used herbal or natural medicine?**

☐ Yes ☐ No

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

☐ Yes ☐ No

10. USE OF ANTIBIOTICS

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

☐ Yes ☐ No ☐ Do not remember

If YES: What did you get the treatment for?
Have you taken many antibiotic treatments, tick for each treatment.

	Treatment 1	Treatment 2	Treatment 3	Treatment 4	Treatment 5	Treatment 6
• Urinary tract infection *(bladder infection, cystitis)*	☐	☐	☐	☐	☐	☐
• Respiratory tract infection *(ear, sinus, throat or lung infection, bronchitis)*	☐	☐	☐	☐	☐	☐
• Other	☐	☐	☐	☐	☐	☐
Treatment duration: number of days	|	|	|	|	|	|

How did you acquire the antibiotics for treatment?
Have you acquired many treatments, tick for each one.

With prescription from a physician/dentist	☐	☐	☐	☐	☐	☐
Without contacting a physician/without prescription:						
· Purchase from a pharmacy abroad	☐	☐	☐	☐	☐	☐
· Purchase over the internet	☐	☐	☐	☐	☐	☐
· Remnants from earlier treatment at home	☐	☐	☐	☐	☐	☐
· From family/friends	☐	☐	☐	☐	☐	☐
· Other ways	☐	☐	☐	☐	☐	☐

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

☐ Yes ☐ No

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

☐ Yes ☐ No

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

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

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

☐ Yes ☐ No

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

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

11. YOUR CIRCADIAN RHYTHM

We will ask you some questions about your sleeping habits

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

☐ Yes ☐ No

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

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐

Then I go to bed at ..... ☐☐:☐☐

I get ready to fall asleep at ..... ☐☐:☐☐

Number of minutes I need to fall asleep ..... ☐☐

I wake up at ..... ☐☐:☐☐

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

Number of minutes I need to get up ..... ☐☐

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

0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐

Then I go to bed at ..... ☐☐:☐☐

I get ready to fall asleep at ..... ☐☐:☐☐

Number of minutes I need to fall asleep ..... ☐☐

I wake up at ..... ☐☐:☐☐

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

Number of minutes I need to get up ..... ☐☐

12. SKIN AND DERMATOLOGY

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

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

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

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

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

☐ Yes ☐ No

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

☐ 1-2 ☐ 3-4 ☐ More than 4 times

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

	Yes	No
Psoriasis	☐	☐
Atopic eczema (children's eczema)	☐	☐
Recurrent hand eczema	☐	☐
Recurrent pimples/spots for several months	☐	☐
Leg or foot ulcer that did not heal for 3-4 weeks	☐	☐

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

☐ Yes ☐ No

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

	Yes	No
Swelling in the ankles or legs, particularly in the evenings	☐	☐
Varicose veins	☐	☐
Eczema (red, itchy rash) on your legs	☐	☐
Leg pain that is getting worse when you are walking and is relieved when you are standing still	☐	☐

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

	Yes	No
Psoriasis	☐	☐
Atopic eczema	☐	☐
Rosacea	☐	☐

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

	Yes	No
Armpits	☐	☐
Under the breasts	☐	☐
Stomach groove/the navel	☐	☐
Around the genitalia	☐	☐
Around the anus	☐	☐
The groin	☐	☐

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

☐ Yes ☐ No

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

	Yes	No
Antibiotic ointment	☐	☐
Antibiotic tablets	☐	☐
Surgical drainage	☐	☐
A larger surgical intervention including skin removal	☐	☐
Surgical laser treatment	☐	☐

Follow-up questions

INFORMATION TO FOLLOW-UP QUESTIONS

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

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

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

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

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

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

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

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

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

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

13. FOLLOW-UP QUESTIONS ON PAIN

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

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

Number of years ☐☐ months ☐☐

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

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

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

- ☐ Head/face
- ☐ Jaw/temporo-mandibular joint
- ☐ Neck
- ☐ Back
- ☐ Shoulder
- ☐ Arm/elbow
- ☐ Hand
- ☐ Hip
- ☐ Thigh/knee/leg
- ☐ Ankle/foot
- ☐ Chest/breast
- ☐ Stomach
- ☐ Genitalia /reproductive organs
- ☐ Skin
- ☐ Other location

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

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

Describe the other cause:

.....

