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The incidence and prevalence of Chronic Fatigue Syndrome, Back Pain of unknown origin, Fibromyalgia, and Myalgia in Norwegian women, and their association to physical activity.

A prospective cohort study of material from the Norwegian Women and Cancer (NOWAC) study.

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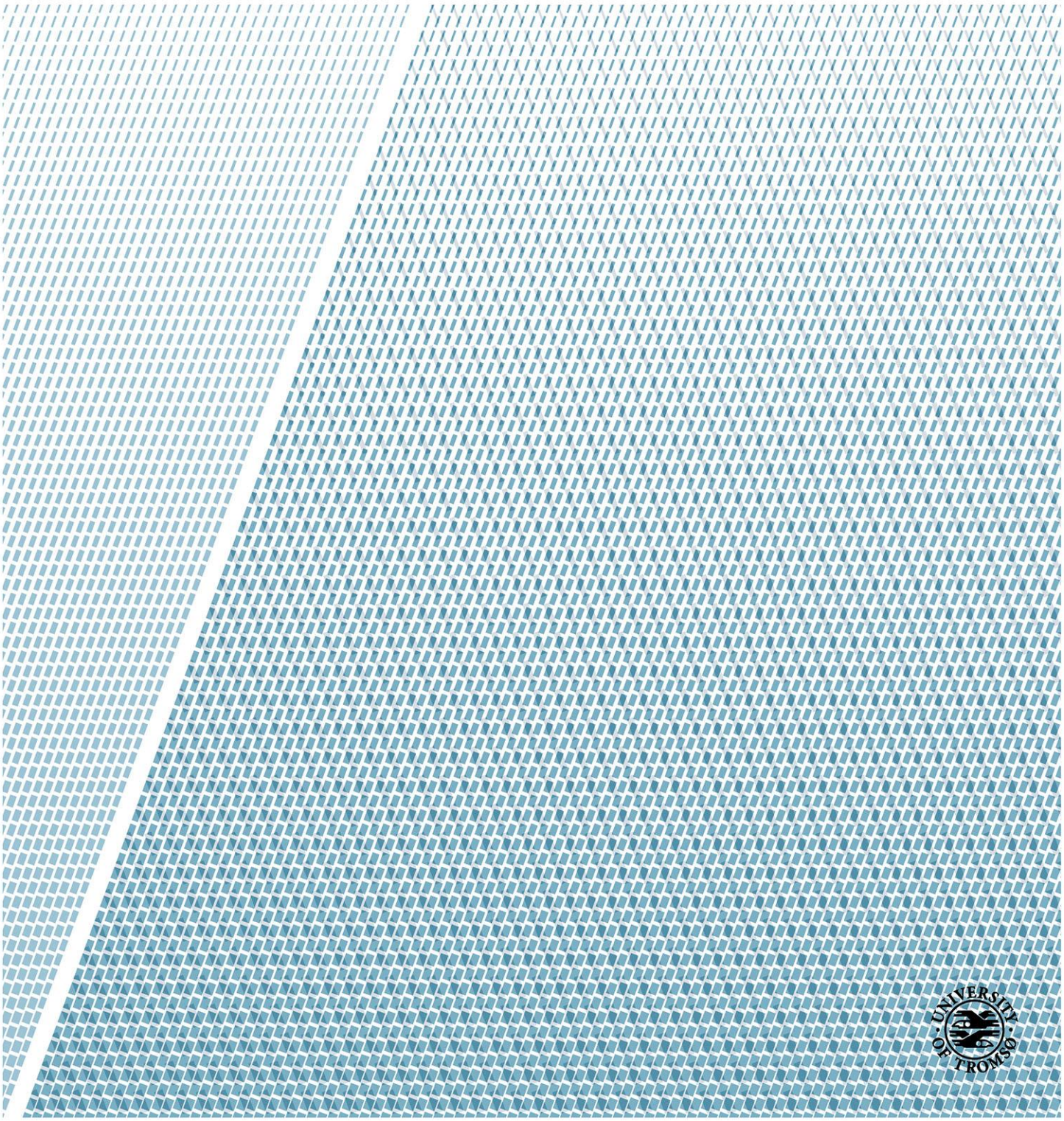

Preface

Finishing this thesis marks the end of two wonderful and highly educative years with the MPH program at the University of Tromsø. We will never be the same again. We are very pleased to end this journey with a thesis topic that lies so close to our physiotherapy hearts.

Working with this thesis has been a pleasant experience which we can truthfully say we have enjoyed. Except for dividing some of the initial proceedings with reading background articles between us, all of the work has been done under four eyes, in the same room, looking at the same screen, reading and formulating the same words. Being able to put two heads together and discuss continuously while working on the statistics and analysis, or the theoretical basis of the thesis, or the discussion of our findings, has been of inestimable worth. Not surprisingly, this manner of working together has proven an excellent form of cooperation, and has not in the slightest deterred us from repeating similar projects together in the future.

We owe a debt of gratitude to our wonderful supervisor Kristin Benjaminsen Borch, who, having just finished her own doctoral thesis, did not flinch from the unnerving task of guiding two such as us through to a product worthy of submitting. Great thanks also to Tonje Braaten and her invaluable help in keeping a cool head when overseeing our methods and analysis. Nils Abel Aars also deserves all due gratitude for countless hours of encouragement and therapy. One for all! Warmest thanks to Caroline Årnes for all patience, providence, and pastries.

Coffee will never be the same again.

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Abstract

Background: Musculoskeletal disorders (MSDs) appear relatively frequent and are costly for society each year, yet they are poorly understood. Four commonly occurring MSDs are Chronic Fatigue Syndrome (CFS), Back Pain (BP) of unknown origin, Fibromyalgia (FM), and muscle pain/Myalgia. There are few Norwegian epidemiologic data on these four outcomes. Physical activity (PA) has been internationally recognized as having a protective effect against chronic disease. The association between PA and these four outcomes is not well understood and the main aim of this study was to investigate this relationship in a large prospective cohort of Norwegian women.

Methods: Self-reported data were gathered from 76 367 women in the nationally representative cohort study the Norwegian Women and Cancer study. Data were gathered on total amount of PA at enrolment and of the four outcome conditions during follow-up, in addition to covariate information. We calculated incidence rate and total prevalence. The association between PA and the four outcomes was assessed using multivariate logistic regression analysis. Prevalent cases were excluded from logistic regression analysis. PA was assessed for trend and as a categorical variable.

Results: Incidence densities per 100 000 person years were calculated to be as follows: CFS 411, BP 1268, FM 287, and myalgia 1509. Total prevalence was found to be 2.58% for CFS, 13.65% for BP, 5.02% for FM, and 17.87% for myalgia. These were comparable to age-standardized rates for the corresponding Norwegian female population. There was a significant trend ($p < 0.001$) that increasing levels of PA were associated with a reduced risk CFS, BP and FM. Compared to moderate PA level, very low levels of PA was significantly associated with increased risk of CFS (OR 1.61 (CI 1.38-1.88)), BP (OR 1.17(CI 1.04-1.31)), and FM (OR 1.30(CI 1.07-1.58)). For CFS, PA levels low (OR 1.31 (CI 1.19-1.44)) and very high (OR 1.18 (CI 1.01-1.38)) were also

associated with an increased risk of PA. The results showed no significant associations between PA and mylagia.

Conclusion: Our study found nationally representative data for incidence and prevalence of CFS, BP, FM, and myalgia in Norwegian women. When compared to moderate levels of total PA, very low PA was associated with an increased risk of CFS, BP, and FM. Low and very high levels of PA were associated with an increased risk of CFS. More studies are needed to confirm the incidence for these outcomes in the Norwegian population, and to investigate the association between these and different types of PA.

Contents

Key words and abbreviations

ACR	The American college of rheumatology
ANOVA	Analysis of variance
BMI	Body mass index
BP	Back Pain
CDC	American Centers for Disease Control and Prevention
CFS/ME	Chronic fatigue syndrome/Myalgic encephalomyelitis
CI	Confidence interval
CNS	Central nervous system
DALY	Disease adjusted life years
FM	Fibromyalgia
ICD	International classification of disease
IHD	Ischemic heart disease
LBP	Low back pain
MI	Myocardial infarction
MSDs	Musculoskeletal disorders
NOWAC	Norwegian Women and Cancer (study)
OR	Odds ratio
PA	Physical activity
RA	Rheumatoid arthritis
SD	Standard deviation
STAMI	Statens Arbeidsmiljøinstitutt (The Norwegian National institute of occupational health)
WHO	World Health Organization

1. Purpose of the thesis

The Norwegian Women and Cancer (NOWAC) study is a longitudinal study originally developed to study the relationship between female cancer and internal and external hormones. The study has self-reported information on women's level of physical activity (PA), as well as prevalence and incidence of some musculoskeletal disorders (MSDs), four of which were of particular interest: chronic fatigue syndrome (CFS), back pain (BP) of unknown origin, fibromyalgia (FM), and myalgia. These conditions are part of the category of disorders which contributes to a large proportion of health care expenses, disability and morbidity in the population (1-4), and yet there is a lack of national epidemiologic data and international understanding as to what might be their cause. At the same time, there is a substantial amount of evidence indicating that PA is a protective factor against many conditions causing morbidity and mortality (5-7). This led us to ask the research questions: *What is the incidence/prevalence of these conditions among Norwegian women? What is the association between levels of physical activity, and chronic fatigue syndrome, back pain of unknown origin, fibromyalgia, and myalgia among Norwegian women?*

2. Introduction

There exists a broad variety of different definitions and groupings when it comes to MSDs today. Commonly included are rheumatic and degenerative conditions such as rheumatoid arthritis (RA), Bechterew, osteoarthritis and osteoporosis. A third and less rigidly defined group, which is often partially or fully included when discussing MSDs, contains the conditions CFS, back pain of unknown origin, FM, and myalgia. These conditions might not seem intuitively connected to each other, but the World Health Organization (WHO) has given some general descriptions on the central characteristics of such ailments, calling them a diverse pathophysiological group linked by anatomy and associations to physical impairments and pain (8). Although MSDs rarely cause mortality in the ill individual compared to many other conditions, they are nevertheless "more prevalent. They are a major cause of pain and reduced quality of life" (9). In Europe, reports have stated 60% of work disability to be caused by MSDs (10), and 2005 numbers from the USA indicated that 50% of above-18 year olds experienced an MSD lasting more than 3 months during the previous year (9). These numbers are more than mirrored in the Norwegian population (2). Norway has a higher prevalence of moderate or strong, chronic pain conditions than most other European countries (2). This group of conditions accounts for 46% of all sick leave and 33% of disability pensions in Norway (11).The Norwegian prevalence for this group of conditions increased by 21% from 1995 to 2000, and were responsible for 49% of the 1-year sick leaves in Norway in 2000 (12). The annual costs of health care for treating MSDs in Norway, including medication, general practitioner visits, examinations and manual treatments, totaled 14.3 billion NOK in 2009 (2). When including all other societal costs – social security benefits, disability pensions, production losses etc. – this sum approached 73 billion NOK, annually. It is apparent that these relatively common ailments, despite being poorly understood, constitute

extensive costs for the society each year, both in form of great amounts of suffering and disability for the affected individuals, as well as vast economic costs for patients, employers and governments.

The one group of MSDs that has remained perhaps the least understood one is that of the 'diffuse' character – the large variety of treatment modalities that exist for chronic pain conditions highlight the present difficulties of treating such conditions effectively (13). For such conditions as the four selected from the questionnaires of the NOWAC study, it is often not possible to set a specific diagnosis, and many patients have ended up being diagnosed according to symptoms (2). CFS, back pain of unknown origin, FM, and myalgia are all extensive problems causing large amounts of suffering and costs while remaining relatively difficult to treat due to the obscure nature of the conditions. Understanding of the epidemiology of chronic pain conditions remains poor despite this being one of the most common causes of contact with the health care services (14). In Norway in 2006, 5% of the new permanent disabilities reported FM as the primary diagnosis (2). The prevalence of chronic widespread pain has been reported to 1% - 15% (15). Devanur and Kerr suggested a world-wide prevalence of CFS between 0.4% - 1.0% (16). The annual prevalence of low back pain (LBP) – typically of unknown origin – is reported as 25% - 60% (10), with a total lifetime prevalence from 11% - 84% (1).

Women have been reported to experience pain-related musculoskeletal conditions more frequently than men (13). Furthermore, MSDs have been reported to be the foremost reason why Norwegian women seek polyclinic care (11). The nature of this difference between the genders and the mechanism behind it is unclear (15).

Woolf and Pfleger reported that higher age causes an increase in the prevalence of many different MSDs, and that they can be affected by lifestyle habits, PA and body tissue composition (8). Mielenz and Alvarez reported that both pain and risk of mortality from certain MSDs could be prevented with regular exercise (13). As the four outcome conditions of our study belong to the same general musculoskeletal category as rheumatic and degenerative conditions, it could be theorized that PA and other lifestyle factors may have a similar impact on the risk of obtaining them.

3. Background and theory

In order to adequately explore the research question, background knowledge was needed regarding the incidence and prevalence of our outcomes, as well as the association of PA to the four different outcomes in our study. We explored what was known about this relationship, and what results were to be expected, as well as where theory might be lacking. Furthermore, we needed explore the relationship between women and the exposure and outcomes used in our study. Finally, we examined whether any of the reported covariates have a potentially confounding effect on the relationship between PA and outcomes.

3.1 Women's health

Health as a worldwide phenomenon displays some differing distribution when separating the genders. Women's health is affected to a different degree by cultural, societal, economic and genetic factors than that of men, causing women to face higher health costs than men due to using more health care (17). Several gender disparities in health are not confined to the developing world but are found consistently in all regions of the globe (17). One such disparity relates to the 'modern epidemic' of MSDs. Women generally have more sickness absence and long-term disability caused by MSDs, and have a suggested increased risk of obtaining chronic MSDs (18).

The cause of the great disparities in MSDs between genders remains unknown, but Meeus et al. pointed out that gender was a potential confounder when studying pain phenomena: this includes women often having lower thresholds, greater ability to discriminate higher pain ratings, and less tolerance of noxious stimuli than males. Furthermore, women report greater levels of pain catastrophizing (19). This does not necessarily mean that women are over-reporting 'normal' experiences as sickness, but could just as easily imply that men are more insensitive and prone to

suppress or be unaware of much of their own bodily experience (20). Furthermore, some authors have suggested the "double-burden" theory as a possible explanation why women experience disabling MSDs more frequently, pointing out that facing stressors both in the occupational and the domestic arena might lead to the development of such conditions (18). Whichever theory one chooses, a potential explanation lies with the fact that women have a lower threshold for seeking out medical attention compared to men (20, 21). Conditions such as CFS and FM have long been recognized to primarily affect women, although there have been suggestions that the number of unreported cases among men are extensive. This could potentially imply a bias towards the null in male prevalence of CFS and MSDs, with unknown numbers of undiagnosed cases.

3.2 Physical activity

PA is internationally recognized as having a protective effect against a broad variety of communicable and non-communicable diseases. According to the WHO;

> Insufficient physical activity is the fourth leading risk factor for mortality. Approximately 3.2 million deaths and 32.1 million DALYs (representing about 2.1% of global DALYs) each year are attributable to insufficient physical activity. People who are insufficiently physically active have a 20–30% increased risk of all-cause mortality compared to those who engage in at least 30 minutes of moderate intensity physical activity on most days of the week (5, p18)

PA has many positive effects on both physiological and psychological processes. Lee et al. reported, among others, cardiorespiratory and muscular fitness, increased functional health and improved cognitive function all to derive from healthy PA (7). Adversely, too little PA leading to a sedentary lifestyle is a risk factor for depression, metabolic syndrome, and all-cause mortality, among others (7).

Increasing PA appears to be protective against morbidity and mortality. The WHO maintains that

there is a dose-response relationship between higher volumes of PA and risk of cardiovascular disease and diabetes (22). However, they also stated that there was a lack of evidence demonstrating an additional preventive effect against non-communicable diseases when exceeding 300 minutes per week of PA (22). The present general consensus of recommendations on daily levels of PA is that people of all ages should participate in 30 minutes of at least moderately strenuous PA, preferably all days of the week (23). Adding more moderate-intensity activity can add to the health benefits gained (24). Of the 31% of adults who are insufficiently active across the globe, there are 6% more women than men (28% and 34%, respectively) (5). These numbers are increased when looking at high-income countries, where a total of 48% of women are insufficiently physically active, and this inactivity increases with age (5, 25). In Norway, approximately 1/3rd of the population was reported to be physically inactive in the decade leading up to the year 2000. This included one in every five women. The number of physically inactive persons has since been declining; as of 2012, 6% of women aged 45-66 years were inactive, compared to 14% of the corresponding men (26). These numbers were slightly higher for younger women, and slightly lower for younger men.

One probable determinant of decreased PA in high-income countries is an increasingly automatized daily life (5). However, Bauman reported that high-income countries, whilst having a lower degree of PA as manual labor, had a higher degree of total leisure time PA (27). This visualizes the fact that PA consists of several subsets of activities. PA as a term is quite general and describes all such "bodily movement that is produced by the contraction of skeletal muscles that increases energy above the basal level" and that significantly increases the amount of energy used (24). Gabriel et al. stated PA to be such activity that "involves human movement, resulting in … increased energy expenditure and improved physical fitness" (28). The same authors sorted

all such movements that are carried out through the day into four sub-categories, depending on the context in which they took place. The suggested categories PA is performed in are exercise/leisure, occupational/educational setting, household/caretaking/domestic, and transportation (24, 28). The U.S Department of Health and Human Services defined exercise as "planned, structured, repetitive and purposive in the sense that improvement or maintenance of one or more components of physical fitness is the objective" (24), with the following aspects of physical fitness having been shown to be health related: "cardiorespiratory fitness", skeletal muscular strength and endurance, as well as body composition and flexibility (24). This describes a link between PA in the form of exercise, and increased health benefits and protective effects. Hallal et al. reported that activity in form of transportation had a protective effect against all-cause mortality and several kinds of morbidity (29). In this respect, PA in commuting could be similar to PA in the form of exercise. Physically intensive work in the occupational setting however, has been shown to be a risk factor for MSDs, and was cautioned against in a report by the Norwegian National Institute for Occupational Health (30). Aas et al. reported that repetitive work and working in awkward positions as well as occupational exposures that induce psychosocial work strain and stress were risk factors for deteriorating health. This problem would be exacerbated in populations that were both inactive and physically unfit (30). PA in the occupational/educational setting thus needs not incur the protective effect of exercise, but might instead have an inverse effect on health. This means that PA consists of different kinds of activity domains that can either promote or possibly deteriorate health.

It has been suggested that level of PA can be a measure to distinguish people's individual health behavior profiles (31). A proposed reason for this is that one can frequently observe a clustering together of positive and negative health behaviors, so that population groups with high levels of

inactivity would also display other hazardous lifestyle characteristics (31). Furthermore, like many other lifestyle variables in society, type of PA is also seen to follow the socioeconomic strata, relating to what amount of time is spent performing the different types of activities included in the general term PA: leisure time PA has been demonstrated to be highest in higher levels of socioeconomic strata, while occupational PA is highest among the lowest socioeconomic strata (32). Since these two have been suggested to have contradictory effects on health, the health effects of PA could be hypothesized to follow socioeconomic stratification.

3.3 Outcomes

The reported outcomes of our study were CFS, BP, FM and myalgia. When looking at the background of these outcomes, we examined the main understanding of these conditions in literature today, as well as epidemiologic data, and their gender distributions. Finally, we investigated how theory links the outcomes to PA.

3.3.1 Chronic fatigue syndrome

CFS is a condition that is marked by persistent and recurring fatigue for more than six months. This is accompanied by secondary symptoms which include impaired memory and concentration, soreness of the throat, sleep-disturbances and headache, as well as chronic, persistent and widespread musculoskeletal pain (19). Modern criteria for diagnosing CFS were suggested by the American Centers for Disease Control and Prevention (CDC) in 1994 (19). A 2006 review of CFS suggested the world-wide prevalence rate to be approximately 0.4-1% (16). Based on the case definition suggested by the CDC in 1994, one community-based study from 1999 in the US by Jason et al. suggested a prevalence rate of 0.522% (33). Another community-based study by

Reyes et al. from 2003 suggested a point prevalence for women of 373 per 100 000 persons (34). They also reported an incidence of 180 per 100 000 persons. Prins et al. reported one incidence rate from 1997 in a US setting to be 0.37% (35). Current epidemiologic data for the Norwegian setting seem to be lacking. As of 2013, the Norwegian prevalence rate of CFS was unknown. Point prevalence, given a similarity to international levels, was estimated at around 10 000 – 20 000 cases by the Norwegian Directorate of Health (36).

Today, the 1994 definition from the CDC is the most widely supported scientific case definition (16, 35). Fatigue is an often emphasized symptom in CFS, but myalgia has been shown to be a just as important and prevalent one as 94% of CFS patients experience muscle aches and pain (19). Such patients' symptoms are typically exacerbated after levels of exercise that had previously been well-tolerated (19). Musculoskeletal pain appeared to be the most disabling aspect of CFS, as this accounted for up to 33% of limitations in activity level (19). Some 35-70% of CFS patients have also been suggested to meet criteria for FM (19).

3.3.1.1 The development and theory of chronic fatigue syndrome

Guidelines for research and clinical evaluation of CFS were revised in 1994 by the CDC, USA, and the International Chronic Fatigue Study Group (37). This was an update of the more restrictive approach employed by the 1988 CFS working case definition suggested by Holmes et al. (38). In the new guidelines, the CDC characterized CFS as consisting of severe and disabling fatigue, and a combination of other symptoms including cognitive impairment, sleep disturbance and musculoskeletal pain (37). There were and are no laboratory tests available to confirm this condition, causing clinicians to have to rely on clinical presentation of symptoms for diagnosis.