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

- ☐ No treatment
- ☐ Analgesic medications/painkillers
- ☐ Physiotherapy/chiropractic treatment
- ☐ Treatment at a pain clinic
- ☐ Surgery
- ☐ Psycho-educative/relaxation training/ psychotherapy
- ☐ Acupuncture
- ☐ Complimentary and alternative medicine *(homeopathy, healing, aromatherapy, etc.*
- ☐ Other treatment

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

How strong would you say that the pain usually is?	No pain	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐	Worst imaginable pain
How strong is the pain when it is in its strongest Intense?	No pain	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐	Worst imaginable pain
To what degree does the pain interfere with your sleep?	No effect	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐	Impossible to sleep
To what degree does the pain interfere with performing common activities at home and at work?	No effect	0 ☐ 1 ☐ 2 ☐ 3 ☐ 4 ☐ 5 ☐ 6 ☐ 7 ☐ 8 ☐ 9 ☐ 10 ☐	Can not do anything

14. FOLLOW-UP QUESTIONS ON SURGERY

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

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

Number ..... ☐

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

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

Surgery in the head/neck/back
- Head/face ..... ☐
- Neck/throat ..... ☐
- Back ..... ☐

Surgery in the chest
- Heart ..... ☐
- Lungs ..... ☐
- Breasts ..... ☐
- Another surgery in the chest region ..... ☐

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

Surgery in the hip/legs
- Hip/thigh ..... ☐
- Knee/leg ..... ☐
- Ankle/foot ..... ☐
- Amputation ..... ☐

Surgery in the shoulder and arm
- Shoulder/overarm ..... ☐
- Elbow/underarm ..... ☐
- Hand ..... ☐
- Amputation ..... ☐

14.03 **Reason for the surgery:**
- Acute illness/trauma ..... ☐
- Planned non-cosmetic operation ..... ☐
- Planned cosmetic operation ..... ☐

14.04 **Where did you have the surgery?**
- The hospital in Tromsø ..... ☐
- The hospital in Harstad ..... ☐
- Other public hospital ..... ☐
- Private clinic ..... ☐

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

Number of years ..... ☐ Months ..... ☐

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

☐ Yes ☐ No

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

☐ Yes ☐ No

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

☐ Yes ☐ No

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

☐ Yes ☐ No

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

How strong pain did you have at the site of surgery <u>before</u> you had surgery	No pain	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	Worst imaginable pain
How strong pain do you normally have at the site of surgery now	No pain	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	Worst imaginable pain
How strong pain do you normally have at the site of surgery when it is most intense	No pain	0 ☐	1 ☐	2 ☐	3 ☐	4 ☐	5 ☐	6 ☐	7 ☐	8 ☐	9 ☐	10 ☐	Worst imaginable pain

15. FOLLOW-UP QUESTIONS ABOUT WORK IN COLD ENVIRONMENT

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

15.01 **Do you feel cold at work?**

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

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

Leisure/hobbies *(hours/week)* ..... ☐☐

Work *(hours/week)* ..... ☐☐

Outdoors, with suitable clothing *(hours/week)* ..... ☐☐

Outdoors, without suitable clothing *(hours/week)* ..... ☐☐

Indoors, with no heating *(hours/week)* ☐☐

In cold, with wet clothing *(hours/week)* ..... ☐☐

Contact with cold objects/tools *(hours/week)* ..... ☐☐

15.03 **What ambient temperature prevents you from:**

	Under °C
Working outdoors	☐☐
Training outdoors	☐☐
Performing other activities outdoors	☐☐

15.04 **Have you during the <u>last 12 months</u> had a frostbite with blisters, sores or skin injury?**

☐ Yes ☐ No

If Yes, how many times? ..... ☐☐

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

☐ Yes ☐ No

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

	Yes	No
At work	☐	☐
In leisure time	☐	☐

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

	Yes	No	Under °C
Breathing problems	☐	☐	☐☐
Wheezy breathing	☐	☐	☐☐
Mucus secretion from lungs	☐	☐	☐☐
Chest pain	☐	☐	☐☐
Disturbance in heart rhythm	☐	☐	☐☐
Impaired blood circulation in hands/feet	☐	☐	☐☐
Visual disturbance *(short term/transient)*	☐	☐	☐☐
Migraine *(short term/transient)*	☐	☐	☐☐
Fingers turning white *(short term/transient)*	☐	☐	☐☐
Fingers turning blue-red *(short term/transient)*	☐	☐	☐☐