In 1994, 14-15.3% of the adult population in the US reported chronic fatigue lasting 2 weeks or longer with no medical cause (37). The CDC at this time suggested defining chronic fatigue as fatigue lasting > 6 months. Persistent or relapsing chronic fatigue had to be of such a nature that it was not alleviated by rest, and resulted in reduction of previous social, occupational, educational and personal activities of a substantial magnitude (35). This chronic fatigue, combined with four or more of the following symptoms; "cognitive impairment, sore throat, tender cervical or axillary lymph nodes, muscle pain, pain in several joints, new headaches, unrefreshing sleep, malaise after exertion", was sufficient cause to assert a case of CFS. This given that the additional symptoms lasted six months or longer. Where the 1988 working case definition had required 8 out of a list of 11 symptoms to be present, the CDC now proposed 4 out of 8 to be sufficient. The CDC group also pointed out the existence of overlapping disorders, amongst others FM, but maintained that such disorders were not sufficient cause to explain chronic fatigue (37). During the early years of the disorder, there has been some controversy surrounding the naming of the illness. Scientists have preferred using CFS, since patients are identified by their symptoms and disabilities, as well as exclusion of other explanatory causes, instead of by objective physical findings or laboratory test results (35). Patients and clinicians, on the other hand, preferred using the term Myalgic Encephalomyelitis (ME). Patients were historically reluctant to the term CFS due to the linkage of this by the WHO to psychiatry in the name Neurasthenia in the ICD system. Due to this, they kept ME classified as a neurological conditions, while patients' organizations began using the name CFS/ME (35). The 1994 report by the CDC was opposed to such a mixing of terms, fearing confusion and undermining of public attention to the disorder. They maintained that more information on pathophysiological processes was needed before changing the name. As of today, the term CFS/ME is commonly used in clinical practice and literature, while ICD-10 codes for two different variants: G93.3 Benign

Myalgic Encephalomyelitis, which is termed as a "postviral fatigue syndrome"; and F48.0 Neurasthenia, which is termed as a neurotic disorder and fatigue syndrome, and is the one specified by the WHO. The diagnostic criteria appear to be similar, but G93.3 must be preceded by an infectious event and is a differential diagnosis to neurasthenia (39).

Several explanatory mechanisms behind CFS have been suggested, such as endocrine disruptions, brain abnormalities, psychiatric comorbidities (depression and anxiety in particular), infectious origins, and that of central pain processing pathways being sensitized (1). It has also been pointed out that serious and stressful life-situations, like losing a job or loved one, often lead up to the disorder (35). Due to both CFS and FM being marked by inter-relation of pain-processing mechanisms, stress regulation and adverse life experiences, they have been suggested for the term "stress disorders" (35). However, the search continues for biological markers and causation (16).

3.3.1.2 Chronic fatigue syndrome and women

CFS has been reported to be a condition primarily affecting women, with a female-male ratio of 6:1 (16). One community based study from Kansas reported point prevalence among US women to be between 0.21-0.54% (34). Bradley et al. reported that women comprised about 70% of the total amount of CFS prevalence (40). Jason et al. reported a female point prevalence of 0.32-0.72% (33). In Norway, health authorities expect women to follow this pattern of higher prevalence and a more severe course of illness (36).

3.3.1.3 Chronic fatigue syndrome and physical activity

The link between pre-diagnosis habitual levels of PA and probability of contracting the disease is not well understood or explored in the literature. One low-powered case-control study by Smith et al. found that individuals who had developed CFS reported higher premorbid levels of PA compared to after having developed the condition (41). In addition, their premorbid levels of PA were rated as high. Premorbid PA levels were reported to be higher than for healthy controls. However, it should be noted that Nijs et al. reported that "continuing to be active despite increasing fatigue is likely to be a crucial step in the development of CFS" (42), implying that PA regardless of adverse warnings given by the body might have a reversed effect. It could be that the patients in the study by Smith et al. continued with high levels of PA despite feeling increasingly fatigued. Furthermore, based on what theory states about PA and its protective effect for so many other conditions, the expected hypothesis would be that higher levels of PA should be protective also for CFS.

Many patients with CFS perceive PA as more exerting than healthy individuals (41). All included articles in a review by Nijs et al. reported reduced habitual PA among patients with CFS compared to healthy controls (42). They also found evidence of reduced peak isometric muscle strength in patients with CFS. They concluded that CFS patients did less amounts of PA during daily life and had less muscle strength. This may not be a surprise, given that too vigorous exercise – as little as a 30% increase - has been demonstrated to trigger relapses, possibly explaining some of the inactivity seen in CFS patients (42). Inactivity and exacerbation seem not to be linked to physiological capacity - Prins et al. suggested that patient inactivity, rather than being caused by physical fitness, actually was caused by perceptions and expectations (35) – that

fearing a relapse of symptoms leads to fear-avoidance behavior towards PA. The level of this kind of behavior was an important determinant of disability (42). Because musculoskeletal pain appears to be the most debilitating factor in CFS, it is intuitive to believe that having CFS would affect the level of PA.

3.3.1.4 Implications of change in diagnostics for the present study

The relatively limited interchangeable use of the terms CFS and ME might have caused some confusion to patients that had received the name of one during diagnosis from a physician, but not the other. We believed this problem to be of limited extent in relation to our study, as the term CFS which was used in the questionnaire was also the one which had been most consistently used throughout the history of the diagnosis, and which remains linked to ME and the ICD-10 today. Any patient diagnosed with ME is likely to be aware of the alternative name. Of possible greater importance is the change in diagnostic criteria in -94, which occurred during the follow-up time for our study. This might have caused some patients to migrate into or out of the diagnostic group at a greater number than usual, due to previous misdiagnosis of a similar condition.

3.3.2 Back pain of unknown origin

Lifetime prevalence of any type of BP has been reported from 11% and up to as high as 84%, and adult yearly incidence in industrialized countries at 5% (1, 3). It is the greatest sub-group within MSDs in Norway, and the one that causes the most sick leave and disability payments (11), with costs at 13-15 billion NOK per year (43). Today there exists international consensus on dividing BP into three categories: 1) specific back pain, 2) back pain of neurologic causes, and 3) non-

specific back pain (back pain of unknown origin) (1, 3, 44). This "diagnostic triage" was suggested by Waddell in 1987 and has been in use since then (45). Specific back pain comprises all BP conditions of known pathologic origins, such as fractures of the back, infections, cancer, and rheumatic/inflammatory conditions (46). Back pains of neurologic causes encompass radiculopathies, spinal stenosis or pain caused by hernia of the intervertebral disc (3, 44). The non-specific group totals 80-90% of all BP cases, and is usually located to the lower back (1, 3, 44). Duration of LBP is divided into acute (< 6 weeks), and chronic (> 12 weeks) (3, 46). These can be both radiating and non-radiating of nature (3, 44). Up to 80% of the population is estimated to experience LBP at some point during life, the lifetime prevalence rate (47), of which 85-90% of LBP cases are of unknown origin (3, 48). In the perused literature, the expressions "back pain" and "low back pain" were used interchangeably, and no great effort was made to separate them when referring to the three categories in the diagnostic triage. Especially the group of non-specific BP was frequently assumed to occur in the lower back (3, 43). With most cases of BP being of unknown origin, and with most cases of BP of unknown origin being located at the lower back, and with most of LBP cases being of unknown origin, it seemed reasonable to assume that most reporting on "back pain of unknown origin" referred to non-specific LBP. Therefore, in our study, the term "back pain" was used as synonymous to this group.

3.3.2.1 The theory of back pain

The theoretical understanding of BP has a long history of difficulties. Waddell mentioned as early as 1987 that there was a lack of the biomechanical and pathologic understanding necessary to identify pathologic or even anatomic sources of pain (49). He suggested distress and illness behavior to be an important part of the condition, improving or deteriorating depending on the

success of the treatment, and stated that BP patients must be seen in light of a biopsychosocial model for illness and disability. Another suggestion was to separate those few with clear pathology from the vast amount of cases that lacked any clear cause. Thiese et al. reported that there is still a lack of consensus on the causes of most cases of LBP (50). Explicit descriptions of classic BP cases are hard to come by in the literature. Epidemiologic studies of BP have difficulties with heterogeneity with their selections, making the phenomenon hard to measure (51). Dionne et al. suggested a two-way definition for prevalence studies on BP: the first, a minimal definition with one "question covering site of low back pain, symptoms observed, and time frame of the measure, and a second question on severity of low back pain" and a more optimal definition "that is made from the minimal definition and add-ons" (51). The NOWAC study does not contain any such measurement instrument for BP, and so prevalence and incidence could not be ascertained in this optimal manner. Nevertheless, the theory from above on what "back pain of unknown origin" probably describes, might justify using this manner of self-reporting as a measure of an approximate incidence and prevalence.

3.3.2.2 Back pain and women

Senie found that women reported higher percentages of BP across all age groups, and that the consequences of BP were higher across all age groups as well. The same was true for women across all levels of socioeconomic status, and that women of low socioeconomic status reported BP even more frequently (52, 53). These gender differences persisted across age, race and ethnicity groups. In Norway, painful conditions of the back were reported as one of the dominating groups of MSDs causing disability in women (54). Shiri et al. reported that obesity in women was a risk factor for BP (10).

3.3.2.3 Back pain and physical activity

It has been reported that subjective measures of PA displayed a protective effect against BP, but primarily when PA was performed as leisure activity (50). The European Guidelines for Prevention in Low Back Pain state that there is a protective effect in leisure PA against BP (55). Thiese et al. found that PA was protective for developing LBP at moderate levels of PA (50). They suggested that there was a ceiling effect for PA, with higher levels not contributing any additional protective effect. Linton et al. also reported consistent evidence for the preventive effect of exercise on neck and back pain (56). Take note that they were talking about exercise in specific. There might be a divide between PA in general, and exercise in particular, when talking about preventive effect. This would be in concordance with the theory of PA, and the reported possible harmful effect of PA in the occupational setting (30). A recommended preventive lifestyle intervention for BP is to undertake moderate exercises multiple times every week and to maintain a physically active lifestyle (48).

3.3.3 Fibromyalgia

The epidemiology of FM has been reported to not be adequately investigated (57). Weir et al. reported to have calculated the first incidence rate (per 1000 years) for a large population. Age adjusted incidence for men was 6.88:1000, and 11.28:1000 for women (57). The diagnostic criteria for FM which are primarily used today are based on revised criteria for FM developed in 1990. These state the following symptoms to be met: “History of widespread pain >3 months”, “Pain in 11 of 18 tender point sites”, and a list of clinical symptoms including fatigue, tenderness, sleep, stiffness, depression, dyscognition, and a reduced quality of life (58). The condition was summed up in a review by Mease from 2005 to be a marked primarily by chronic, widespread

pain, and multiple tender points throughout the body. Together with Ablin et al. he also described a range of other symptoms, including sleep disturbance, fatigue, irritable bowel syndrome, headaches, and mood disorders (59, 60). The most recurring symptoms were pain, fatigue and sleep disturbances. Virtually all patients described severe fatigue despite adequate sleep, which normally worsened by mid-afternoon. Mease also reported poor sleep patterns (59). Recurring descriptions of the condition by patients are typically likened to having the flu, together with a generalized pain sensation (58). The level of disability and impairment attained from the disease is high; Mease reported that FM patients scored lower than all others when compared to patients with RA, osteoarthritis, permanent ostomies, chronic obstructive pulmonary disease, and type 1 diabetes (59). Furthermore, the disability one gets from FM does not seem to change over time (59).

FM is often reported to coexist with other similar pain syndromes, such as headache and irritable bowel syndromes, depression, and CFS (61). 22% of FM patients have been reported to have depressions also (58). Especially CFS and FM appear to have substantial overlap of symptoms, and 50-70% of FM patients were reported to have a current or past diagnosis of CFS (61). 80% of FM patients will fulfill the criteria for CFS also (58). Thus, epidemiologic assessments of FM prevalence and incidence suffer from some uncertainty due to the extensive overlap of symptoms with CFS (13). Mielenz and Alvarez suggested this measurement bias to be one of underreported FM, but this could possibly go both ways.

3.3.3.1 History and theory of fibromyalgia

The first differentiation from the general ‘muscular rheumatisms’ commonly referred to in the

1800s, to the term “fibrositis”, occurred in 1904 (62). It was then suggested that the condition was one of fibrous muscle tissue inflammation (62). The first modern description of the “fibromyalgia syndrome” was presented in 1972, when Smythe described fibrositis symptoms as including tender points and widespread pain, along with certain clinical information, and specifying sites of tender points (62). This led to an increased interest surrounding the condition, with the term “fibromyalgia” appearing in 1976. Research continued until 1990, when the Multicenter Criteria Committee, headed by the American College of Rheumatology (ACR), developed the consensus definition of the condition FM as seen previously (63). Although theories of causation remained diverse, these criteria and definitions of the FM syndrome have remained relatively unchanged since the ACR report. By 1999, there had been no pathophysiological findings in muscle- or soft tissue to indicate localized pathology. Thus it was reported in 1999 that the search for causation was shifting towards neuroscience (61). By 2004, authors stated that “the pathogenesis of this disorder now is accepted to be an aberration of central neurohormonal functions, particularly central sensitization” (62). A 2005 review stated possible precipitating causes to be stress, medical illness, pain conditions, neurotransmitter and neuroendocrine disturbances (59). They too pointed towards a sensitization of the central nervous system (CNS), as well as the periphery, as the main disturbance. Genetic factors have also been suggested as an underlying cause (13).

3.3.3.2 Fibromyalgia and women

As in many other chronic widespread pain conditions, women are also overrepresented in FM, with a suggested rate of 7:1 for women compared to men (57). This ratio was based on the 1995 prevalence of Wolfe et al., who reported a total point prevalence of 2% for both sexes, but 3.4%

for women and 0.5% for men (64). In Norway, prevalence from one epidemiologic study was reported at 3.2%, with the prevalence of women being 5%, and with women making up 90% of adult FM patients (2). The form of prevalence rate was not clear but appeared to be total prevalence within selection. Women with FM also comprise the largest national group of new disability pensions (4, 54). In total, around 1750 new disability pensions are due to FM each year in Norway (2). Particular risk factors for women have been suggested to include autoimmune disorders, systemic inflammatory conditions, as well as endometriosis (13). The exact reason why women seem to be affected more often than men - or become more disabled by the condition than men - is unknown. As previously discussed, underreporting among men could inflate the women-men ratio and make it appear as if women were overrepresented in FM.

3.3.3.3 Fibromyalgia and physical activity

According to general advice for prevention of MSDs, varied PA has a well-documented preventive effect for MSDs, including FM (2). Obtaining the diagnosis of FM has demonstrated an association with low levels of PA. This was despite the fact that increased PA had been demonstrated to reduce pain and improve quality of life in these patients (13, 65). Premorbid levels of PA and the association with developing FM have not been well explored in literature. The previously mentioned case-control study by Smith et al. suggested a high premorbid pattern of PA for those participants that developed FM (41). It must be reiterated that their study had problems with statistical power. FM patients also report that experienced pain prevents them from being as physically active as recommended. The same patients are most frequently seen to be physically inactive (13). Women report lower levels of physical fitness, but do not report lower levels of PA (2). According to Lærum et al., women with FM also reported that PA

increased pain and exhaustion more to a larger extent than healthy women (2).

3.3.4 Muscle pain/myalgia

The outcome reporting item of muscle pain/myalgia was the outcome included in our study which had the most room for individual interpretation. Asking a lay person to define what 'muscle pain' is, might possibly gather as many answers as persons asked. Even in clinic, muscle pain is a broad category to diagnose (66). There are several possible sub-categories of muscle pain disorders which frequently overlap, causing diffuse and indistinct boarders of definitions. It was not clear from the item in the questionnaire what muscle pain referred to, as no definition was given for respondents to align themselves to. We therefore looked at some broad terms used in clinic to describe muscle pain conditions in an attempt to demonstrate the variation inherent in the term 'muscle pain' for purposes of discussion. However, it must be kept in mind that no such clarification was offered to respondents in the NOWAC study.

Frequently used terms for muscle pain both within clinic and literature include myalgia, myofascial pain, myofascial pain syndrome, muscle soreness, delayed onset muscle soreness, myofascial trigger points, regional soft tissue pain, and localized muscle pain, amongst others (39, 66-70). Causes for these types of muscle pain are almost as diverse as the terminology itself. Literature often uses the terms myalgia and myofascial pain interchangeably to describe localized muscle pain, although ICD 10 employs the former (39). Parfitt et al. defined myalgia as "acute, local, noninflammatory pain" in musculature (69). The term is thus often used to describe a localized pain condition in musculature that can have a number of causes but usually follows an approximately similar pattern of manifestation. Myofascial pain, also referred to in clinic as

"regional soft tissue pain" (66), is pain which comes from muscles or their fascia (67). Myalgia often presents with localized pain in the form of muscle "foci", giving rise to a feeling of stiffness in the area in combination with a deep aching sensation which is aggravated by using the affected muscles (67). The presence of "foci" (or myofascial triggerpoints) has previously been a presumption for the diagnosis, although no sufficiently validated diagnostic criteria for identifying trigger points have been developed (67). Bennett reported that such muscular pain was often caused by overuse, repetitive strain or acute muscle injury (67). Borg-Stein and Simons also reported that onset may follow an incident of trauma or injury, or appear more gradually (71). They can also be of an infectious nature, or be caused by medication use (68), but appears to be most often used as a differential term for conditions of non-traumatic, non-infectious and non-pathogenic origin. Localized muscle pain problems can be temporary, although some authors reported the tendency of lasting pain to develop into what was termed "myofascial pain syndrome" (67). Borg-Stein reported myofascial pain syndrome to be a condition characterized by pain arising from several myofascial trigger points in possible tandem with other pain generators, thereby indicating a condition that might be more widespread than single localized muscle pains (66). Brukner and Khan referred to this as a common local pain disorder (70).

The pathophysiological causes behind localized myofascial pain are still not fully understood (67). In clinic, the most important step is to identify possible underlying morbidity for the symptom of myalgia (68). Schmerling attempted to divide myalgia into groups on basis of suspected etiology: myalgia with diffuse or localized symptoms. Conditions causing the diffuse variants were listed as "systemic rheumatic disease, fibromyalgia, infection, medication use, metabolic derangements, hypothyroidism, psychiatric causes", while localized myalgia were theorized to be caused by "strenuous activity, soft tissue disease, pyomyositis, myofascial pain

syndrome, muscle infarction, and compartment syndrome" (68). The author thus included conditions beyond the narrow types of "localized muscle pain" in the attempt to chart possible causes (68).

The discrimination between individuals with myalgia and FM is not overly good (67), but the important difference is the absence of a global pattern of widespread pain, fatigue and sleep disturbance in myalgia (71). This difference in distribution of muscle pain gives cause to say that myalgia can be a condition separate from those of CFS, FM and diffuse BP. However, it is also clear that patients with chronic pain conditions may report myalgia as a symptom of their condition. Borg-Stein reported that women and men had the same prevalence rates of myofascial pain (66).

Based on these diverse definitions and proposed causes of muscle pain conditions, we expected muscle pain in some form or other to occur regardless of level of PA. Possibly some causations will be more common with certain levels of PA than others, such as muscle pain due to delayed onset muscle soreness after activity in people with lower PA groups (70). The diversity of muscle pain conditions and causes implies that all individuals are prone to experience a form of this phenomenon at some point or points during life.

In conclusion, what respondents were referring to when returning information on "muscle pain/myalgia" might include a variety of causes and conditions. The term "muscle pain" appears to be too broad for useful registering of one discrete condition, as respondents might be thinking of any number of the conditions described above when reporting this - there is no guarantee for how respondents choose to interpret the questionnaire item. This might question the usefulness of

"muscle pain/myalgia" as an outcome measurement, but the fact remains that however they wished to define it, respondents in the NOWAC study were reporting this phenomenon. We therefore chose to explore the available data.

3.3.5 Overlap of chronic fatigue syndrome and fibromyalgia

It is evident that there is a substantial overlap of these two conditions. Patients are at risk of being diagnosed to either one when presenting with symptoms that are common for both, such as fatigue and musculoskeletal pain. Perhaps one of the main differences is the gravity of either of these two symptoms, with those experiencing the most pain being categorized as FM, and vice versa. Due to their similarity, some have suggested combining the two conditions:

> "Van Houdenhove (2003) even concluded that there is preliminary evidence for a relationship between CFS/FM and complex regional pain syndrome type I, based on many clinical features similar with CFS and FM, such as a predominance in women, frequent traumatic onset and allodynia or hyperalgesia." (19)

Both conditions were included as separate outcomes in our study. Similar associations between these two outcomes and PA might strengthen the suggestions of Van Houdenhove.

3.4 Covariates

The following are covariates as reported by respondents in the study. Possible association with PA and the outcomes we were looking for is examined in further detail below.

3.4.1 Age

Taffet reported on broadly predictable changes brought on by ageing that were associated with an

increased susceptibility to many diseases. This effect was modified by factors such as genetics, lifestyle, and exposure through the environment (72). Age has been found to be a risk factor for some chronic pain conditions (13). It has been reported that musculoskeletal pain is most frequently present in the age group 40-60 years (2). Deyo reported BP to be more frequent in the age group above 45, but also stated that it became less prevalent among the oldest participants (52). Dionne et al. reported a similar curvilinear trend for BP of benign and mixed causes according to age groups (51).

PA is now recognized as a crucial element in maintaining health among older adults while reducing their risk of developing a number of chronic conditions (73). Dumith et al. found prevalence of inactivity to be greatest in women and to increase by age (25). However Norwegian numbers from 2008-2009 indicated that women and men were not significantly different with regards to physical inactivity (74), except for groups aged 70 and above, which were significantly more inactive than younger age groups.

3.4.2 Body mass index

Like ageing, increasing body mass index (BMI) is also recognized as a risk factor for much of morbidity and mortality. The WHO states that:

> "Mortality rates increase with increasing degrees of overweight, as measured by BMI. To achieve optimal health, the median BMI for adult populations should be in the range of 21 to 23 kg/m2, while the goal for individuals should be to maintain a BMI in the range 18.5 to 24.9 kg/m2, and moderate to severe risk of co-morbidities for a BMI greater than 30 kg/m2. There is increased risk of co-morbidities for BMIs in the range of 25.0 to 29.9 kg/m2" (5)

1 in 5 Norwegians were reported to be obese in 2011. There was no significant difference

between genders, except for a female dominance in the older age groups (75). Senie reported an increasing pattern of chronic diseases corresponding to the rapid rise of obesity of human populations during the recent decades (53).

Obesity and PA are correlated to each other. Increased physical inactivity causes increased BMI and prevalence of obesity, and obesity in itself can be a factor limiting level of PA due to motivational and exertional difficulties (76). Shiri et al. observed that leisure time PA decreased with obesity, which again increased the risk of BP. Thus, PA is important to individuals who are obese or overweight in order to prevent BP (10). Shiri et al. found that obesity but not excess weight increased the risk of radiating BP (10). The effect of abdominal obesity for this condition was seen in women in particular (10). There seemed to be a difference in magnitude of risk between overweight and obesity. Of the other three outcomes in our study, the link between increased BMI and disease is not well understood, but on a general basis it has been suggested that higher levels of BMI – possibly obesity – is a risk factor for MSDs (75).

There exists some controversy surrounding the association between BMI and morbidity. Janssen et al. stated that it was waist circumference, and not BMI in itself, that explained the health risk in obesity (77). BMI as a measure does not differentiate between body tissue composition, but only the ratio of weight and height. Overweight and obesity on the other hand are descriptions of an unhealthy body composition consisting of excess body fat. Shiri et al. reported that waist circumference may be a better measure of obesity compared to BMI (10).

3.4.3 Education

Education is a social determinant of health, both in form of what knowledge an individual has

access to and the possibility of understanding and applying it, but more importantly by the way it gives access to occupation and salary, and the lifestyle associated with these. As a social determinant of health, a lack of education has proven to be a risk factor for mortality and morbidity (5). Frydenberg et al. found that MSDs were less prevalent among persons with higher education, compared to those of lower education levels (78). Explanations included less physical straining work in higher education occupations, and possible lifestyle differences between lower and higher educated persons (78). Higher education was inversely associated with prevalence of BP (2). Prins et al. reported a higher prevalence of CFS in adults with lower education (35).

In Norway, shorter lengths of education was associated with inactivity; the shorter the length of education, the less leisure time the person was likely to spend on PA (79). Studies on the Norwegian population in 2012, reported 18% of those with lowest education levels to be inactive, compared to only 6% of those with the highest (26).

3.4.4 Alcohol

Alcohol overuse is one of the major risk factors for non-communicable diseases (5). There is little theory indicating that alcohol exposure is a risk factor for MSDs. Moderate alcohol intake has in some cases been shown to reduce the risk of ischemic heart disease (80). Association between alcohol consumption and morbidity is complex and dependent on both pattern of, as well as amount of, the consumption (5).

3.4.5 Smoking

Cigarette smoking remains one of the most important modifiable risk factors for chronic disease today, along with physical inactivity (31). There are currently 1.3 billion smokers, most of which live in developing countries (81). Smoking as a social determinant of health also displays variation in prevalence within population subgroups. Lower socioeconomic groups have a higher prevalence of smoking (31). The WHO reported that higher levels of daily smoking was found to be associated with lower levels of educations (5). Smoking is also a risk factor for experiencing acute myocardial infarction, cancer, and diabetes (81, 82).

There is an association between cigarette smoking and risk of muscle pain (83). Independently of confounding factors, early disability pension due to musculoskeletal conditions and low back diagnoses was associated with persistent smoking (84). Reports indicated daily smoking to be a risk factor for onset of severe BP (15, 85). Two early epidemiologic studies in Norway reported that smoking was associated with increased levels of musculoskeletal pain (86, 87). Eriksen et al. reported that young and middle-aged persons who smoked experienced more and worse pain when they smoked compared to when they did not (75).

The majority or articles included in a meta-analysis on smoking and levels of PA indicated that smoking and PA are inversely related – more smoking led to less PA (31). Kaczynski et al. reported finding some weak evidence that smoking was associated with lower levels of PA in women (31). Early reports by Conway and Cronan found that current smokers engaged in less overall exercise per week than nonsmokers (88).

3.5 Comorbidities

Respondents in the NOWAC study reported on some sets of other morbidities, including diabetes and ischemic heart disease (IHD). Cancer data was gathered from the Norwegian Cancer Registry. These comorbidities were included in the present study to be assessed as modification factors.

3.5.1 Diabetes

There are primarily two types of diabetes – type 1 and 2. Of these, 80-90% is type 2, which is dependent upon a genetic susceptibility (89). Risk factors for diabetes 2 include physical inactivity, smoking and obesity. This causes the disease often to be referred to as the lifestyle-induced type (89). Prevalence of known type 2 diabetes among Norwegian women was reported at 3.5-4% in 2007-2008 (90). Health authorities presume the prevalence of unknown type 2 diabetes to be approximately the same. Diabetes is a risk factor for IHD, especially among women (90).

MSDs have been reported to occur more frequently in diabetes patients (91). Cagliero et al. reported MSDs to be present in almost 40% of diabetic patients (92). However, this group of conditions, as we have seen, is quite diverse. Diabetes, type 2 mellitus in particular, affects the connective tissues in the body (92, 93). As such, several comorbidities often occur alongside it. These include a number of joint and skeletal disorders (80) of local and known origin. These types of conditions are not marked by the sort of global, diffuse patterns as those of interest to our study, and diabetes has not been explicitly reported as a risk factor for these types of MSDs. However, regional musculoskeletal disease can possibly exacerbate patterns of global

musculoskeletal pain, in which case diabetes can be thought of as an indirect risk factor for developing diffuse MSDs like the outcomes of our study. Furthermore, Abate et al. suggested the presence of a subclinical, low-grade systemic inflammation state in conditions of obesity and metabolic disorders (94). In addition to affecting the musculoskeletal apparatus, it could be theorized that such a systemic state might exacerbate diffuse, global musculoskeletal ailments.

Diabetes has been shown to be associated with physical inactivity, with an adjusted relative risk of 1.20 for being inactive if diabetes is present (7). Exercise as diabetes treatment is considered one of the cornerstones in an optimal treatment regime (95).

3.5.2 Cancer

Cancers are one of the leading causes of mortality in the non-communicable disease group (5). The causes of cancer are many and consist of an interaction between genetics, lifestyle habits and the environment (96). Risky lifestyle factors include previously mentioned smoking, obesity, alcohol, and physical inactivity (5). Inactivity and obesity have been shown to increase the risk of several types of cancer by as much as 25% (5), and especially colon and breast cancer (7). Norwegian women have a slightly lower prevalence of total cancers than men (54.1% versus 45.9%) (97). When measured in five-year periods, cancer incidence in Norwegian women had risen by 2% by the end of 2011 (97).

Cancer in the musculoskeletal system is liable to be a cause for musculoskeletal pain/myalgia and disability. However, only 1% of all musculoskeletal pain reported in Norway was cancer-related (2). Cancer is an exclusion criterion for a diagnosis of CFS (35, 36) – in some cases symptoms

can be of a similar nature. It is also an exclusion criterion for BP, according to already established definitions. FM is a diagnosis of exclusion, when inflammation or damage are not present to explain the widespread pain (98), and as such should not be diagnosed in tandem with a cancer diagnosis. Cancer does not appear to be mentioned specifically as a precipitating factor for our four outcome conditions.

3.5.3 Ischemic heart disease

IHD was reported in the questionnaires of the NOWAC study by questions of angina and myocardial infarction (MI) status. Physical inactivity is a strong predictor for coronary heart disease (99), in addition to other previously described lifestyle habits. Raised blood pressure is an important risk factor for developing cardiovascular disease (5). IHD follows typical patterns of socioeconomic status, with conditions occurring more often and impacting more severely in low-resource settings (5).

High blood pressure is a demonstrated risk factor for BP (50). Furthermore, psychosocial stress can be a risk factor for chronic widespread pain, and high blood pressure might function as a symptom of such stress. The literature does not draw clear links between IHD and the MSDs serving as outcomes in our study. However, IHD follows the same distribution in society as the other typical risk factors for MSDs. This contributes to create a possible picture of the person at risk for these conditions.

Keeping all this theory in mind, we now move on to assess the association between levels of PA and the four outcomes we have described above.

4. Materials and methods

We planned and performed a prospective cohort study based on data from the NOWAC study. Information regarding the NOWAC study and its participants was obtained from the NOWAC study homepage on the internet, as well as articles describing the cohort (100-105).

4.1 The Norwegian Women and Cancer study

All data material used in our study was gathered from the NOWAC study, headed by the Department of Community Medicine at The Arctic University of Norway, University of Tromsø. The NOWAC study is a longitudinal cohort study originally started in 1991 to investigate possible associations between internal and external hormones and female cancer (100). Data were obtained through self-administered questionnaires which participants receive per mail. All women born between 1921-1961 were sampled randomly from the Norwegian Central Person Register which contains information on all Norwegian inhabitants including a unique birth-number which consists of a date of birth and five individualized personal numbers and personal numbers (100).

4.1.1 Questionnaires in the Norwegian Women and Cancer study

Participants in the NOWAC study were invited to attend the initial round of questionnaires, with the possibility to be contacted at later occasions for further follow-up. At the present time there exists one baseline and two follow-up rounds of questionnaires. Each round was separated by 4-8 years of follow-up time. Several series of questionnaires (2-8 pages long) were developed and sent to participants, most containing questions on diet, exogenous hormone use, other diseases,

reproductive information, smoking habits, and alcohol consumption. Information on cancer status was then linked to participants from the Norwegian Cancer Registry. All series of questionnaires asked for self-reported PA. Many series also asked for information on prevalence and incidence of the MSDs serving as outcome measurements in our study: CFS, BP, FM, and myalgia. Some series were developed as part of validation studies, with questions differing somewhat in accordance with the nature of such studies. Some series were shorter forms, focusing only on such things as cancer and exogenous hormone use, or cancer and diet.

4.1.2 Participants and follow-up in the Norwegian Women and Cancer study

Baseline invitations were performed during the years 1991-1997. 102 540 women aged 30-70 years returned filled-in questionnaires, a total of 57%. An expansion of the cohort with 60 000 new invites was performed during the years 2003-2004, returning 27 400 filled-in questionnaires by women aged 45-60 years. An additional expansion was done during 2007, inviting another 88 000 women, of whom 42 600 – 48.4% - returned a filled-in questionnaire.

The first follow-up began in 1998 and continued through 2002. During this time, 80 693 women returned a filled-in questionnaire, yielding a response rate of 81%. The second follow-up was done during 2004-2005. A total of 47 586 filled-in questionnaires were returned. Figure 4.1 displays the different series of questionnaires and the rounds of follow-up to which they belong, as well as the years in which these series were administered.

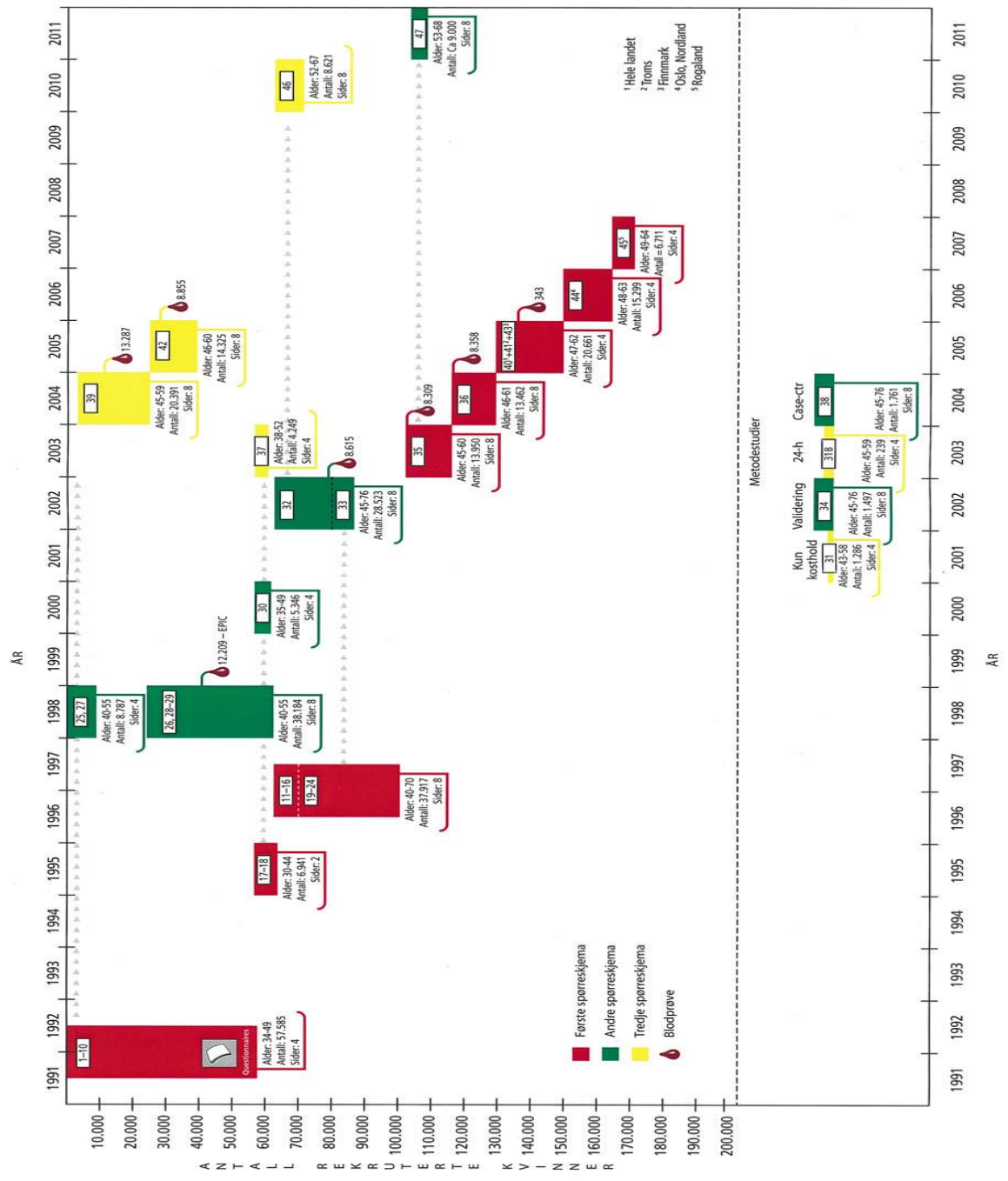


Figure 4.1: Cohort enrolment in the NOWAC study: participants, questionnaires, and baseline/follow-ups (101).

4.2 Inclusion and exclusion in present study

For the present study, only questionnaire series from the NOWAC study containing relevant baseline exposure levels of PA, and follow-up endpoint information on MSDs, were included.

This caused data material for our study to be obtained from baseline, series 1-5, 8-16, 19-24, 35; first follow-up, series 25-29, 32-33, 47; and second follow-up, series 38-39, 42, 46. Figure 4.2 displays the flow of participants eligible for our study produced by those series that contained relevant data on exposure and outcome.

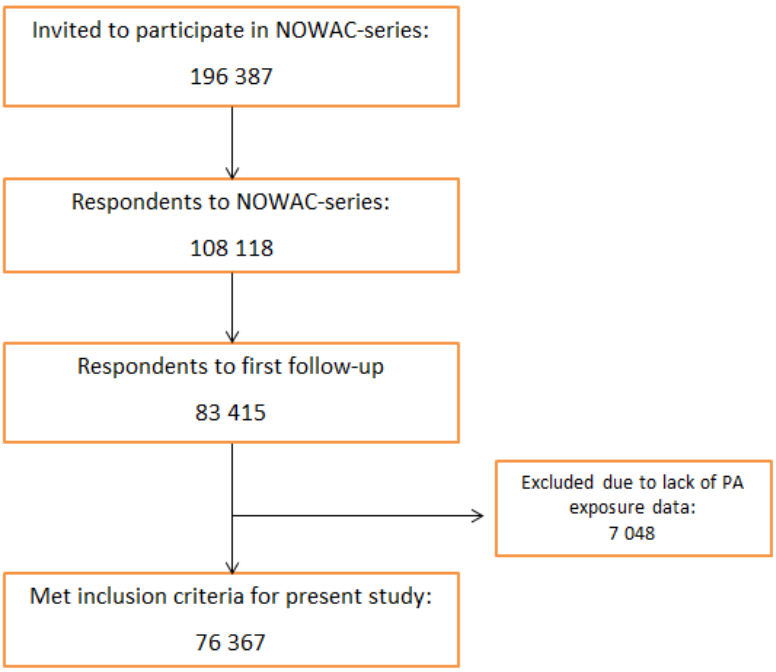


Figure 4.2: Flow chart of participants in present study.

Out of the present total invited participants of 196 387 women, all those who responded on baseline and follow-ups totaled 83 415 respondents. Inclusion criteria for our study was reporting on PA at baseline. This gave a final study sample of 76 367 women with information from baseline and follow-up. These were the women returning information on PA at baseline, as well as returning questionnaires containing questions about the four outcomes during follow-up. Characteristics of participants, including their reported level of PA at enrolment, were obtained from baseline questionnaires.

There was a drop-out of included participants between the first and second follow-up. Of participants responding to first follow-up, 46% did not respond to the second follow-up.

Exclusion criteria for analysis were set according to outcome status. As cumulative incidence during the study period was the outcome of interest, prevalent cases at the time of enrolment were excluded from the corresponding analysis of that outcome.

4.3 Analysis of data

The following outlines how variables were gathered and coded from the NOWAC study and what statistical methods were used to assess the information.

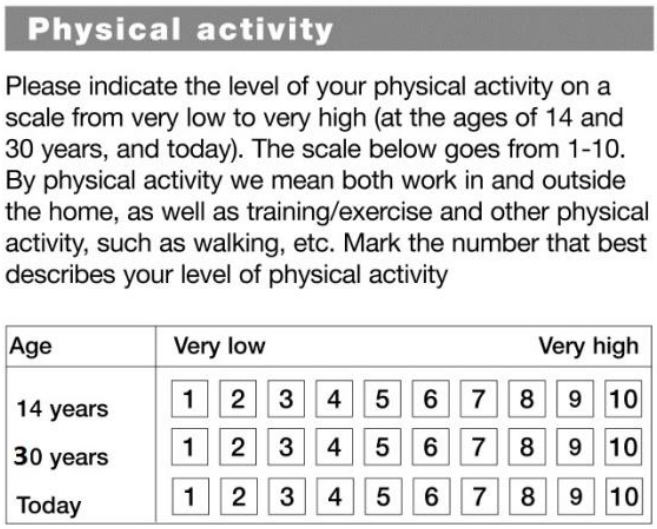
4.3.1 Exposure and outcomes in the material

When measuring PA in large populations, it can be acceptable to use different kinds of survey on grounds of practicality, feasibility and economics (24). Reports must be converted into a measurement metrics that allows ranking of degree of PA according to each other (24). In our study, PA was measured per self-reporting in a questionnaire. See appendix A for an example questionnaire from the NOWAC study.

4.3.1.1 Physical activity measurement

The exposure variable for level of PA was obtained from a ten-point scale included in the original questionnaires. Participants were asked to "*indicate your level of physical activity on a scale from 'very low' to 'very high'. The scale below runs from 1-10. By physical activity is meant both work*

in the home as well as occupational activity, exercise, and other forms of physical activity such as taking walks, hikes, and so forth. Indicate that number which best represents your level of physical activity" (figure 4.3). PA level existed in the data set as a ten-point variable but was recoded into a five-category variable as preparation for analysis. Reported levels 1-2 were coded as "very low", levels 3-4 were coded as "low", levels 5-6 were coded as "moderate", levels 7-8 were coded as "high", and levels 9-10 were coded as "very high". Category "moderate" was used as reference group in logistic regression analysis. This manner of recoding PA has previously been demonstrated on the same dataset and appears to be a functional manner of preparing the variable for logistic regression analysis (106, 107). Due to the reporting that moderate PA might be more protective for MSDs than high and low levels of PA, the moderate group was used as reference category in the logistic regression model for BP. This was also the largest of the groups, and therefore served well as a reference group.



Physical activity

Please indicate the level of your physical activity on a scale from very low to very high (at the ages of 14 and 30 years, and today). The scale below goes from 1-10. By physical activity we mean both work in and outside the home, as well as training/exercise and other physical activity, such as walking, etc. Mark the number that best describes your level of physical activity

Age	Very low									Very high
14 years	1	2	3	4	5	6	7	8	9	10
30 years	1	2	3	4	5	6	7	8	9	10
Today	1	2	3	4	5	6	7	8	9	10

Figure 4.3: Example of reporting item on physical activity from NOWAC questionnaire.

4.3.1.2 Outcome measures

Outcome variables were included in the questionnaire under the following description: "*For the*

following conditions, tick off the box for which year the condition arose or report the year of the period before [study period start]". Selectable options included boxes for all the years of the period including one marked "before the year [study period start]". This allowed the onsets of the diseases to be assessed, and the production of four different outcome-variables coded "no", "incidence" and "prevalence", with prevalence defined as all cases in the years before baseline. Based on these, participants with prevalence could be censored in logistic regression analysis.

4.3.2 Confounders

Confounders in the study as previously discussed were deemed of importance to the outcomes at hand and included in statistical modeling to assess their confounding effect on the association between levels of PA and the outcomes:

Age at enrolment was derived from respondents' year of birth. Age was recoded into age groups of 10 units per group, giving a total of five groups: 30-39, 40-49 , 50-59, 60-69, and 70-79. The final two age groups, 60-69 and 70-79, were combined as the oldest enrolled participants were 70 years of age and few in numbers. The reference category of age was set to the second level, 40-49 years.

BMI at enrolment was calculated from respondents' specification of current height and weight. BMI was recoded into the following categories in accordance with the WHO classification of BMI: "normal weight (BMI = 18.5-24.99)"; "underweight (BMI < 18.5)"; "overweight (BMI = 25-29.99)" and "obese (BMI $\geq$ 30)" (108). The category for normal weight was used as reference category in logistic regression analysis.

Length of education was obtained by asking participants about their total length of education or vocational training. Education was grouped as following: “0-9 years”, “10-12 years” and “≥ 13 years”. Category 1 was used as reference category in logistic regression analysis.

Alcohol consumption was recorded by asking participants whether they were completely abstinent, or if not then how often they consumed one unit of beer (½ liter), wine (1 glass) or spirits (drinks), on average during the last year. Options included “never/seldom”, “1 per month”, “2-3 per month”, “1 per week”, “2-4 per week”, “5-6 per week” and “1+ per day”. Consumption was then calculated into grams per day. The data was recoded into four groups: “0.1-3.9 grams per day”, “complete abstinence”, “4-10 grams per day” and “> 10 grams per day”. Category “0.1-3.9” was used as reference category in logistic regression analysis.