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

	Decrease	No effect	Improve
Concentration	☐	☐	☐
Memory	☐	☐	☐
Finger sensitivity *(feeling)*	☐	☐	☐
Finger dexterity *(motor)*	☐	☐	☐
Control of movement *(for example tremor)*	☐	☐	☐
Heavy physical work	☐	☐	☐
Long-lasting physical work	☐	☐	☐

16. USE OF NON-PRESCRIPTION PAINKILLERS

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

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

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

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

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

Acetylsalicylates: *(Aspirin,Dispril, Globoid)*

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

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

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

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

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

Naproxen: *(Ledox, Naproxen)*

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

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

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

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

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

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

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

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

	Yes	No
Paracetamol	☐	☐
Acetylsalicylates	☐	☐
Ibuprofen	☐	☐
Naproxen	☐	☐
Phenazone with caffeine	☐	☐

16.04 **Where do you usually purchase painkillers?**

- ☐ Pharmacy
- ☐ Grocery
- ☐ Petrol stations
- ☐ Abroad
- ☐ Internet

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

☐ Yes ☐ No

17. FOLLOW-UP QUESTIONS ABOUT SKIN DISEASES

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

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

No complaint — 0 1 2 3 4 5 6 7 8 9 10 — Worst imaginable complaints

17.01 **Psoriasis**
- How much are you affected by your psoriasis today? ☐☐☐☐☐☐☐☐☐☐☐
- How much are you affected by your psoriasis when it is most severe? ☐☐☐☐☐☐☐☐☐☐☐

17.02 **Atopic eczema**
- How much are you affected by your atopic eczema today? ☐☐☐☐☐☐☐☐☐☐☐
- How much are you affected by your atopic eczema when it is most severe? ☐☐☐☐☐☐☐☐☐☐☐

17.03 **Hand eczema**
- How much are you affected by your hand eczema today? ☐☐☐☐☐☐☐☐☐☐☐
- How much are you affected by your hand eczema when it is most severe? ☐☐☐☐☐☐☐☐☐☐☐

17.04 **Acne**
- How much are you affected by your acne today? ☐☐☐☐☐☐☐☐☐☐☐
- How much are you affected by your acne when it is most severe? ☐☐☐☐☐☐☐☐☐☐☐

17.05 **Abscesses**
- How much are you affected by your abscesses today? ☐☐☐☐☐☐☐☐☐☐☐
- How much are you affected by your abscesses when it is most severe? ☐☐☐☐☐☐☐☐☐☐☐

17.06 **Here is a list of factors that might trigger or exacerbate abscesses, tick for what you think apply to you:**

	Yes	No
Stress/psychological strain	☐	☐
Narrow/tight clothing	☐	☐
Menstrual periods	☐	☐
Pregnancy	☐	☐
Other	☐	☐

17.07 **How many episodes of abscesses do you usually have per year?** (tick once)

☐ 0-1 ☐ 4-6
☐ 2-3 ☐ More than 6

17.08 **How old were you when you got abscesses for the first time?**

☐ 0-12 years ☐ 26-35 years
☐ 13-19 years ☐ 36-50 years
☐ 20-25 years ☐ Older than 50 years

17.09 **If you no longer have abscesses, how old were you when it disappeared?**

☐ 0-12 years ☐ 26-35 years
☐ 13-19 years ☐ 36-50 years
☐ 20-25 years ☐ Older than 50 years

FEEDBACK

Should you wish to give us a written feedback on either the questionnaire or The Tromsø Study in general, you are welcome to do it here:

Thank you for your help

Tromsø-undersøkelsen

The Tromsø Study
Department of community medicine, University of Tromsø
9037 TROMSØ
Telephone: 77 64 48 16
Telefax: 77 64 48 31
Email: tromsous@ism.uit.no
www.tromso6.no