Smoking was registered by asking if they were current smokers. Our study used the variable displaying current smoking status, coded as “never”, “former” and “current”. Category “never” was used as reference category in logistic regression analysis. The first 10 series of questionnaires in the NOWAC study did not ask about current smoking habits, but derived this from respondents reporting how many cigarettes they were currently smoking per day.

Diabetes at enrolment was reported by participants in response to being asked “Have you had any of the following diseases” and being prompted to report starting age if they had. This allowed for coding of diabetes as a dichotomous “no/yes” prevalence variable for inclusion in logistic regression analysis.

Cancer was not included as a question in the original baseline series as NOWAC is linked

directly to the cancer registries. Cancer status for participants was obtained directly from the National Cancer Registry. Any type of cancer present in history was coded into a dichotomous "no/yes" prevalence variable for inclusion in logistic regression analysis.

Ischemic heart disease was combined from respondents' reporting of present angina or myocardial infarction in the same dimension as diabetes. These were combined to create a dichotomous "no/yes" IHD variable to determine prevalence at baseline, for inclusion in logistic regression analysis.

4.4 Statistical methods

The following outlines the statistical methods used to assess the data gathered from the NOWAC study. This included both the descriptive statistics used to gain an overview of the distribution of variables within the selection, and the logistic regression analysis used to assess the association between exposure and outcomes.

4.4.1 Descriptive statistics

Descriptive statistics were used to obtain information on the study participants. Means and standard deviations were used to assess the dispersion of data, or median and percentiles if data were asymmetrically spread or prone to outliers. Groups were compared and trends were tested using ANOVA for continuous variables. For ordinal or nominal variables, the non-parametric Kruskal-Wallis test was used to compare groups. Variables were grouped according to levels of PA, to more easily compare the groups of exposure in relations to each other.

We calculated an incidence rate for all four outcomes. The entire cohort was divided into 4 sub cohorts in order to estimate the person-time between the different questionnaire series from baseline through second follow-up. This was done because the different sub cohorts had different follow-up times. Case accumulation was assumed to occur at a constant rate during the years of follow-up. All participants not experiencing the outcome accounted for as many years of person time as there were follow-up years. Total person-time was summed for all sub cohorts, and number of incident cases divided by it in order to obtain incidence rate for each outcome. Incidence rate was reported per 100 000 person-years.

Prevalent cases were reported for each outcome. In order to make rates more easily applicable to the mother population, prevalence rates were then age standardized using direct standardization based on 2013 numbers of corresponding age groups for the female population of Norway, gathered from Statistics Norway (109). We also reported prevalence rates for all four outcomes, as rates per 100 000. Since prevalence rates were based on reporting from baseline measurements performed during several different time periods between 1991-2003, they are aggregate rates for all of the periods. We note that our sample included age groups 30-70. Mean age of participants at enrolment was reported for each outcome.

4.4.2 Logistic regression models

All statistical analysis was performed using IBM SPSS Statistics v. 21 for Windows. Microsoft Excel 2010 for Windows was used for creating tables and figures of results.
Initially a cox proportional hazard regression was considered, but deemed unfit due to inconsistencies in reporting of time at onset of disease between first and second follow-up.

Logistic regression was selected as the main method of analyzing the strength of association due to the dichotomous nature of the outcomes of interest (110). This would also allow controlling for possible confounders. Four logistic regression models were made, one with each of the four different outcomes as the dependent variable: CFS, BP, FM, and myalgia. Prevalent cases were excluded for the one diagnose examined as endpoint in each of the four models. Acceptable alpha level was set to 5%. Linear trend of PA was reported first, before categorical comparison of PA levels was performed. Odds ratios (ORs) and 95% confidence intervals (CIs) were reported. Hosmer-Lemeshow tests were done to assess the goodness-of-fit of the model.

Univariate analysis of covariates against each of the four outcomes was performed preliminary. This was done to assess the predictive power of the covariates for outcomes. Significant variables were then included one by one in building a model for each outcome. Insignificant variables were finally added to the model to check for new significance levels. A correlation matrix was then created to assess the correlation levels between PA and confounders. All such predictors that were significant and also correlated to PA were to be further assessed as possible confounders to be adjusted for in the final model. When building the final models, covariates that had a confounding effect of a certain magnitude on the main estimate of association were included. The level of confounding deemed necessary for a covariate to be included was set at 5%. Confounding was determined comparing age-adjusted ORs for PA to ORs for PA when including each of the covariates separately. If ORs changed by 5% or more for any of the PA level associations with the outcomes, the covariate was considered to have a confounding effect on the association between PA and the outcomes, and was subsequently included in the final model. In cases of doubt, when several levels lay close to but below the 5% level, we chose to include the covariate on basis of previously described theoretical knowledge. If a covariate was found to be a

confounder for the association to one of the outcomes, it was included in all four models. In the end, based on assessment of confounders as well as theory, we ended up with four identical models containing age, as well as the following lifestyle factors: BMI, education levels, alcohol consumption, and smoking. Of these, smoking was the only variable not reaching the 5% confounding level, but was included in analysis nevertheless based on previous knowledge that smoking and levels of PA are closely related.

Sensitivity analysis was performed in order to assess what effect including participants with one or several comorbidities would have on the ORs of PA. These comorbidities were diabetes, cancer and IHD. We ran analysis of the main models while including a filter that removed participants with each of the comorbidities. Persons with comorbidities were excluded first separately for each condition, and then together, and ORs of PA compared. The differences in ORs were compared using Wald statistics. No significant differences were found and therefore comorbidity covariates were left out of the model.

4.4.2.2 Missing in analysis

In order to censor prevalent cases of each of the four outcomes, values corresponding to prevalence were set to system missing. This caused a proportion of cases to be missing in each of the four models equal to the proportion of prevalence for each of the four outcomes. Additional cases became missing when all adjustment variables were included in the models, due to non-item reply for respondents on some of these. Proportion of excluded cases due to prevalence and missing due to non-item response on confounding factors are reported in table 4.1.

Table 4.1 Proportion missing cases in analysis due to prevalent cases of chronic fatigue syndrome (CFS), back pain (BP), fibromyalgia (FM) and myalgia, as well as for non-item response:

	CFS	BP	FM	Myalgia
Excluded prevalent cases:	2.6 %	13.6 %	5 %	17.9 %
No. of cases:	1968	10422	3837	13649
Missing due to non-item response:	22.6 %	20.1 %	21.9 %	18.9 %

5. Results

This chapter presents all descriptive and analytical results from statistical analysis of the data.

5.1 Descriptive statistics of data

Descriptive data in our selection was divided in distribution of outcome variables, and distribution of other covariates in the selection.

5.1.1 Descriptive statistics of outcomes

Table 5.1 reports the distribution of the main outcomes of interest among the participants, grouped by reported levels of PA.

Total number of incident and prevalent cases, as well as prevalence rates and age standardized prevalence rates for each outcome, is reported in table 5.1. Mean age for the four outcomes were as follows: For CFS, 48.6 (standard deviation (sd) 8.2) years; for BP, 48.3 (sd 8.6) years; for FM, 49.1 (sd 7.9) years; for myalgia, 48.3 (sd 8.3) years. These averages were slightly higher than mean age of the entire sample, at 46.9 years. Reported prevalence rates are valid for populations of this mean age respectively for each outcome.

PA levels at baseline were distributed as follows: Very low = 5.1%; low = 21.1%; moderate = 41.9%; high = 25.4%; very high = 6.6%, totaling 76367 participants. This appeared to be approximately normally distributed as seen in the curve on figure 5.1.

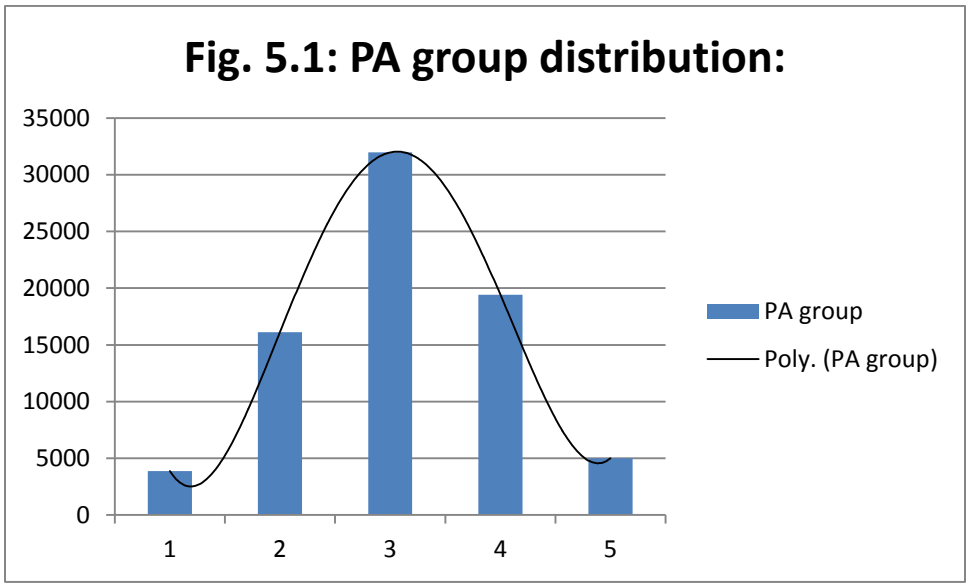


Figure 5.1 Number of respondents within each physical activity (PA) group. Normal distribution curve is displayed.

Chronic fatigue syndrome:

The incidence rate for CFS was 411 per 100 000 person-years. There were 3229 new cases during follow-up, 4.2% of the sample. 2.58% reported prevalent CFS at enrolment, quite similar to the age standardized prevalence of 2.62%. Prevalent cases were excluded from analysis when CFS was the outcome. Incidence followed an apparently normally distributed pattern across PA groups due to the magnitude of the group size as seen in table 5.1. However, the relative incidence of CFS within each PA group was as follows: Very low = 6.6%; low = 4.9%; moderate = 3.9%; high = 3.7%; very high = 4.6%, as seen in figure 5.2.

Back pain:

Incidence rate for BP was calculated to be 1268 per 100 000 person-years. The total number of incident cases of reported BP was 8353, 10.9% of the sample, during the follow-up time. 13.65% reported prevalent BP at enrolment, as compared to the age standardized rate of 14.22%. Prevalent cases were excluded from analysis when BP was the outcome. Incidence again

followed an apparently normally distributed pattern across PA groups due to the magnitude of the group size. However, the relative incidence of BP within each PA group was as follows: Very low = 11.8%; low = 11.3%; moderate = 11%; high = 10.3%; very high = 11%, as seen in figure 5.2.

Fibromyalgia:

The incidence rate of FM was calculated to be 287 per 100 000 person-years. Number of new cases of reported FM was 2194, 2.9% of the sample. 5.02% of the sample reported prevalent FM at enrolment, quite similar to the age standardized prevalence rate 5.03%. Prevalent cases were excluded from analysis when FM was the outcome. Incidence followed an apparently normally distributed pattern across PA groups due to the magnitude of the group size. However, the relative incidence of FM within each PA group was as follows: Very low = 3.7%; low = 3%; moderate = 2.8%; high = 2.6%; very high = 3%, as seen in figure 5.2.

Myalgia:

Finally, incidence rate for myalgia was calculated to be 1509 per 100 000 person-years. The total number of new cases of reported myalgia was 9363, 12.3% of the sample. 17.87% reported prevalent myalgia at enrolment into the NOWAC study. Age standardized prevalence rate was 18.09%, which was quite close. Prevalent cases were again excluded from analysis when myalgia was the outcome. Incidence followed an apparently normally distributed pattern across PA groups due to the magnitude of the group size. The relative incidence of myalgia within each PA group was as follows: Very low = 12.8%; low = 12.2%; moderate = 12.3%; high = 12.1%; very high = 12.8%, as seen in figure 5.2.

The patterns of total and relative incidence were quite similar for all four diagnoses. Common for all diagnoses were dropping incidence levels from PA group “very low” to group “high”, with a late increase in incidence from group “high” to group “very high”. With CFS, incidence level for group “very high” was higher than for group “moderate”. For BP, incidence level for group “very high” was identical to that of group “moderate”. For FM, incidence level for group “very high” was identical to that of group “low”. For myalgia, incidence level for group “very high” was identical to that of group “very low” and the highest of all the groups. As with incidence, BP and myalgia had the highest rates of prevalence compared to the other two. Mean age in prevalent cases was higher for all four outcomes than for the study sample as a whole. SDs of mean age in prevalent cases suggested that most prevalent cases (95% CI) were approximately between 32 and 64 years of age.

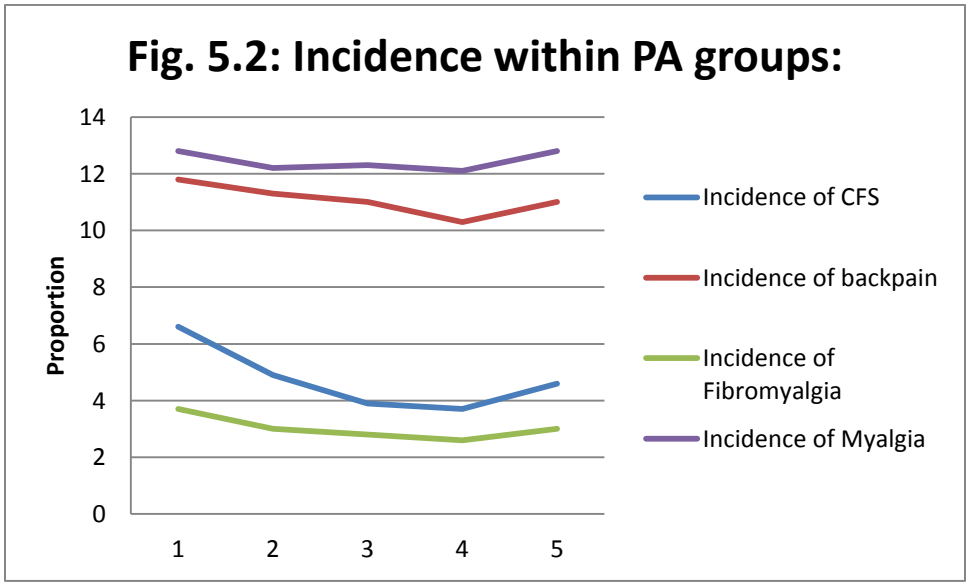


Figure 5.2 Incidence of outcomes within each physical activity (PA) group.

Table 5.1 Distribution of incidence and prevalence for outcomes, and across physical activity (PA) groups:

PA group:	Total(proportion):	Very low	Low	Moderate	High	Very high
Group total n =	76367 (100%)	3869 (5.1%)	16104 (21.1%)	31968 (41.9%)	19413 (25.4%)	5013 (6.6%)
Chronic fatigue syndrome:						
Proportion incidence within PA group	3229 (4.23%)	6.6 %	4.9 %	3.9 %	3.7 %	4.6 %
Incidence rate (per 100 000 person-years)	411.41					
Prevalence	1968 (2.58%)					
Age standardized prevalence	2.62%					
Back pain:						
Proportion incidence within PA group	8353 (10.94%)	11.8 %	11.3 %	11.0 %	10.3 %	11.0 %
Incidence rate (per 100 000 person-years)	1267.85					
Prevalence	10422 (13.65%)					
Age standardized prevalence	14.22%					
Fibromyalgia:						
Proportion incidence within PA group	2194 (2.87%)	3.7 %	3.0 %	2.8 %	2.6 %	3.0 %
Incidence rate (per 100 000 person-years)	287.06					
Prevalence	3837 (5.02%)					
Age standardized prevalence	5.03%					
Myalgia:						
Proportion incidence within PA group	9363 (12.26%)	12.8 %	12.2 %	12.3 %	12.1 %	12.8 %
Incidence rate (per 100 000 person-years)	1509.14					
Prevalence	13649 (17.87%)					
Age standardized prevalence	18.09%					
Total cases incidence+prevalence	56616					

5.1.1.1 Combination of outcome conditions in participants

Table 5.2 displays the different combinations of outcomes that appeared in participants, both prevalent and incident cases. Each category is exclusive, meaning no participant could be in more

than one category at the same time. CFS appeared 1015 times by itself, and 4182 times in combination with one or more other conditions. BP appeared 7236 times by itself, and 11539 times in combination with one or more other conditions. FM appeared 988 times by itself, and 5043 times in combination with one or more other conditions. Myalgia appeared by itself 9495 times, and 13517 times in combination with one or more other conditions. Both CFS and FM appeared to occur less frequently alone than they did in combination with other conditions. Both myalgia and BP appeared to occur frequently both alone and in combination with other conditions.

CFS and FM appeared exclusively together only in 90 respondents. However, they appeared together in 1347 respondents alongside additional conditions.

Table 5.2 Combination of outcomes in participants with frequency and proportions:

Outcome combinations:	Frequency:	Proportion:
M[1]	9495	12.4
F[2]	988	1.3
CFS[3]	1015	1.3
BP[4]	7236	9.5
M-F	1512	2.0
M-CFS	1042	1.4
M-BP	6761	8.9
F-CFS	90	.1
F-BP	445	.6
CFS-BP	423	.6
M-CFS-BP	1280	1.7
M-F-BP	1649	2.2
M-F-CFS	366	.5
F-CFS-BP	74	.1
M-F-CFS-BP	907	1.2
Healthy	43084	56.4
Total	76367	100.0

[1]Myalgia [2]Fibromyalgia [3]Chronic fatigue syndrome [4]Back pain

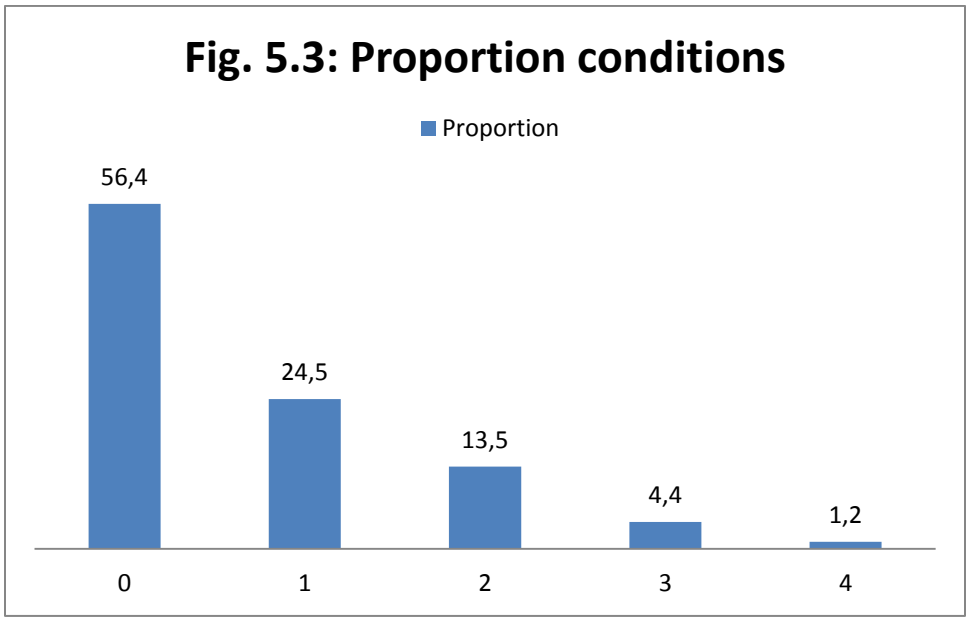


Figure 5.3 Proportion of participants having 0, 1, 2, 3, and 4 simultaneous outcome conditions.

5.1.2 Descriptive statistics of study population

Mean follow-up time between baseline and first follow-up was 6.4 years. Mean follow-up time between first follow-up and second follow-up was 6.7 years. For the time interval between baseline and second follow-up, the mean follow-up time was 13.1 years. Max follow up time was 15 years.

The distribution of covariates according to levels of PA is reported in table 5.3.

Maximum age at enrolment was 70 years, minimum was 34. Mean age was 46.9 (sd 8.4). Age differed significantly between groups of PA ($p< 0.001$). Test for linear trend was also significant ($p< 0.001$) and indicated a trend of decreasing age with increased PA. Participants registering at "very low" activity level were 47.8 years of age on average, and participants reporting a "very high" activity level were on average 46.3 years of age. 100% of the participants registered data

on the age-item, as birth year was obtained from the Norwegian Central Person Register.

Maximum BMI registered at enrolment was 69.5 and minimum was 12. Mean BMI among respondents was 23.6 (sd 3.6). BMI differed significantly between groups of PA ($p< 0.001$). Test for linear trend was also significant ($p< 0.001$) and indicated a trend of decreasing BMI with increased PA. Participants reporting a "very low" activity level had an average BMI of 25.4, whereas participants reporting a "very high" activity level had an average BMI of 22.7. Response rates for BMI were 86.9%.

Maximum length of education at enrolment was 40 years, minimum was 0. Mean years of education was 12.2 (sd 3.4). Education displayed a different distribution than BMI and age. While the difference between the groups was significant ($p<0.001$), these displayed a significant quadratic trend ($p< 0.001$) across PA levels, as shown in figure 5.4. Post Hoc tests reveal groups 1 and 5 ("very low" and "very high") to be quite similar (not significantly different, $p=0.74$). Furthermore, groups 2 and 3 ("low" and "moderate") were significantly different from groups 1, 4 and 5, but quite similar to one another ($p=1.000$). Of these, the "moderate" group had the smallest standard deviation (3.5 vs 3.3). In all groups, "high" was the only one significantly different from all the others (greatest $p=0.012$). The total response rate for length of education was 95.8%.

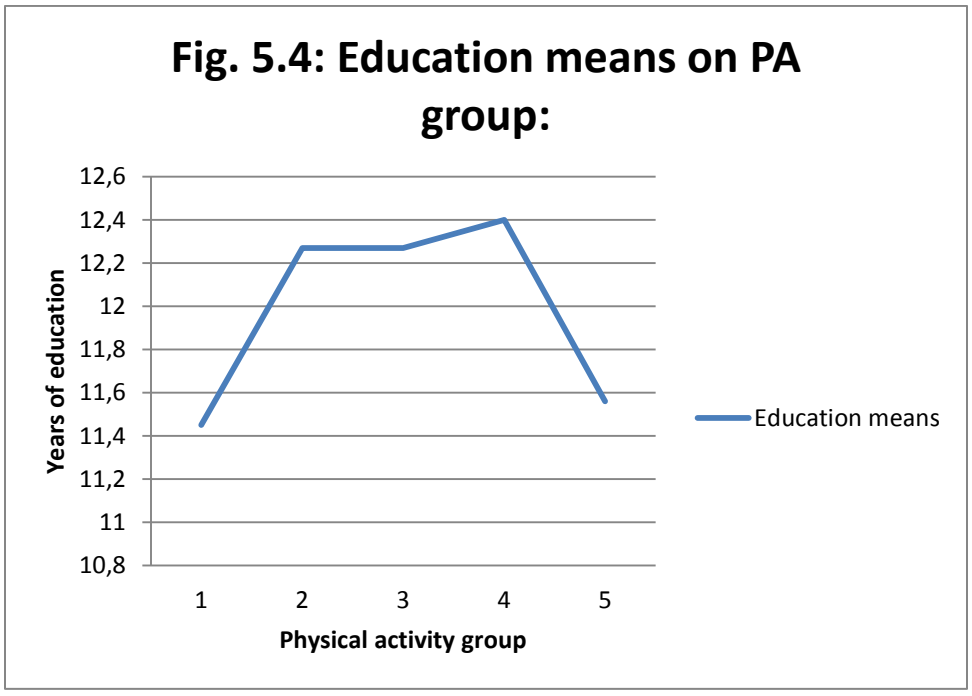


Figure 5.4 Mean education length within physical activity (PA) groups.

Maximum alcohol consumption at enrolment was 203.8 grams per day, minimum was 0. Median alcohol consumption was 1.6 grams per day (90 percentile = 8.3). Because alcohol consumption was not normally distributed and had a few extreme values, median and percentiles was chosen as the measure of dispersion. When comparing groups, alcohol consumption means were significantly different between groups of PA ($p<0.001$). Post Hoc tests gave significant differences between groups "very low" and "very high"; "Low" to "moderate" and "very high"; "moderate", in addition to "low", also to "very high"; "high" to "very high"; and "very high" to all other categories, setting it apart as seen in figure 5.5. Test for linear trend remained significant with $p< 0.001$. Response rates for alcohol were 83.8%.

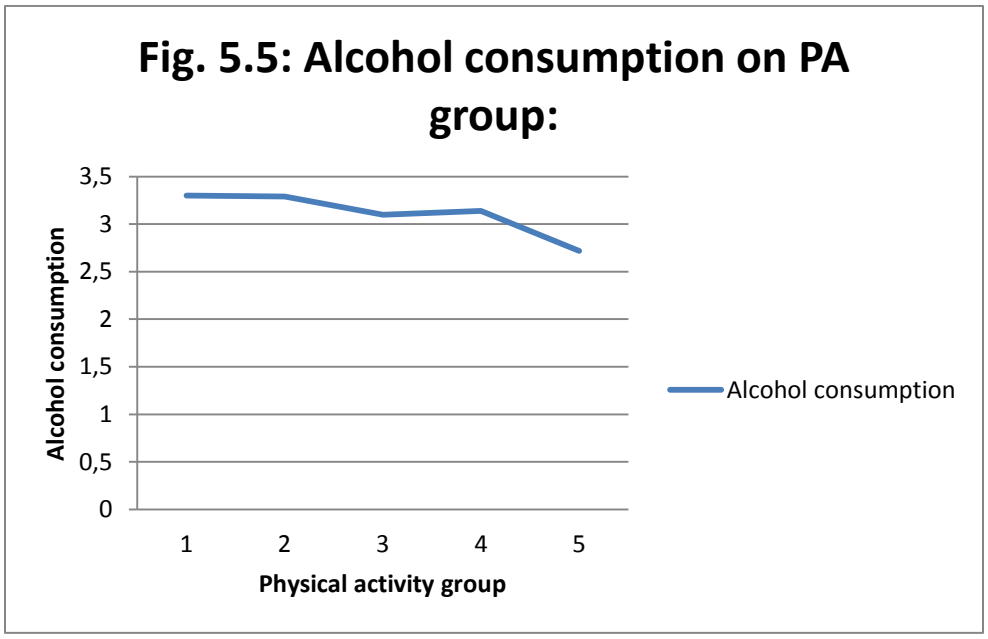


Figure 5.5 Level of alcohol consumption within physical activity (PA) groups.

Smoking as reported at baseline differed significantly between groups "never", "former" and "current" on PA groups ($p<0.001$). Figure 5.6 displays the variation in proportion of the three categories between the five groups. The Kruskal-Wallis non-parametric test indicated a falling mean rank from PA group 1-4, before an increase appeared between group 4 and group 5. This indicated that there were progressively fewer 1's and 2's (former, current) from group 1-4, before the number again increased to group 5. This could be explained by the increasing proportion current smokers in group 5. Response rates for smoking were 98.9%.

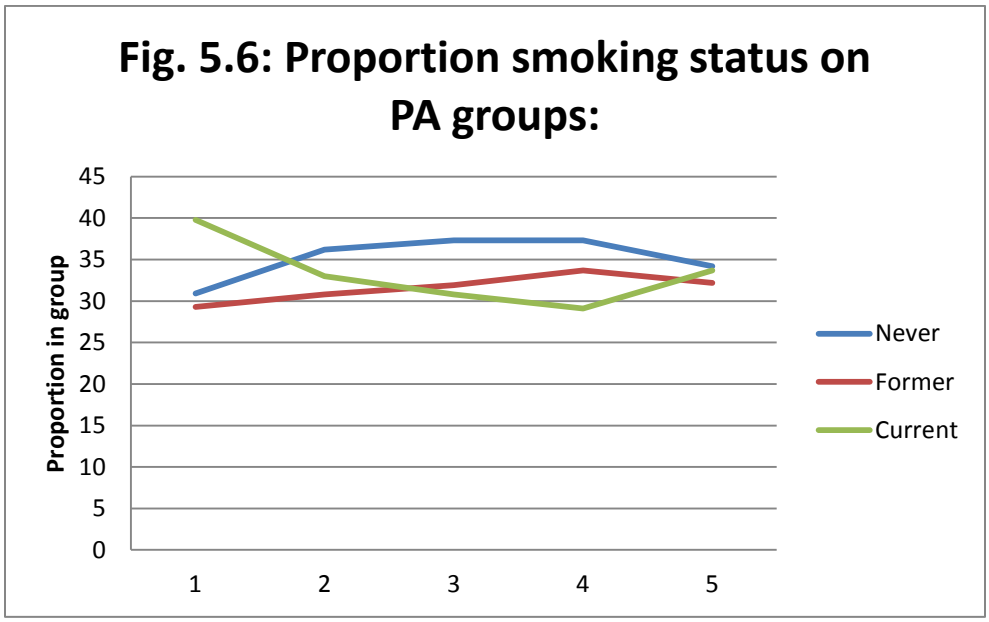


Figure 5.6 Proportion of never, former, and current smokers within physical activity (PA) groups.

Diabetes at baseline was reported as not present or present. There was a mildly sloping trend towards smaller prevalence in higher PA groups. The Kruskal-Wallis test was significant with $p<0.001$. All mean ranks in the test decreased progressively with higher PA group. Total response rates for diabetes were 99.3%.

Cancer was reported as any form of cancer present at enrolment. There was a decreasing trend in prevalence with higher PA group association. The Kruskal-Wallis test was significant with $p<0.001$. All mean ranks in the test decreased progressively with higher PA group. Total response rates for cancer were 100%.

IHD was reported as any present condition of ischemic heart disease at enrolment. This included myocardial infarction and angina. The distribution of IHD was similar to that of current smokers

in that mean rank dropped from PA group 1-4, before increasing and becoming larger than group 3 in group 5. The Kruskal-Wallis test was significant at $p< 0.001$. Total response rates for IHD was 98.8%. As this was an ordinal variable and had to be compared using non-parametric tests, it was not possible to ascertain the individual difference between groups.

Table 5.3 Distribution of covariates according to physical activity (PA) groups[1] (reported as means and sd, or proportion and total group numbers. Total n respondents and proportion of total study population is reported for each variable):

PA group:	n	Very low	Low	Moderate	High	Very high	% total:
Age	76367	47.8 (8.8)	47.4 (8.6)	46.8 (8.4)	46.6 (8.2)	46.3 (8.2)	100.0 %
Group n=		3869	16104	31968	19413	5013	
BMI	66339	25.4 (4.9)	24.5 (4.0)	23.5 (3.4)	23 (3.1)	22.7 (3.1)	86.9 %
Group n=		3519	14277	27911	16309	4323	
Education (years)	73153	11.5 (3.4)	12.3 (3.5)	12.3 (3.3)	12.4 (3.4)	11.6 (3.3)	95.8 %
Group n=		3688	15375	30653	18617	4820	
Alcohol Consumpt[2] (grams)	64027	3.3 (7.4)	3.3 (5.3)	3.1 (4.5)	3.1 (4.5)	2.7 (4.6)	83.8 %
Group n=		3431	13874	26847	15704	4171	
Smoking[3] (% current)	75491	39.8	33	30.8	29.1	33.7	98.9 %
Group n=		3805	15911	31638	19187	4950	
Diabetes[4] (% yes)	75803	6.2	3.7	2.4	2.1	2.1	99.3 %
Group n=		3817	15948	31756	19301	4981	
Cancer[5] (% yes)	76367	10.3	9.8	8.7	8.2	8.1	100.0 %
Group n=		3869	16104	31968	19413	5013	
IHD[6] (% yes)	75485	5.2	3.0	1.9	1.7	2.0	98.8 %
Group n=		3791	15859	31647	19241	4947	
Tot. pop.:							76367

[1] PA grouped "very low" – "very high".
[2] Alcohol consumption as measured in grams per day.
[3] Smoking status at enrolment, reported as proportion "current" smoker.
[4] Proportion diabetes at enrolment, "yes".
[5] Proportion any cancer at enrolment, "yes".
[6] Proportion of reported ischemic heart disease (myocardial infarction or angina) (IHD) at enrolment, "yes".

5.2 Logistic regression analysis

Results for age-adjusted and multivariable adjusted analysis are presented in table 5.4. Moderate level of PA was used as reference group to which all other PA groups were compared. Hosmer-Lemeshow test results are reported in table 5.4. These indicate adequate goodness-of-fit for all four models.

5.2.1 Main findings Chronic fatigue syndrome

When adjusted for age, significant ORs were 1.90 (CI 1.65 – 2.19) for PA level very low, 1.34 (CI 1.22 – 1.47) for PA level low, and 1.16 (CI 1.01 – 1.35) for PA level very high. Significance for PA trend was < 0.001 in age adjusted model. When adjusted for multivariate model, remaining significant ORs were 1.61 (CI 1.38 – 1.88) for PA level very low, 1.31 (CI 1.19 – 1.44) for PA level low, and 1.18 (CI 1.01 – 1.38) for PA level very high. P for trend in multivariate model remained significant at < 0.001. The OR indicated a protective association between increasing levels of PA and CFS at 0.899.

5.2.2 Main findings Back pain

When adjusted for age, significant ORs were 1.20 (CI 1.08 – 1.34) for PA level very low, 1.08 (CI 1.02 – 1.15) for PA level low, and 0.90 for PA level high (CI 0.85 – 0.96). Significance for PA trend was significant at < 0.001 in age adjusted model. When adjusted for multivariate model, only the OR of PA level very low remained significant at 1.17 (CI 1.04 – 1.31). P for trend in multivariate model remained at < 0.001, with an OR of 0.945.

5.2.3 Main findings Fibromyalgia

When adjusted for age, only PA level very low was significant with an OR of 1.49 (CI 1.24 – 1.78). Significance for PA trend was < 0.001 in age adjusted model. When adjusted for multivariate model, this changed to OR 1.30 (CI 1.07 – 1.58). P for trend in multivariate model was significant 0.008. The OR indicated a protective association between increasing levels of PA and myalgia at 0.936.

5.2.4 Main findings myalgia

When adjusted for age, only PA level very low was significant with an OR of 1.20 (CI 1.08 – 1.33). Significance for PA trend was < 0.001 in age adjusted model. The results were not significant adjusting for multivariate model, but remained close at OR 1.11 (CI 0.99 – 1.25). Other CIs lay generally close to the boarder of significance in myalgia, as seen in table 5.4. P for trend in multivariate model was not significant.

Table 5.4 Odds ratios (OR) and confidence intervals (CI) in age-adjusted and multivariate adjusted models for physical activity (PA) on chronic fatigue syndrome (CFS), back pain (BP), fibromyalgia (FM) and myalgia:

	Age-adjusted:		**Multivariable adjusted[1]:**		
	OR (CI)	P for trend[2]	OR (CI)	P for trend[2]	Goodness-of-fit[3]
CFS					0.097
PA		< 0.001		< 0.001	
Very low	1.90 (1.65 – 2.19)		1.61 (1.38 – 1.88)		
Low	1.34 (1.22 – 1.47)		1.31 (1.19 – 1.44)		
Moderate	1.00 (ref.)		1.00 (ref.)		
High	0.95 (0.86 – 1.04)		1.00 (0.90 – 1.11)		
Very High	1.16 (1.01 – 1.35)		1.18 (1.01 – 1.38)		
BP					0.919
PA		< 0.001		< 0.001	
Very low	1.20 (1.08 – 1.34)		1.17 (1.04 – 1.31)		
Low	1.08 (1.02 – 1.15)		1.07 (0.99 – 1.14)		
Moderate	1.00 (ref.)		1.00 (ref.)		
High	0.90 (0.85 – 0.96)		0.95 (0.89 – 1.01)		
Very High	0.95 (0.86 - 1.05)		0.93 (0.84 – 1.04)		
FM					0.775
PA		< 0.001		0.008	
Very low	1.49 (1.24 – 1.78)		1.30 (1.07 – 1.58)		
Low	1.12 (1.00 – 1.25)		1.09 (0.96 – 1.23)		
Moderate	1.00 (ref.)		1.00 (ref.)		
High	0.91 (0.82 – 1.02)		0.96 (0.85 – 1.08)		
Very High	1.05 (0.88 – 1.25)		0.99 (0.81 – 1.19)		
Myalgia					0.229
PA		< 0.001		0.230	
Very low	1.20 (1.08 – 1.33)		1.11 (0.99 – 1.25)		
Low	1.06 (1.00 – 1.13)		1.03 (0.97 – 1.10)		
Moderate	1.00 (ref.)		1.00 (ref.)		
High	0.95 (0.90 – 1.00)		0.99 (0.93 – 1.05)		
Very High	1.01 (0.92 – 1.11)		1.05 (0.95 – 1.16)		

[1] Covariates in multivariate model: age, BMI, education, alcohol consumption, smoking.
[2] Linear test for trend.
[3] Goodness-of-fit as assessed with Hosmer-Lemeshow test. A non-significant result at the 5% level indicates model has adequate fit.

6. Discussion

Our study set out to explore whether there was an association between self-reported PA and incidence of CFS, BP, FM, and myalgia among Norwegian women. The following discussion interprets the results from statistical description and analysis of data, with suggested explanations of results. Identified strengths and limitations in the present study were also assessed, as well as some implications for further research.

6.1 Main findings

Our study found that increasing levels of PA were significantly associated with a lowered risk of CFS, BP, and FM when assessed for trend. When comparing lower and higher PA levels to PA level moderate, we found that the lowest level of PA was associated with an increased risk of CFS, BP, and FM. For CFS, three out of four PA groups were significantly associated with increased risk of CFS, namely PA levels "very low", "low" and "very high". For myalgia, no PA levels were associated with an increased risk of the outcomes compared to moderate.

6.1.1 Descriptive statistics

Distribution of PA levels at enrolment was seemingly normally distributed. The largest group was those reporting to be moderately active, and there were more women in the two highest PA level groups than there were in the two lowest ones. According to Statistics Norway we would have expected at least approximately 6% of women to report "very low" levels of PA, given that this could be described as being physically inactive (26). Surprisingly, 5.1% reported being inactive, which marks this sample, consisting of women reporting baseline information from

1991 to 2003, as more active than the national average in 2012. In 1998, 39% of Norwegian women aged 25-66 reported exercising less than once a week (111), therefore we would have expected the normal distribution to be skewered more towards inactivity in our selection, but surprisingly found higher levels of PA to be more common among these women. The largest reported change in PA level in Norway the last two decades was from 2002 – 2005 when the proportion inactive women aged 45 – 66 fell from approximately 33% to around 24% (111). This implied no large changes in PA levels among women up until 2002.

There was a significant difference in age between groups of PA, with a trend of decreasing age with increasing activity. Participants reporting "very low" PA were on average 1.5 years older than participants reporting "very high" PA. It follows that total PA levels often decrease when age increases because older people statistically move less (25).

There was a similar pattern for the distribution of BMI in the selection, with "very low" PA having a BMI on average 2.7 greater than those women reporting very high PA. This put group "very low" at an average BMI of 25.4, which was above the WHO threshold for defining overweight (108). Decreasing PA during daily living increases the risk of gaining weight in an ever more sedentary society (76), and according to Shiri et al. a higher BMI will in turn decrease leisure time spent on PA (10), and thus further increase the health risks for this group.

Alcohol consumption followed a diminishing linear trend, with consumption decreasing with higher levels of PA. Women reporting very high PA levels consumed the least alcohol and were consistently different from all other groups. Alcohol consumption dropped with increased PA, indicating a possibly healthier lifestyle with those that were the most active. This would be in line

with Kaczynski et al. when they suggested that level of PA could be a measure to identify the health profiles of different people (31).

We would have expected trends similar to these covariates on PA for the other covariates included in the statistical model: education, smoking, and comorbidity. If PA levels indicate health profiles as suggested, then they could also be a measure of socioeconomic status (32). In that case, education, smoking, and comorbidity, which are also socioeconomically distributed, should follow the same patterns as BMI and alcohol in our study. Unexpectedly, they did not.

Mean education level increased from PA group "very low" to group "high", but then dropped to a level below that of "moderate" for PA group "very high". Granted, the difference was only 0.8 years between the two, but the deviation from the linear trend was quite noticeable as well as statistically significant.

Proportion of current smokers decreased significantly with increasing PA levels except for the highest one where it increased to a level similar to those with the lowest PA levels. At the same time, proportion of never smokers followed a completely reverse trend, where those reporting very high PA levels once more came out similar to those with low PA levels. Since smoking has also been reported to be associated with lower socioeconomic status (31), this finding further indicated that PA in our study was not a linear proxy for socioeconomic status among participants. Regarding the nature of our exposure variable, being composed of several kinds of physical activity, we would not necessarily have expected PA alone to function as such a proxy.

In addition to some lifestyle factors, health and disease also follow a social gradient to a certain

extent (112), especially IHD and diabetes (90). In our results, comorbidities did not contribute to any great extent in identifying what type of people PA group very high consisted of. Interestingly, incidence of all four outcomes followed a similar pattern to that of smoking. They decreased according to PA levels before consistently rising again from women reporting high levels of PA to those reporting very high levels, placing the incidence in group "high" somewhere between the levels of "very low" and "low", or "low" and "moderate".

Of all PA groups, it was clear that the women who report "very low" PA appeared to be the ones with the most risk factors associated to them, as they scored consistently worse for important predictors of mortality and morbidity, such as BMI, education, smoking, and alcohol consumption. They also reported the highest levels of all comorbidities as well as outcomes. All these factors combined to suggest that this PA group was composed of those who most often are defined as belonging to lower socioeconomic strata, and have health profiles that reflect this. This suggested that PA corresponds to socioeconomic status and therefore to health profiles in the lower groups of PA levels.

In thread with possibly not being a linear proxy, higher PA seemingly stopped denoting higher levels of socioeconomic status in PA group "very high". As mentioned, women in PA group "very high" had an excess of smoking, less education, and more morbidity. It was interesting that PA did not continue to follow the simple, linear trend for covariates that are socioeconomically distributed. As mentioned previously, part of the explanation for this might be found in the measure of PA levels itself. Participants in the NOWAC study were asked to report their total amount of PA in daily living, which was specified to include PA when working at home or in an occupational setting, as well as exercise, and other forms of PA that could include activity when

commuting or during leisure time. As explored in the theory surrounding PA levels, Beenackers et al. found that those who spent the most time doing leisure time PA had the highest socioeconomic status (32). The findings of Bauman further indicated that those in high income countries which did not have physically intensive manual labor spent more time on leisure PA than those who did (27). Beenackers et al. further reported those with the lowest levels of education and socioeconomic status to also be those who were prone to having the most physically intensive work in the occupational setting. It has also been suggested that being physically active throughout the work-day might increase the desire to relax and be physically inactive during leisure time (79). Furthermore, those that have a physically intensive occupation would have to report that they are physically active throughout the work-day for several hours each day, most days of the week. From this it is possible to hypothesize that women who had a physically intensive occupation could be prone to categorize themselves as very physically active. It is possible that women reporting very high PA levels would be classified in a lower group if we had only been looking at leisure time PA, and by proxy, socioeconomic status.

Studies have demonstrated that self-reported PA might be an acceptable way to rate PA level in a female population. Borch et al. reported a correlation between self-reported PA and objectively measured PA (113). This could indicate that the women reporting very high levels of PA actually did have this activity level. Subsequently, this might enhance their physical fitness, thus allowing them to reap the health benefits associated with such PA derived fitness. A possibly high level of physical fitness even among individuals with characteristics of lower socioeconomic strata, such as our "very high" group, could be explained by the increased popularity of leisure time PA in Norway. Levels of leisure time PA have increased in Norway during the last decade (26), and it has been demonstrated that high-income countries have a higher degree of total leisure time PA

(5). On the other hand, we have demonstrated participants in the present study who reported the very highest levels of PA to also display some lifestyle habits and incidences of morbidity that marked them as persons with health profiles possibly belonging to lower socioeconomic strata, suggesting they would not necessarily enjoy a protective effect of their PA level. Given their distribution of covariates and morbidities, we hypothesized that the sub-group type of PA they performed had a higher degree of influence over their health status than their total amount of PA did. This theory was supported by the systematic review of Beenackers et al. (32).

6.1.2 Outcomes

According to the cross tabulation of outcomes, the two outcomes CFS and FM appeared more often in combination with one or more other outcomes than by themselves. BP and myalgia appeared most often by themselves, but also frequently in combination with the other two. CFS and FM are the two outcomes that more closely resemble 'syndromes', and which are similar to one another. The 'symptomatic' conditions, BP and myalgia, appeared by far most frequently, which should be no surprise considering their nature as pain symptoms. CFS and FM rarely figured on their own: approximately1/4th of CFS cases appeared without any of the other three, while approximately 1/5th of FM cases did. They also rarely appeared solely together: 0.1% of the study sample reported having both FM and CFS without having any of the two symptoms. 1.8% of the study sample reported having both FM and CFS in combination with one or both of the other two outcomes. This amounted to 1437 total cases of double-diagnosis of CFS in combination with FM, and was unexpected given the rather clearly defined diagnostic criteria separating the conditions from one another, as described previously.

The fact that most cases of CFS and FM appeared in combination with one or both of the pain-symptoms could be explained by the fact that they could be symptoms of CFS and FM. Participants with CFS or FM could in the preliminary stages of these conditions experience cases of BP and/or myalgia as symptoms of these syndromes, but not identify them as such due to not having received a diagnosis of CFS or FM at that time. Both myalgia and BP lack the structured diagnostic criteria that CFS and FM have, and are diagnoses of exclusion. CFS and FM are diagnoses one receives from a physician, while BP and myalgia are common ailments that most people experience one or more times throughout their lifetime, and for which it is not required to get a doctors affirmation that one is experiencing.

Theory on CFS and FM stated that they are two separate conditions and two discrete categories. However, theory has also demonstrated that they are similar with regards to symptoms and criteria, and that many patients who qualify for one also qualify for the other. It was unexpected that out of some 9000 total cases of CFS and FM, almost 1500 of these appeared at the same time with one another. We would have thought physicians to be more restrictive in the diagnostic process when one of these two conditions is already present. However, for a portion of cases – the prevalent ones - we did not know at what time conditions appeared in our sample; if they were diagnosed simultaneously or with a long interval. It should also be commented that we assume most of CFS and FM cases to have been diagnosed by a physician. Any reported case of these conditions that was not, we would not consider being a reliable incident case. However, we have no information whether participants had actually been diagnosed by a physician. An interesting subject for future research would be to assess diagnostic practices in the health care services today regarding double-diagnosis of CFS and FM, given that the overlap of these two in the current sample was representative for the general population.

The age standardized prevalence rates appeared to be quite similar overall to the prevalence rates of the selection in our study. The prevalence rates of 2.58% for CFS, 13.65% for BP, 5.02% for FM, and 17.87% for myalgia are comparable to the age standardized rates of 2.62%, 14.22%, 5.03% and 18.09% respectively. This implies that the age groups of our study are representative of the mother population, Norwegian women.

6.1.2.1 Chronic fatigue syndrome

Incidence rate and prevalence rate for CFS were in our study calculated to be 411 per 100 000 person years and 2.58%. Due to the gender differences in incidence and prevalence for this condition (16), numbers would most likely be lower for the Norwegian population as a whole. Incidence rates for both genders combined have been suggested to lie between 180-370 per 100 000 person-years in other international settings (35). Other studies have reported female prevalence rates of CFS in two American settings to lie between 0.37% - 0.52% (33, 34). These studies performed telephone surveys of large local cohorts and performed clinical examinations of smaller subgroups of fatigued individuals to confirm or rule out a diagnosis of CFS. One review suggested world-wide prevalence rates at 0.4-1.0% for both genders combined (16) – this would be higher if for women only. The nationally representative prevalence rate of 2.58% found in our study was substantially higher than that of previously mentioned international studies. When interpreting this prevalence rate it is important to keep in mind that it was an aggregate of reported prevalence from several different time periods from both the 1990's and the 2000's. If the understanding and diagnostics of CFS differed to a significant degree across these time periods, that might have affected our calculated prevalence rate. However, as seen in the theoretical basis of CFS, this was unlikely to have had any large effect on our figures. Keeping

aware of the possible limitations of these numbers, they are nevertheless potentially some of the first indications of the level of CFS prevalence in Norwegian women. Norwegian health authorities have assumed national prevalence to follow international levels (36), while our numbers demonstrated national levels to be higher than those of other settings.

As expected, multivariate p for trend displayed a significantly lowered risk of experiencing the outcome when increasing level of PA, starting from very low levels. When adjusted for in the multivariate logistic regression model, PA groups "very low", "low", and "very high" were significant predictors of CFS when compared to group "moderate". Despite changes in ORs, no changes in statistical significance occurred when compared to the age-adjusted model. As expected, "very low" and "low" displayed an adverse effect on the risk of getting CFS when compared to "moderate", with ORs 1.61 and 1.31 respectively. Unexpectedly, "very high" also displayed this kind of adverse effect, with an OR of 1.18. It is also interesting to note that being in PA group "high" made no significant difference from being in PA group "moderate".

Previous knowledge was lacking with regards to the association of levels of PA on the risk of developing CFS – a best estimate of what relationship PA might have was that moderate levels of PA could be hypothesized to have a protective association when compared to lower levels. Nijs et al. suggested that continued activity despite an increasing sense of sickness and loss of well-being might increase the likelihood of developing the condition (42). Therefore, we might also expect that those at risk of developing the disease would be more likely to do so the higher their activity level is. At a certain point, more activity might cause certain people to become sicker, faster. Therefore, the presence of a threshold level in PA's protective effect might be plausible given the relatively limited knowledge available.

Based on theory of PA in general, and hypothesis on PA's association with CFS in specific, the results of the present study seemed to fit the pattern. Lower levels of PA progressively increased the risk of developing the condition, with sedentary levels giving the highest risk. PA levels higher than moderate seemed to have a diminishing protective association, with the uppermost levels of PA exacerbating the risk of developing CFS. This indicated that the theorized threshold level might exist, and be located somewhere between PA levels "high" and "very high" in our selection. While the women reporting high levels of PA did not have a risk that was significantly different from that of "moderate", "very high" did. This also indicated that comparing groups of PA and their association to the risk of developing CFS was more accurate than looking at p for trend of PA.

However, it is by no means certain that this increased risk was attributable to a possible threshold level in PA alone. PA group "very high" had some other characteristics that have been previously theorized to make this group have a generally higher risk of contracting disease. As demonstrated, PA group "very high" had a distribution of covariate factors that in some cases made this group's characteristics more similar to the lowest PA groups than to PA group "high". For women reporting very high PA levels that had a distribution of confounders placing them in higher socioeconomic strata, theory has indicated that most PA time is spent on leisure time activity (32). As they reported the very highest level of PA, their threshold for refraining from activity could be thought to be quite high as well – making them more likely to insist on maintaining a high level of activity despite a sense of sickness and loss of well-being. This might have explained their increased risk of developing CFS, given that they have one. On the other hand, descriptive statistics displayed how many in the PA group "very high" possibly fit into lower socioeconomic strata, with all the added hardships this entails. Physically intensive

occupations often have a negative impact upon health (30), and stress and dramatic life changes have been shown to result in an increased risk of developing CFS (35).

Based on our results, we suggest the hypothesis that lower levels of PA as compared to moderate levels are a risk factor for developing CFS as for many other diseases and disorders. We also suggest the presence of a possible threshold level in the extreme high PA levels, where PA stops being a protective factor and assumes the role of a risk factor for developing CFS. It is unclear whether this threshold level was attributable to amount of PA in itself, or the type of PA that different socioeconomic groups most frequently performed. This last suggestion is based on limited available knowledge and the findings of our study, and would be suitable for further exploration by other studies.

6.1.2.2 Back pain

Previously discussed theory indicated that incidence and prevalence of BP would be higher in women than men (53). Incidence rate and prevalence rate for BP in our study were found to be 1268 per 100 000 person-years and 13.65%, respectively. Our incidence rate was low compared to incidence rates of other studies. Being a conservative estimate, this prevalence was still within the previously reported lifetime prevalence rates 11-84% (1, 3) reported in a systematic review of population prevalence of LBP. One reason why a lower prevalence was reported here than in some other studies, might be the fact that some of the highest age groups were not included. Prevalence of BP has been demonstrated to remain constant across all age groups (53). Most likely, our low numbers were attributable to the fact that mean age of participants reporting BP prevalence in our study was 48.3 (± 8.6) years, and included age groups were 34-70. This means

that those who reported prevalent BP had on average only lived slightly more than half of their expected lifetime in which to experience BP. If the reported constancy of prevalence across age groups is correct, this means that some of our participants were yet to experience BP at a later point in life. Our prevalence might be lower than some other reported prevalence rates due to our study looking solely at BP of unknown origin. In addition, it is possible that the women of our study had a high threshold for reporting an experience as BP due to the non-explanative phrasing of the BP item in the questionnaire. Senie however reported that women in general reported higher consequences of BP (53), which might indicate that they were more liable to report cases of BP. Overall, we might still have expected a higher reported prevalence of BP than what was the case.

Results from multivariate logistic regression analysis showed a significant P for trend, indicating a lower risk of experiencing BP with increased PA level. Categorical comparison displayed a significantly increased risk of BP for PA groups "very low" and "low", as well as a reduced risk for PA group "high", when adjusting for age. When including additional confounders however, only PA group "very low" remained significant for increased risk of BP. This result seemed to be mostly in concordance with what theory suggested, that moderate levels of PA could be protective against BP when compared to lower levels (50). A ceiling effect to this protective effect has been suggested, so that higher levels of PA do not necessarily lower the risk of BP any further (50, 55). This theory predicted that we might have expected low PA levels also to be a risk factor of BP when compared to moderate, but this was not found in our study. Thiese et al. also reported very high levels of PA to be a risk factor for developing BP of equal importance to very low levels (50). The fact that PA group "very high" was not a statistically significant risk factor in our study, and that its OR and CI were quite different from those of "very low", was

unexpected. This is especially true when considering how similar group "very low" and "very high" were with regards to the descriptive characteristics of these two groups. With so many similar risk factors, we would have expected results for these two PA groups from the present analysis to resemble one another more closely. Yet it remained that the only mentionable factor separating these two groups was their level of PA. Thus, theory outlined two levels of risk; that of low levels of PA and that of moderate levels, and suggested the risk of very high levels of PA to resemble that of low. Yet in our study we found that very high level of PA did not have significantly different risk of BP than that of moderate. This might be a topic of interest for future studies. Additionally, the difference between our study and previously discussed theory might serve to point out the difference between total levels of PA and PA as leisure time activity/exercise.

The fact that very low level of PA was a risk factor for experiencing BP could be explained by the adverse effect that inactivity has on the musculoskeletal system. Lee et al. reported on the correlation between PA and cardiorespiratory and muscular fitness, as well as a positive effect on the composition of body tissues (7). Sedentary individuals have been shown to have an unhealthier body mass and composition (7), and Shiri et al. documented the association between obesity and increased risk of BP, an association increasingly present in women (10). As well as being significantly associated with an increased risk of BP, the women in our study reporting very low levels of PA also had the highest mean BMI in the selection. Their stated activity level indicated that their heightened BMI was not attributable to excessive muscle tissue, but probably to that of unhealthy body composition. These women also had the shortest length of education, indicating that among them would be found a higher number of individuals working in more physically intensive occupational settings. This form of PA might adversely affect health and

well-being (30, 32). Further explanation for the effect of inactivity on risk of BP could be found in the biopsychosocial understanding of this condition. As discussed in relation to CFS, those who reported a very low level of PA had certain characteristics identifying them as belonging to certain socioeconomic strata, to which is connected some social determinants of health in form of habit, culture and economy (112, 114). These social determinants can be understood as causes of lowered PA. For instance, those who reported PA levels "very low" were also those who smoked the most (31), which was not surprising given their low levels of education; a relationship that has previously been well demonstrated (115, 116). Smoking is a risk factor for developing BP by itself (15, 84), adding to the burden of disease in this group. But more than being only a determinant of BP in itself, smoking is also associated with lowered levels of PA (31, 88), given the effect of smoking on the cardiorespiratory system which is crucial for the ability to perform physically intensive activity. As confounders have been controlled for in the statistical modeling, it might appear as if the association between PA and risk of BP remained important, but that the level of PA itself could be a result of underlying causes.

There were some unexpected results with regards to the association of very high PA levels to the risk of BP. These results should be interpreted with the understanding that what was meant by BP in the NOWAC questionnaire, and subsequently understood by the participating women to be so, did not necessarily reflect what is meant by such terms in other studies. As previously discussed, the NOWAC study does not contain any explicit definition of what is meant with BP beyond being of unknown origin. Therefore it is possible that prevalence and incidence were not ascertained in an optimal manner. BP of unknown origin remains a subjective experience and a condition defined by exclusion of other, known causes of BP. What the women of our study chose to define and report as BP would be subject to individual interpretation. We suggest that

further population based work should take care to standardize a definition of ‘back pain of unknown origin’.

6.1.2.3 Fibromyalgia

Incidence rate and total prevalence were also calculated for FM. We calculated them to be 287 per 100 000 person-years and 5.02%, respectively. As before, numbers were based on women only, and will therefore be higher than those of the Norwegian population as a whole due to the previously discussed higher risk for FM in women. These rates remain conservative estimates. Of the international studies reporting FM prevalence, many reported that of the US national setting. Several of these reported identical rates (57, 59, 117), and they all referred to the same original source; that of Wolfe et al. from 1995. They conducted an interview of 3006 subjects in Wichita, Kansas. 391 of these underwent physical examination in order to diagnose FM on basis of ACR criteria (64). This was the study reporting a prevalence rate of 3.4% in women and 0.5% in men. Our prevalence rate of 5.02% for women is representative of the Norwegian female population. There are few present comparative epidemiologic numbers of female rates for FM in the Norwegian population, but one source reported a female prevalence rate of 5% (2). Subjects with prevalent FM in our study had an average age of 49.1 (±7.9) years and were between 34-70 years of age. Our numbers add to the limited epidemiological knowledge of FM in Norway today, and imply that as with CFS, FM numbers may be higher in the population than what has previously been reported.

Multivariate p for trend again displayed a significantly lowered risk of experiencing the outcome with increasing level of PA, starting from very low levels. As with CFS, the models for FM did

not differ in terms of significance of PA levels between age adjusted and multivariate adjusted models. When performing categorical comparison, the only statistically significant association between PA and FM was found for level "very low", with an OR of 1.30. In both models, the CI for group "low" was close to being significant, and its overlap of 1 was skewered towards the right so that we would have expected "low" level of PA to also be a risk factor for developing FM. As for all other outcomes, moderate PA levels were the reference levels, indicating that being less than moderately active was a risk factor associated with developing FM. Higher levels of PA did not display statistically significant associations with FM. However, while the CI of "high" was somewhat skewered towards the left, indicating a potentially protective association, that of "very high" was more ambiguous. The fact that neither "very high" nor "low" displayed statistical significance was surprising, given the close relationship between FM and CFS regarding the nature of the conditions and the people who develop them (19, 61). With a suggested overlap of up to 80% of patients who fit the diagnostic criteria of both FM and CFS (59), and given the previously discussed characteristics of PA group "very high", we would have expected the association between PA and these two outcomes to closely resemble one another.

Among other theories, the review by Mease from 2005 suggested precipitating causes of FM to be stress, medical illness, and pain conditions (59). We know that PA by itself alleviates and could prevent such processes in the body when composed of the protective kind of activity. At the same time, inactivity is associated with a higher prevalence of depression, anxiety, MSDs, and other painful conditions (7, 118-120). It is possible to theorize that this pathophysiological sum of inactivity could be a predictor for developing FM based on the scarce evidence base for causes of FM, combined with the well-known generally adverse effects of inactivity.

In addition to these possible physiological and psychological causes, Lærum et al. have suggested that the development of FM must be interpreted in a biopsychosocial model with a combination of physiological, psychological, and cultural aspects of daily living as possible explanations (2). As we have reported above, inactive respondents in our study have characteristics corresponding to that of low socioeconomic status and are through this at higher risk of multiple causes of morbidity and mortality.

We did not expect to see non-significant findings for PA groups "low" and "very high". For the socioeconomic argument to be strengthened, based on what we have previously discussed on PA group "very high", this group should have displayed a risk similar to that of the risk of CFS for this group. Possibly, CFS and FM differ with respect to the protective effect of PA. Adding to this is the fact that the central aspect of CFS is fatigue, which is the theoretical explanation of why very high activity level might increase the risk of developing CFS (42). In FM, widespread pain is more central than fatigue, which might not be as easily exacerbated by more activity as is fatigue. Similarity of risk factors for these two conditions would be an interesting topic for further research. These results suggested that maintaining CFS and FM as two separate conditions might be appropriate.

For both "low" and "very high", we must also keep in mind that "moderate" PA was the group to which they were compared. Thus, our results showed that there was little difference in associated risk of developing FM between being in PA group "low", "moderate", "high", and "very high". This could imply a possible threshold level for FM indicating that any higher activity level is better than very low activity when it comes to reducing the risk of developing FM. However, this is not a phenomenon that has been previously suggested by theory behind FM - despite being

suggested in general theory about the effect of PA. Thus, caution should be used when inferring to the clinical importance of levels of PA for risk of developing FM.

6.1.2.4 Myalgia

Our study calculated an incidence rate and prevalence rate of 1509 per 100 000 person-years and 17.87%, respectively. Muscle pain/myalgia is another condition that could occur several times in the same individual during life. In the NOWAC study, it was not possible for one individual to report any outcome more than once. Therefore, incidence rate would most likely have been higher had the NOWAC study allowed for multiple reporting of conditions which can be recurrent. Respondents reporting prevalent cases were between 34-70 years of age and had a mean age of 48.3 (± 8.3) years. Estimates remain conservative as discussed, and only apply to women. Myalgia was the phenomenon most frequently reported by the women in our study. Due to some methodological issues when describing muscle pain/myalgia as a reporting item, and standardizing this as a measurement, comparative numbers of incidence and prevalence are difficult to find. Participants in our study were asked to report whether they had experienced 'muscle pain (myalgia)' at any point during a given time interval. How the respondent chose to interpret this question would determine what was reported as muscle pain/myalgia, rather than the clinical or theoretical understanding of what muscle pain/myalgia is. In fact, muscle pain differs from the other conditions relevant to our study in that it, to an even larger extent than BP, is a symptom and cannot be described as a syndrome or disease in itself. Theory states that causes of muscle pain/myalgia are many and diverse. In the cross-tabulation of outcomes, myalgia was constantly present in all the largest groups of combined outcomes, indicating that it might be frequently reported in people who have experienced other MSDs in which musculoskeletal pain

is a central symptom.

For myalgia, multivariate analysis of PA levels displayed a protective but not statistically significant trend for increasing PA levels. Regarding PA groups, group "very low" was statistically significantly associated with an increased risk of reporting myalgia, when adjusted for age. This significance disappeared once the multivariable logistic regression model was included. Evaluating ORs, only PA group "high" had a protective association beyond that of comparator "moderate", whilst all other levels indicated increased risk of experiencing the outcome. No groups reached statistical significance. We do not regard these results as unexpected, given the inherent ambiguity of the outcome item in question.

Most people will experience what can be termed 'muscle pain' at one or several times during their lives (68). It was therefore unexpected that reported numbers of incidence and prevalence of muscle pain were not higher than what was reported in our study, although in the case of prevalence, there still remained time at risk for most respondents and so the rate might still have increased in time. Including both incident and prevalent cases, more than 20 000 women reported having experienced a phenomenon identifiable as muscle pain or myalgia. While this was unexpectedly few, it remained the largest reported outcome group, indicating that it was the most commonly occurring outcome. This was to be expected, given its position as a symptomatic condition. In our study, it was evident that level of PA was not strongly associated with risk of experiencing this outcome. All PA groups experience it to a similar degree. This could still mean that *some* types of muscle pains are more frequent in certain PA level groups than others, but the manner in which myalgia was defined leaves the item too broad and unspecific to differentiate

between types of muscle pain. The heterogeneity of what has been reported could be seen as too high to be compounded into one outcome measurement which could accurately measure one discrete phenomenon. Sources of muscle pain could include delayed onset muscle soreness after strenuous exercise, as a symptom of pathophysiological processes, as a result of injury, due to MSDs of unknown origin, and as early signs of the other three outcomes of our study. In the same way the term 'muscle pain' is too general, so also the term 'myalgia' could be too narrow. It is not certain that the lay-woman was capable of identifying what condition was meant by this term, and might therefore underreport cases of myalgia owing to the fact that she had never received such a diagnosis by a physician. The fact that incidence and prevalence rates were unexpectedly low might indicate that the presence of the term 'myalgia' in the questionnaire item was confusing for some respondents and deterred them from reporting this or identifying experienced conditions with this term. This is a hypothesis which could be explored in a validation-type study.

Results regarding myalgia from our study need to be interpreted cautiously, as what was meant by respondents when reporting having experienced muscle pain/myalgia might be any number of pain conditions, resulting from an equal number of different causes. We can by these results register how large a proportion of the included women report experiencing a phenomenon they identify as muscle pain/myalgia. Future projects should strive to define and more clearly describe what condition is the desired object of questions regarding muscle pain, to ease respondents' understanding and allow accurate reporting. This ambiguity regarding the term myalgia is reflected in the current evidence base surrounding the phenomenon as described in theory.

6.2 Main strengths and limitations of our study

There were a number of possible strengths and limitations associated with our study. These mainly related to the NOWAC study from which data material was gathered, and the type of methodology applied when analyzing this.

The NOWAC study is based on self-reported data, which is time-efficient and incurs a lower cost than other forms of measurement (110). Because the results of our study depended on what information respondents chose to disclose, so too did the internal validity. External validity depended on whether the selection was representative for that of the source population, namely Norwegian middle-aged women.

6.2.1. Strengths of our study

One of the strengths of our study was that data from participants had been internally and externally validated. The sample was drawn randomly from the source population. Self-reported data involve an amount of uncertainty regarding the reliability of information given by respondents. This can be attributed to a self-selection bias that can occur in studies based on voluntary participation, giving the "healthy volunteer effect" (105). According to previously performed studies, the NOWAC study population did not differ significantly from the corresponding age groups of the source population from which it was drawn, except for a slightly higher level of mean education length (105). Due to the representative nature of the NOWAC study, results from our study will be possible to generalize to the female population of Norway in corresponding age groups, and can therefore be used as basis of future hypotheses and development of evidence bases. Epidemiologic data described in our study will be valid for the

main population, meaning that our study contributes important information on both prevalence and incidence rates in the Norwegian female population that have previously been scarce.

Respondent rates for enrolment and follow-ups in the NOWAC study were about 55% and 80% respectively. There was a dropout between baseline measurements and first and second follow-up due to participants electing not to return a filled-in questionnaire. Examinations were done to test whether the differences in response rates affected the distribution of exposure variables in the samples. No statistically significant differences were found (105). This indicates that dropout rates should not be a problem due to the established validity of remaining participants.

For inclusion into the present study, only participants reporting PA levels at baseline fit the inclusion criteria. 74.5% of the original cohort baseline participants met inclusion criteria for participation in our study. Of those returning a filled-in questionnaire during the first follow-up, 54% were included in the second follow-up. Descriptive statistics of covariates were gathered from participants in the second follow-up and manually compared to those of the baseline participants. Statistical comparison was beyond the scope of our study, but manual inspection indicated marginal differences between baseline and second follow-up participants. Perhaps most importantly, participants in the second follow-up were slightly younger on average, causing such variables as BMI and morbidity to also be slightly differently distributed than in the baseline population. Second follow-up participants were never more than 4.6 years younger on average than baseline (in PA group "very low"), which was to be expected given that a mean follow up time of 13.1 years between baseline and second follow-up would most likely cause a proportion of the oldest participants at baseline enrolment to drop out by the time of the second follow-up, due to death or other reasons. However, Lund et al. reported older women in some settings to

have higher response rates (105). This might indicate a potential bias in the data, but we maintain that attrition rates are normal and expected for this type of studies, and that differences appeared to be small in our study.

To ascertain the validity of the exposure variable used in our study, the correlation between self-reported PA and objectively measured PA have previously been validated (113). They concluded that there were "modest correlations compared with criterion measures, making this self-report instrument suitable to differentiate general PA levels in an adult female population in Norway" (113). This indicated that the manner of measuring the exposure variable chosen for our study is a reliable method of measuring levels of PA in populations and therefore was suitable to rank the participants' PA level. The NOWAC study was not designed to look at PA as a primary exposure. Nevertheless, it has the advantage of asking for a summary measure of total PA based on the same kind of sub-categories of PA that have been suggested in theory (24, 28), yielding an exposure measurement that accounts for all these diverse forms of PA. Possibly, future studies can attempt to differentiate between the sub-categories of PA to explore the individual effect estimates of these with regards to risks. In particular, the difference between leisure versus occupational PA might be interesting to investigate, given their potentially inverse nature in relation to health as suggested by theory.

Validation studies have been performed for many of the covariates of interest to our study (103):

With self-reported BMI, one study found underestimation of weight and overestimation of height to occur in women (121). Younger women underestimated their weight the most. Those who were underweight more often reported a higher weight, and those who were obese more often

reported a lower weight. However, regarding the present study, work has been done to validate self-reported BMI as a measurement of women's height and weight. Borch referred to personal communication with Dr. Eiliv Lund and Mrs. Nicolle Mode, University of Tromsø, Norway, regarding so far unpublished results (122). They suggested that BMI appears to be a valid measure in the NOWAC study when compared to height and weight measured by health professional staff.

A study by Rylander et al. concluded self-reported diabetes in the NOWAC study to be a valid measurement of presence of diabetes. They also concluded that missing answers could be reliably interpreted as not having the disease (123).

Through personal communication, Dr. Lund reported that among 50 self-reported MI, 35 (70%) were verified through medical case histories as definitely having had a MI. Possible MI was identified in 2 cases (4%), 3 (6%) were definite or possible MI cases (not specifiable) and 6 (12%) were angina pectoris cases. Only 5 cases were identified as definitely not having had MI (10%) (Unpublished). Assuming that the participants were not systematically different from the non-participants, self-reported MI may overall be considered more or less valid among Norwegian women of the NOWAC study (Professor Eiliv Lund, ISM, UiT; personal communication).

Social desirability bias has been suggested to cause underreporting of smoking in self-reports, thus creating a possible bias towards the null (124). Regardless, as smoking is not measured by amount, but rather by absolute status (never – former – current), underreporting of former/current was not likely to occur to any large extent.

Mean follow up time between baseline measurements and the two rounds of follow-up was sufficiently long to allow for the development of outcomes in participants and therefore for the detection of incident cases. The fact that exposure was measured at baseline also gave a certain temporal indication between exposure and outcomes, and could serve to form a causal hypothesis on the relationship between exposure and outcome variables.

One of the strengths in our study was its large and representative number of participants. Robust numbers of respondents significantly lowered the chance of random errors affecting the effect estimates from analysis. This also implied that the epidemiologic data on incidence and prevalence discovered in our study were equally robust, and would resemble the corresponding distributions in the source population. Accounting for the different time periods when calculating incidence rate also allowed for a more precise calculation. The information gathered through the NOWAC study also had the benefit of allowing us to control for important lifestyle factors as possible confounders. Sensitivity analysis of comorbidity covariates allowed us to apply logistic regression for dichotomous outcomes with the smallest possible model, in accordance with the principle of parsimony (125). Use of exposure variable and confounders in our study was done in concordance with what previous studies on the same study population have demonstrated (122), and appeared to be appropriate for these types of variables as discussed in section 4.

6.2.2 Limitations of our study

We identified some possible limitations associated with our study.

As discussed, there were missing data for some covariates included in our study. Several kinds of

bias may be associated with non-item response for lifestyle data. Missing cases in analysis are reported in table 4.1. No action was taken to impute for missing data in the covariates. The highest amount of proportion missing data was 22.6%. Descriptive statistics in our study identified alcohol to be the variable most prone to non-item response, causing these participants to be missing from analysis when alcohol was included in the logistic model. This was understandable given that some series of the NOWAC study did not include alcohol as a reporting item. There was a possibility that there were some systematic similarities between these missing participants that we were unaware of and which could have caused a bias in our results. These possibilities of bias when reporting lifestyle habits may have served to skewer the distribution of confounding factors and underestimate their effect on the association between PA and the outcomes of interest. Previously discussed validation studies indicate that much of the data material might be free of substantial amounts of bias.

Studies have found that alcohol is often underreported in studies with self-administered responses. The "social desirability bias" has been shown to cause respondents to not reply accurately on items regarding alcohol consumption. Respondents tend to underreport and/or underestimate their own levels of consumption, frequency of drinking, and daily reported consumption, as well as the consequences of drinking (126). This means it should be expected that actual alcohol consumption is higher than what is apparent from self-reporting.

One possible limitation of the exposure measurement was the wide time-span that the study gathered baseline information from. The first baseline was gathered in 1991, while the most recent one was done in 2003. Those of our selection that participated in baseline reporting at some point after the year 2000 could have had a rather different lifestyle with regards to PA and

leisure time PA, than those who did so in the early 90's. A possible implication of this is that one should be cautious with assuming homogeneity in a baseline group spanning two decades with regards to the different sub-categories within PA. What became contained within the exposure measurement of total PA could be quite different depending on whether this was measured in the 1990's or 2000's. Results from analysis will have to be interpreted with this in mind. Sub-group analysis on PA between the decades was beyond the scope of our study, but a study on PA and risk of postmenopausal breast cancer in the NOWAC study by Borch et al. found no large differences in distribution of covariates over PA level (122).

Another possible limitation with regards to exposure and confounders was the fact that these were all gathered from baseline. Max follow-up time was 15 years, giving participants at most these many years to change their lifestyle habits and therefore confounding the association of PA to outcomes by an unknown magnitude due to having a true exposure that was of a different magnitude than what was reported at baseline.

Theory suggests some difficulties with regards to the four different outcomes of interest. Firstly, the NOWAC study is not designed to measure these four conditions as outcomes, which was evident in the ambiguity regarding these reporting items as discussed above. Secondly, there was some development of diagnostic routines regarding both CFS and FM during the 1990s. This could imply that some unknown proportion of the reported incidence found in our study was actually attributable to recent diagnosis of pre-existing conditions being identified during the same period that the first baseline information was gathered for our study. This could underestimate prevalence and overestimate incidence of these conditions among Norwegian women. However, our study set out to investigate the association between self-reported PA and

self-reported MSDs. For future studies, it would be interesting to validate self-reported MSDs with general practitioners' confirmations or patient journal information.

We expect that there might be some residual confounding that has not been adjusted for in our analysis, possibly due to the distance in time between baseline and follow-ups, or due to other confounding variables having not been included in analysis.

6.3 Implications for further research

Our study implies that there are data available for calculating prevalence and incidence of common causes of disability and sick leave among Norwegian women. Future studies should attempt to verify prevalence and incidence rates of the outcomes of our study.

PA appeared to be differently associated with each of the four outcomes of our study. Future studies should take this into consideration and keep them separate as outcome measures. Validation studies can attempt to establish the validity of self-reported outcomes by comparing self-reported information with patient journals or possibly by establishing the conditions through physical examination.

It has been reported that "the contradictory inequalities for total PA may partially be explained by the contrasting socioeconomic patterns found for leisure time PA and occupational PA" (32). It would be interesting for future studies to investigate each of these two PA categories' individual associations with risk of developing MSDs.

Finally, the NOWAC study by the nature of its design only examines health effects of exposures on outcomes for women. Regarding knowledge of the great disparities between genders for the outcomes investigated in our study, it will be interesting to compare Norwegian genders to each other.

6.3 Conclusion

In a nationally representative cohort of Norwegian women aged 34-70, incidence densities per 100 000 person-years were calculated to be as follows: CFS 411, BP 1268, FM 287, and myalgia 1509. Prevalence rates were found to be 2.58% for CFS, 13.65% for BP, 5.02% for FM, and 17.87% for myalgia. These were comparable to age-standardized rates for the corresponding Norwegian female population. In logistic regression analysis, when compared to moderate PA levels, we found that very low PA levels were associated with an increased risk of CFS, BP, and FM. Low PA levels were associated with an increased risk of CFS. Very high PA levels were associated with an increased risk of CFS.

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Appendix A:

KVINNER OG KREFT

Høst 2003

KONFIDENSIELT

Hvis du samtykker i å være med, sett kryss for JA i ruten ved siden av. Dersom du ikke ønsker å delta kan du unngå purring ved å sette kryss for NEI og returnere skjemaet i vedlagte svarkonvolutt.
Vi ber deg fylle ut spørreskjemaet så nøye som mulig.

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

Med vennlig hilsen
Eiliv Lund
Professor dr. med

Jeg samtykker i å delta i spørreskjemaundersøkelsen JA ☐ NEI ☐

Forhold i oppveksten

I hvilken kommune har du bodd lengre enn ett år?

Kommune: **Alder**

1. Fødested: ..... Fra ..... år til ..... år
2. ..... Fra ..... år til ..... år
3. ..... Fra ..... år til ..... år
4. ..... Fra ..... år til ..... år
5. ..... Fra ..... år til ..... år
6. ..... Fra ..... år til ..... år
7. ..... Fra ..... år til ..... år

Kroppstype i 1. klasse. (Sett ett kryss)

☐veldig tynn ☐tynn ☐normal ☐tykk ☐veldig tykk

Menstruasjonsforhold

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

Hvor mange år tok det før menstruasjonen ble regelmessig?

☐ Ett år eller mindre ☐ Mer enn ett år
☐ Aldri ☐ Husker ikke

Har du regelmessig menstruasjon fremdeles?

☐ Ja ☐ Har uregelmessig menstruasjon
☐ Vet ikke (menstruasjon uteblitt pga. sykdom o.l.)
☐ Bruk av hormonpreparat med østrogen
☐ Nei

Hvis Nei;

har den stoppet av seg selv? ..... ☐
operert vekk eggstokkene? ..... ☐
operert vekk livmoren? ..... ☐
annet? ..... ☐

Alder da menstruasjonen opphørte? ..... år

Graviditeter, fødsler og amming

Har du noen gang vært gravid? Ja ☐ Nei ☐

Hvis Ja; fyll ut for hvert barn du har født opplysninger om fødselsår og antall måneder du ammet (fylles også ut for dødfødte eller for barn som er døde senere i livet). Dersom du ikke har født barn, fortsetter du ved neste spørsmål.

Barn	Fødselsår	Antall måneder med amming	Barn	Fødselsår	Antall måneder med amming
1			5		
2			6		
3			7		
4			8		

Bruk av hormonpreparater med østrogen i overgangsalderen

Har du noen gang brukt østrogen-tabletter/plaster? ..... Ja ☐ Nei ☐

Hvis Ja; hvor mange år har du brukt østrogentabletter/plaster i alt? ..... år

Hvor gammel var du første gang du brukte østrogentabletter/plaster? ..... år

Bruker du tabletter/plaster nå? ..... Ja ☐ Nei ☐

Hvor pålitelig anser du kildene nedenfor å være når det gjelder informasjon om østrogenbehandling?

	Lite pålitelig	Pålitelig	Meget pålitelig	Vet ikke/ usikker
Allmenpraktiserende lege	☐	☐	☐	☐
Gynekolog	☐	☐	☐	☐
Apotek	☐	☐	☐	☐
Radio/TV	☐	☐	☐	☐
Ukeblader/aviser	☐	☐	☐	☐
Slekt/venninner	☐	☐	☐	☐

Bruker du soyapreparater mot plager i overgangsalderen? ..... Ja ☐ Nei ☐

UTFYLLENDE SPØRSMÅL TIL ALLE SOM HAR BRUKT ELLER BRUKER PREPARATER MED ØSTROGEN I FORM AV TABLETTER ELLER PLASTER.

Hvis du har svart «nei» på spørsmålene om hormonbruk i overgangsalderen, kan du gå videre til spørsmålene under «**P-piller**». Har du svart «ja», ber vi deg om å utdype dette nærmere ved å svare på spørsmålene nedenfor. For hver periode med sammenhengende bruk av samme hormonpreparat håper vi du kan si oss hvor gammel du var da du startet, hvor lenge du brukte det samme hormonpreparatet og navnet på dette. Dersom du har tatt opphold eller skiftet merke, skal du besvare spørsmålene for en ny periode. Dersom du ikke husker navnet på hormonpreparatet sett «usikker». For å hjelpe deg til å huske navnet på hormonpreparatene ber vi deg bruke den vedlagte brosjyre som viser bilder av hormonpreparater som har vært solgt i Norge. Vennligst oppgi også nummer på hormontabletten/plasteret som står i brosjyren.

Periode	Alder ved start	Brukt samme hormontablett/plaster/ Sammenhengende år	måned	Nr.	Hormontablett/ plaster/ (se brosjyre) Navn
1.					
2.					
3.					
4.					
5.					

P-pillebruk

Har du brukt p-piller eller minipiller? Ja ☐ Nei ☐

Bruker du p-piller nå? Ja ☐ Nei ☐

For p-pillebruk ønsker vi å få vite navnet på p-pillen, årstallet du startet å bruke den og hvor lenge du brukte dette merket sammenhengende. Dersom du har hatt opphold eller skiftet merke start på ny linje. For å hjelpe deg å huske navnet ber vi deg bruke den vedlagte brosjyren. Vennligst oppgi nummeret på p-pillen.

Periode	Alder ved start	Brukt samme hormontablett/plaster/ Sammenhengende år	måned	Nr.	Hormontablett/ plaster/ (se brosjyre) Navn
1.					
2.					
3.					
4.					
5.					
6.					

Hormonspiral

Har du noen gang brukt hormonspiral (Levonova)? Ja ☐ Nei ☐

Hvis Ja; hvor mange hele år har du brukt hormonspiral i alt? ☐☐

Hvor gammel var du første gang du fikk innsatt hormonspiral? ☐☐

Bruker du hormonspiral nå? Ja ☐ Nei ☐

Østrogenpreparat til lokal bruk i skjeden

Har du noen gang brukt østrogen-krem/stikkpille? Ja ☐ Nei ☐

Hvis Ja; bruker du krem/stikkpille nå? Ja ☐ Nei ☐

Andre legemidler

Bruker du noen av disse legemidlene daglig nå?

Fontex, Fluoxetin Ja ☐ Nei ☐

Cipramil, Citalopram Ja ☐ Nei ☐

Seroxat, Paroxetin Ja ☐ Nei ☐

Zoloft Ja ☐ Nei ☐

Fevarin Ja ☐ Nei ☐

Cipralex Ja ☐ Nei ☐

Hvis Ja; hvor lenge har du brukt dette legemidlet sammenhengede? Måneder ☐☐ År ☐☐

Har du benyttet noen av disse legemidlene tidligere? Ja ☐ Nei ☐

Hvis Ja; hvor lenge har du benyttet disse legemidlene i alt? År ☐☐

Sykdom

Har du eller har du hatt noen av følgende sykdommer?

	Ja	Nei	Hvis ja: Alder ved start
Kreft	☐	☐	☐☐
Høyt blodtrykk	☐	☐	☐☐
Hjertesvikt/hjertekrampe	☐	☐	☐☐
Hjerteinfarkt	☐	☐	☐☐
Slag	☐	☐	☐☐
Sukkersyke (diabetes)	☐	☐	☐☐
Depresjon (oppsøkt lege)	☐	☐	☐☐

Selvopplevd helse

Oppfatter du din egen helse som; (Sett ett kryss)

Meget god ☐ God ☐ Dårlig ☐ Meget dårlig ☐

Røykevaner

Har du i løpet av livet røykt mer enn 100 sigaretter til sammen? Ja ☐ Nei ☐

Hvor gammel var du da du tok din første sigarett? ☐☐

Hvis Ja, ber vi deg om å fylle ut for hver aldersgruppe i livet hvor mange sigaretter du i gjennomsnitt røykte pr. dag i den perioden.

Antall sigaretter hver dag

Alder	0	1-4	5-9	10-14	15-19	20-24	25+
10-14	☐	☐	☐	☐	☐	☐	☐
15-19	☐	☐	☐	☐	☐	☐	☐
20-29	☐	☐	☐	☐	☐	☐	☐
30-39	☐	☐	☐	☐	☐	☐	☐
40-49	☐	☐	☐	☐	☐	☐	☐
50+	☐	☐	☐	☐	☐	☐	☐

	Ja	Nei
Røyker du daglig nå?	☐	☐
Røykte noen av dine foreldre når du var barn?	☐	☐

Hvis Ja, hvor mange sigaretter røykte de til sammen pr. dag? ☐☐

Brystkreft i nærmeste familie

Har noen nære slektninger hatt brystkreft?

	Ja	Nei	Vet ikke	Alder ved start
Datter	☐	☐	☐	☐☐
Mor	☐	☐	☐	☐☐
Søster	☐	☐	☐	☐☐

Mammografiundersøkelse

Har du vært til undersøkelse av brystene med mammografi Ja ☐ Nei ☐

Hvis Ja;
hvor gammel var du første gangen? (hele år) ☐☐

Hvor mange ganger har du vært undersøkt?

-etter invitasjon fra Mammografiprogrammet ☐☐

-etter henvisning fra lege ☐☐

-uten henvisning fra lege ☐☐

Har du silikoninnlegg i brystene? Ja ☐ Nei ☐

Hvis Ja;
hvor mange år har du hatt det? ☐☐

Har du hatt silikoninnlegg tidligere? Ja ☐ Nei ☐

Hvis Ja;
hvorfor fjernet du innlegget? ☐

Fysisk aktivitet

Vi ber deg angi din fysiske aktivitet etter en skala fra svært lite til svært mye. Skalaen nedenfor går fra 1-10. Med fysisk aktivitet mener vi både arbeid i hjemmet og i yrkeslivet, samt trening og annen fysisk aktivitet som turgåing o.l. Sett kryss over det tallet som best angir ditt nivå av fysisk aktivitet.

Alder	Svært lite									Svært mye
14 år	1	2	3	4	5	6	7	8	9	10
30 år	1	2	3	4	5	6	7	8	9	10
I dag	1	2	3	4	5	6	7	8	9	10

Hvor mange timer pr. dag i gjennomsnitt går eller spaserer du utendørs?

	sjelden aldri	mindre enn 1/2 time	1/2-1 time	1-2 timer	mer enn 2 timer
Vinter	☐	☐	☐	☐	☐
Vår	☐	☐	☐	☐	☐
Sommer	☐	☐	☐	☐	☐
Høst	☐	☐	☐	☐	☐

For hver av følgende aktiviteter du deltar i, ber vi deg oppgi hvor mange minutter pr. dag du bruker i gjennomsnitt til hver av aktivitetene.

Fritidsaktivitet	Vinter	Vår	Sommer	Høst
Se på TV	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Lesing	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Håndarbeid/hobby	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Hagearbeid	☐☐☐	☐☐☐	☐☐☐	☐☐☐
Dusj/bad/egenpleie	☐☐☐	☐☐☐	☐☐☐	☐☐☐

Høyde og vekt

Hvor høy er du? (i hele cm.) ☐☐☐

Hvor mye veide du da du var 18 år? (i hele kg.) ☐☐☐

Hvor mye veier du i dag? (i hele kg.) ☐☐☐

Kosthold

Påvirker noen av følgende forhold kostholdet ditt?
(sett gjerne flere kryss)

- ☐ Er vegetarianer/veganer
- ☐ Har anoreksi
- ☐ Spiser ikke norsk kost til daglig
- ☐ Har allergi/intoleranse
- ☐ Har bulimi
- ☐ Kronisk sykdom
- ☐ Prøver å gå ned i vekt

Vi er interessert i å få kjennskap til hvordan kostholdet ditt er vanligvis. Kryss av for hvert spørsmål om hvor ofte du i gjennomsnitt siste året har brukt den aktuelle matvaren, og hvor mye du pleier å spise/drikke hver gang.

Hvor mange glass melk drikker du vanligvis av hver type? (Sett ett kryss pr. linje)

	aldri/ sjelden	1-4 pr. uke	5-6 pr. uke	1 pr. dag	2-3 pr. dag	4+ pr. dag
Helmelk (søt, sur)	☐	☐	☐	☐	☐	☐
Lettmelk (søt, sur)	☐	☐	☐	☐	☐	☐
Ekstra lettmelk	☐	☐	☐	☐	☐	☐
Skummet (søt, sur)	☐	☐	☐	☐	☐	☐

Hvor mange kopper kaffe/te drikker du vanligvis av hver sort? (Sett ett kryss for hver linje)

	aldri/ sjelden	1-6 pr. uke	1 pr. dag	2-3 pr. dag	4-5 pr. dag	6-7 pr. dag	8+ pr. dag
Kokekaffe	☐	☐	☐	☐	☐	☐	☐
Traktekaffe	☐	☐	☐	☐	☐	☐	☐
Pulverkaffe	☐	☐	☐	☐	☐	☐	☐
Espresso o.l.	☐	☐	☐	☐	☐	☐	☐
Svart te	☐	☐	☐	☐	☐	☐	☐
Grønn te	☐	☐	☐	☐	☐	☐	☐

Hvor mange glass vann drikker du vanligvis?
(Sett ett kryss for hver linje)

	aldri/ sjelden	1-3 pr. uke	4-6 pr. uke	1 pr. dag	2-3 pr. dag	4+ pr. dag
Springvann	☐	☐	☐	☐	☐	☐
Flaskevann u/kullsyre	☐	☐	☐	☐	☐	☐
Flaskevann m/kullsyre	☐	☐	☐	☐	☐	☐

Hvor mange glass appelsinjuice, saft og brus drikker du vanligvis? (Sett ett kryss for hver linje)

	aldri/ sjelden	1-3 pr. uke	4-6 pr. uke	1 pr. dag	2-3 pr. dag	4+ pr. dag
Appelsinjuice	☐	☐	☐	☐	☐	☐
Saft/brus med sukker	☐	☐	☐	☐	☐	☐
Saft/brus sukkerfri	☐	☐	☐	☐	☐	☐

Hvor ofte spiser du yoghurt (1 beger)? (Sett ett kryss)

☐ Aldri/sjelden ☐ 1 pr. uke ☐ 2-3 pr. uke ☐ 4+ pr. uke

Hvor ofte spiser du kornblanding, havregryn eller müsli? (Sett ett kryss)

☐ Aldri/sjelden ☐ 1-3 pr. uke ☐ 4-6 pr. uke ☐ 1 pr. dag

Hvor mange skiver brød/rundstykker og knekkebrød/skonrokker spiser du vanligvis?
(1/2 rundstykke = 1 brødskive) (Sett ett kryss for hver linje)

	aldri/ sjelden	1-4 pr. uke	5-7 pr. uke	2-3 pr. dag	4-5 pr. dag	6+ pr. dag
Grovt brød	☐	☐	☐	☐	☐	☐
Kneipp/halvfint	☐	☐	☐	☐	☐	☐
Fint brød	☐	☐	☐	☐	☐	☐
Knekkebrød o.l.	☐	☐	☐	☐	☐	☐

Nedenfor er det spørsmål om bruk av ulike påleggstyper. Vi spør om hvor mange brødskiver med det aktuelle pålegget du pleier å spise. Dersom du også bruker matvarene i andre sammenhenger enn til brød (f. eks. til vafler, frokostblandinger, grøt), ber vi om at du tar med dette når du besvarer spørsmålene.

På hvor mange brødskiver bruker du? (Sett ett kryss pr. linje)

	0 pr. uke	1-3 pr. uke	4-6 pr. uke	1 pr. dag	2-3 pr. dag	4+ pr. dag
Syltetøy	☐	☐	☐	☐	☐	☐
Brun ost, helfet	☐	☐	☐	☐	☐	☐
Brunost, halvfet/mager	☐	☐	☐	☐	☐	☐
Hvitost, helfet	☐	☐	☐	☐	☐	☐
Hvitost, halvfet/mager	☐	☐	☐	☐	☐	☐
Kjøttpålegg, Leverpostei	☐	☐	☐	☐	☐	☐
Rekesalat, italiensk o.l.	☐	☐	☐	☐	☐	☐

På hvor mange brødskiver pr. uke har du i gjennomsnitt siste året spist? (Sett ett kryss pr. linje)

	0 pr. uke	1 pr.uke	2-3 pr.uke	4-6 pr.uke	7-9 pr.uke	10+ pr.uke
Makrell i tomat, røkt makrell	☐	☐	☐	☐	☐	☐
Kaviar	☐	☐	☐	☐	☐	☐
Sild/Ansjos	☐	☐	☐	☐	☐	☐
Laks (gravet/røkt)	☐	☐	☐	☐	☐	☐
Annet fiskepålegg	☐	☐	☐	☐	☐	☐

Hva slags fett bruker du vanligvis på brødet?
(Sett gjerne flere kryss)

- ☐ Bruker ikke fett på brødet
- ☐ Smør
- ☐ Hard margarin (f. eks. Per, Melange)
- ☐ Myk margarin (f. eks. Soft, Vita, Solsikke)
- ☐ Smørblandet margarin (f.eks. Bremyk)
- ☐ Brelett
- ☐ Lettmargarin (f. eks. Soft light, Letta)
- ☐ Middels lett margarin (f. eks. Olivero, Omega)

Dersom du bruker fett på brødet, hvor tykt lag pleier du smøre på? (En kuvertpakke med margarin veier 12 gram).
(Sett ett kryss)

☐ Skrapet (3 g) ☐ Tynt lag (5 g) ☐ Godt dekket (8 g) ☐ Tykt lag (12 g)

Hvor ofte spiser du frukt? (Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr.mnd.	1 pr.uke	2-4 pr.uke	5-6 pr.uke	1 pr.dag	2+ pr. dag
Epler/pærer	☐	☐	☐	☐	☐	☐	☐
Appelsiner o.l.	☐	☐	☐	☐	☐	☐	☐
Bananer	☐	☐	☐	☐	☐	☐	☐
Annen frukt	☐	☐	☐	☐	☐	☐	☐

Hvor ofte spiser du ulike typer grønnsaker?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr.mnd.	1 pr.uke	2 pr.uke	3 pr.uke	4-5 pr.uke	6-7 pr. uke
Gulrøtter	☐	☐	☐	☐	☐	☐	☐
Kål	☐	☐	☐	☐	☐	☐	☐
Kålrot	☐	☐	☐	☐	☐	☐	☐
Brokkoli/blomkål	☐	☐	☐	☐	☐	☐	☐
Blandet salat	☐	☐	☐	☐	☐	☐	☐
Tomat	☐	☐	☐	☐	☐	☐	☐
Grønnsaksblanding (frossen)	☐	☐	☐	☐	☐	☐	☐
Andre grønnsaker	☐	☐	☐	☐	☐	☐	☐

For de grønnsakene du spiser, kryss av for hvor mye du spiser hver gang. (Sett ett kryss for hver sort)

- gulrøtter	☐ 1/2 stk.	☐ 1 stk.	☐ 1 1/2 stk.	☐ 2+ stk.
- kål	☐ 1/2 dl	☐ 1 dl	☐ 1 1/2 dl	☐ 2+ dl
- kålrot	☐ 1/2 dl	☐ 1 dl	☐ 1 1/2 dl	☐ 2+ dl
- brokkoli/blomkål	☐ 1-2 buketter	☐ 3-4 buketter	☐ 5+ buketter	
- blandet salat	☐ 1 dl	☐ 2 dl	☐ 3 dl	☐ 4+ dl
- tomat	☐ 1/4	☐ 1/2	☐ 1	☐ 2+
- grønnsakblanding	☐ 1/2 dl	☐ 1 dl	☐ 2 dl	☐ 3+ dl

Hvor mange poteter spiser du vanligvis (kokte, stekte, mos)? (Sett ett kryss)

☐ Spiser ikke/spiser sjelden poteter
☐ 1-4 pr. uke ☐ 5-6 pr. uke ☐ 1 pr. dag ☐ 2 pr. dag
☐ 3 pr. dag ☐ 4+ pr. dag

Hvor ofte bruker du ris og spagetti/makaroni ?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr. mnd.	1 pr. uke	2 pr. uke	3+ pr. uke
Ris	☐	☐	☐	☐	☐
Spagetti, makaroni	☐	☐	☐	☐	☐

Hvor ofte spiser du grøt ? (Sett ett kryss)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2-6 pr. uke	1+ pr. dag
Risengrynsgrøt	☐	☐	☐	☐	☐	☐
Annen grøt (havre o.l.)	☐	☐	☐	☐	☐	☐

Fisk

Vi vil gjerne vite hvor ofte du pleier å spise fisk, og ber deg fylle ut spørsmålene om fiskeforbruk så godt du kan. Tilgangen på fisk kan variere gjennom året. Vær vennlig å markere i hvilke årstider du spiser de ulike fiskeslagene.

	aldri/ sjelden	like mye hele året	vintrer	vår	sommer	høst
Torsk, sei, hyse, lyr	☐	☐	☐	☐	☐	☐
Steinbit, flyndre, uer	☐	☐	☐	☐	☐	☐
Laks, ørret	☐	☐	☐	☐	☐	☐
Makrell	☐	☐	☐	☐	☐	☐
Sild	☐	☐	☐	☐	☐	☐
Annen fisk	☐	☐	☐	☐	☐	☐

Med tanke på de periodene av året der du spiser fisk, hvor ofte pleier du å spise følgende?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2+ pr. uke
Kokt torsk, sei, hyse, lyr	☐	☐	☐	☐	☐
Stekt torsk, sei, hyse, lyr	☐	☐	☐	☐	☐
Steinbit, flyndre, uer	☐	☐	☐	☐	☐
Laks, ørret	☐	☐	☐	☐	☐
Makrell	☐	☐	☐	☐	☐
Sild	☐	☐	☐	☐	☐
Annen fisk	☐	☐	☐	☐	☐

Dersom du spiser fisk, hvor mye spiser du vanligvis pr. gang? (1 skive/stykke = 150 gram)

Kokt fisk (skive) ☐1 ☐1,5 ☐2 ☐3+

Stekt fisk (stykke) ☐1 ☐1,5 ☐2 ☐3+

Hvor mange ganger pr. år spiser du fiskeinnmat?
(Sett ett kryss pr. linje)

	0	1-3	4-6	7-9	10+
Rogn	☐	☐	☐	☐	☐
Fiskelever	☐	☐	☐	☐	☐

Dersom du spiser fiskelever, hvor mange spiseskjeer pleier du å spise hver gang? (Sett ett kryss)

1	2	3-4	5-6	7+
☐	☐	☐	☐	☐

Hvor ofte bruker du følgende typer fiskemat?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2+ pr. uke
Fiskekaker/pudding/boller	☐	☐	☐	☐	☐
Plukkfisk/fiskegrateng	☐	☐	☐	☐	☐
Frityrfisk/fiskepinner	☐	☐	☐	☐	☐
Andre fiskeretter	☐	☐	☐	☐	☐

Hvor stor mengde pleier du vanligvis å spise av de ulike rettene? (Sett ett kryss for hver linje)

- fiskekaker/pudding/boller (stk.) (2 fiskeboller=1 fiskekake)	☐ 1	☐ 2	☐ 3	☐ 4+
- plukkfisk, fiskegrateng (dl)	☐ 1-2	☐ 3-4	☐ 5+	
- frityrfisk, fiskepinner (stk.)	☐ 1-2	☐ 3-4	☐ 5-6	☐ 7+

I tillegg til informasjon om fiskeforbruk er det viktig å få kartlagt hvilket tilbehør som blir servert til fisk. Hvor ofte bruker du følgende til fisk? (Sett ett kryss pr. linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. mnd.	1 pr. uke	2+ pr. uke
Smeltet smør	☐	☐	☐	☐	☐
Smeltet eller fast margarin/fett	☐	☐	☐	☐	☐
Seterrømme (35%)	☐	☐	☐	☐	☐
Lettrømme (20%)	☐	☐	☐	☐	☐
Saus med fett (hvit/brun)	☐	☐	☐	☐	☐
Saus uten fett (hvit/brun)	☐	☐	☐	☐	☐

For de ulike typene tilbehør du bruker til fisk, vær vennlig å kryss av for hvor mye du vanligvis pleier spise.

- smeltet smør (ss)	☐ 1/2	☐ 1	☐ 2	☐ 3	☐ 4+
- smeltet margasin (ss)	☐ 1/2	☐ 1	☐ 2	☐ 3	☐ 4+
- seterrømme (ss)	☐ 1/2	☐ 1	☐ 2	☐ 3	☐ 4+
- lettrømme (ss)	☐ 1/2	☐ 1	☐ 2	☐ 3	☐ 4+
- saus med fett (dl)	☐ 1/4	☐ 1/2	☐ 3/4	☐ 1	☐ 2+
- saus uten fett (dl)	☐ 1/4	☐ 1/2	☐ 3/4	☐ 1	☐ 2+

Hvor ofte spiser du skalldyr (f. eks. reker, krabbe og skjell)**?** (Sett ett kryss)

☐ Aldri/sjelden ☐ 1 pr. mnd ☐ 2-3 pr. mnd ☐ 1+ pr. uke

Andre matvarer

Hvor ofte spiser du reinkjøtt?

☐ Aldri/sjelden ☐ 1 pr. mnd. ☐ 2-3 pr. mnd. ☐ 1 pr. uke
☐ 2-3 pr. uke ☐ 4+ pr. uke

Hvor ofte spiser du følgende kjøtt- og fjærkreretter? (Sett ett kryss for hver rett)

	aldri/ sjelden	1 pr.mnd.	2-3 pr.mnd.	1 pr.uke	2+ pr.uke
Steik (okse, svin, får)	☐	☐	☐	☐	☐
Koteletter	☐	☐	☐	☐	☐
Biff	☐	☐	☐	☐	☐
Kjøttkaker, karbonader	☐	☐	☐	☐	☐
Pølser	☐	☐	☐	☐	☐
Gryterett, lapskaus	☐	☐	☐	☐	☐
Pizza med kjøtt	☐	☐	☐	☐	☐
Kylling	☐	☐	☐	☐	☐
Andre kjøttretter	☐	☐	☐	☐	☐

Dersom du spiser følgende retter, oppgi mengden du vanligvis spiser: (Sett ett kryss for hver linje)

- steik (skiver)	☐ 1	☐ 2	☐ 3	☐ 4+
- koteletter (stk.)	☐ 1/2	☐ 1	☐ 1,5	☐ 2+
- kjøttkaker, karbonader (stk.)	☐ 1	☐ 2	☐ 3	☐ 4+
- pølser (stk. à 150g)	☐ 1/2	☐ 1	☐ 1,5	☐ 2+
- gryterett, lapskaus (dl)	☐ 1-2	☐ 3	☐ 4	☐ 5+
- pizza m/kjøtt (stykke à 100 g)	☐ 1	☐ 2	☐ 3	☐ 4+

Hvor mange egg spiser du vanligvis i løpet av en uke?(stekte, kokte, eggerøre, omelett) (Sett ett kryss)

☐ 0 ☐ 1 ☐ 2 ☐ 3-4
☐ 5-6 ☐ 7+

Hvor ofte spiser du iskrem? (til dessert, krone-is osv.) Sett et kryss for hvor ofte du spiser iskrem om sommeren, og et kryss for resten av året)

	aldri/ sjelden	1-3. pr.	2-3 pr. mnd.	1 pr. uke	2+ pr. uke
-Om sommeren	☐	☐	☐	☐	☐
-Resten av året	☐	☐	☐	☐	☐

Hvor mye is spiser du vanligvis pr. gang? (Sett ett kryss)

☐ 1dl ☐ 2 dl ☐ 3 dl ☐ 4+ dl

Hvor ofte spiser du bakevarer som boller kaker, wienerbrød eller småkaker (Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 mnd.	1 pr. uke	2-3 pr uke	4-6 pr. uke	1+ pr. dag
Gjærbakst (boller)	☐	☐	☐	☐	☐	☐
Wienerbrød, kringle	☐	☐	☐	☐	☐	☐
Kaker (bløtkaker)	☐	☐	☐	☐	☐	☐
Pannekaker	☐	☐	☐	☐	☐	☐
Vafler	☐	☐	☐	☐	☐	☐
Småkaker, kjeks	☐	☐	☐	☐	☐	☐

Hvor ofte spiser du dessert? (Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 mnd.	1 pr. uke	2-3 pr uke	4-6 pr. uke	1+ pr. dag
Pudding sjokolade/karamell	☐	☐	☐	☐	☐	☐
Riskrem, fromasj	☐	☐	☐	☐	☐	☐
Kompott, fruktgrøt, hermetisk frukt	☐	☐	☐	☐	☐	☐
Jorbær (friske, frosne)	☐	☐	☐	☐	☐	☐
Andre bær (friske, frosne)	☐	☐	☐	☐	☐	☐

Hvor ofte spiser du sjokolade? (Sett ett kryss)

	aldri/ sjelden	1-3 mnd.	1 pr. uke	2-3 pr uke	4-6 pr. uke	1+ pr. dag
Mørk sjokolade	☐	☐	☐	☐	☐	☐
Lys sjokolade	☐	☐	☐	☐	☐	☐

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

☐ 1/4 ☐ 1/2 ☐ 3/4 ☐ 1 ☐ 1,5 ☐ 2+

Hvor ofte spiser du snacks? (Sett ett kryss)

	aldri/ sjelden	1-3 pr. mnd.	1 pr. uke	2-3 pr. uke	4-6 pr. uke	7+ pr. uke
Potetchips	☐	☐	☐	☐	☐	☐
Peanøtter	☐	☐	☐	☐	☐	☐
Andre nøtter	☐	☐	☐	☐	☐	☐
Annen snacks	☐	☐	☐	☐	☐	☐

Tran og fiskeoljekapsler

Bruker du tran (flytende)? Ja ☐ Nei ☐

Hvis ja; hvor ofte tar du tran?
Sett ett kryss for hver linje.

	aldri/ sjelden	1-3 pr. mnd.	1 pr. uke	2-6 pr. uke	daglig
Om vinteren	☐	☐	☐	☐	☐
Resten av året	☐	☐	☐	☐	☐

Hvor mye tran pleier du å ta hver gang?

☐ 1 ts. ☐ 1/2 ss. ☐ 1+ ss.

Bruker du tranpiller/kapsler? Ja ☐ Nei ☐

Hvis ja; hvor ofte tar du tranpiller/kapsler?
Sett ett kryss for hver linje.

	aldri/ sjelden	1-3 pr. mnd.	1 pr. uke	2-6 pr. uke	daglig
Om vinteren	☐	☐	☐	☐	☐
Resten av året	☐	☐	☐	☐	☐

Hvilken type tranpiller/kapsler bruker du vanligvis, og hvor mange pleier du å ta hver gang?

Antall

Navn _____ |__|

Bruker du fiskeoljekapsler? (omega-3) Ja ☐ Nei ☐

Hvis ja; hvor ofte tar du fiskeoljekapsler?

aldri/ sjelden	1-3 pr. mnd.	1 pr. uke	2-6 pr. uke	daglig
☐	☐	☐	☐	☐

Hvilken type fiskeoljekapsler bruker du vanligvis, og hvor mange pleier du å ta hver gang?

Navn _____ antall |__|

Varm mat

Hvor mange ganger i løpet av en måned spiser du varm mat?

Antall

Til frokost ..... |__|

Til lunsj ..... |__|

Til middag ..... |__|

Til kvelds ..... |__|

Kosttilskudd

Hvor ofte bruker du kosttilskudd?
(Sett ett kryss pr. linje)

Navn på vitamin/mineraltilskudd:	aldri/ sjelden	1-3 pr. mnd.	1 pr. uke	2-6 pr. uke	daglig
_____	☐	☐	☐	☐	☐
_____	☐	☐	☐	☐	☐
_____	☐	☐	☐	☐	☐

Alkohol

Er du totalavholdskvinne? Ja ☐ Nei ☐

Hvis Nei, hvor ofte og hvor mye drakk du i gjennomsnitt siste året? (Sett ett kryss for hver linje)

	aldri/ sjelden	1 pr. mnd.	2-3 pr. uke	1 pr. uke	2-4 pr. uke	5-6 pr. uke	1+ pr. dag
Øl (1/2 l.)	☐	☐	☐	☐	☐	☐	☐
Vin (glass)	☐	☐	☐	☐	☐	☐	☐
Brennevin (drink)	☐	☐	☐	☐	☐	☐	☐
Likør/Hetvin	☐	☐	☐	☐	☐	☐	☐

Sosiale forhold

Er du: (Sett ett kryss)

☐ gift ☐ samboer ☐ ugift ☐ skilt ☐ enke

Hvor mange års skolegang/yrkesutdannelse har du i alt, ta med folkeskole og ungdomsskole? |__|

Hvor mange personer er det i ditt hushold? ..... |__|

Hvor høy er bruttoinntekten i husholdet pr. år?

under 150.000 kr.	☐	151.000-300.000 kr.	☐
301.000-450.000 kr.	☐	451.000-600.000 kr.	☐
601.000-750.000 kr.	☐	over 750.000 kr.	☐

Hva er din arbeidssituasjon? (sett kryss)

☐ Arbeider heltid ☐ Arbeider deltid ☐ Pensjonist

☐ Hjemmearbeidende ☐ Under utdanning ☐ Uføretrygdet

☐ Under attføring ☐ Arbeidssøkende

Yrke: _____

Hvordan var de økonomiske forhold i oppveksten?

☐ Meget gode ☐ Gode

☐ Dårlige ☐ Meget dårlige

Arbeider du utendørs i yrkessammenheng? Ja ☐ Nei ☐

Hvis Ja;
hvor mange timer pr. uke? .....Sommer .....vinter

Solvaner

Får du fregner når du soler deg? ..... Ja ☐ Nei ☐

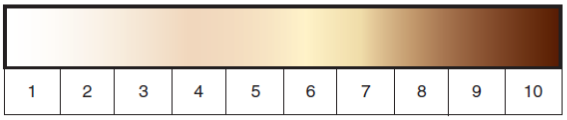
Hvilken øyefarge har du? (sett ett kryss)

☐ brun ☐ grå, grønn eller blanding ☐ blå

Hva er din opprinnelige hårfarge? (sett ett kryss)

☐ mørkbrunt, svart ☐ brun ☐ blond, gul ☐ rød

For å kunne studere effekten av soling på risiko for hudkreft ber vi deg gi opplysninger om hudfarge
Sett ett kryss på det tallet under fargen som best passer din naturlige hudfarge (uten soling)



1	2	3	4	5	6	7	8	9	10

Hvor mange ganger pr. år er du blitt forbrent av solen slik at du har fått svie og blemmer med avflassing etterpå? (ett kryss for hver aldersgruppe)

Alder	Aldri	Høyst 1 gang pr. år	2-3 g. pr. år	4-5 g. pr. år	6 eller flere ganger
Før 10 år	☐	☐	☐	☐	☐
10-19 år	☐	☐	☐	☐	☐
20-29 år	☐	☐	☐	☐	☐
30-44 år	☐	☐	☐	☐	☐
45+ år	☐	☐	☐	☐	☐

Hvor mange uker soler du deg pr. år i syden?

Alder	Aldri	1 uke	2-3 uker	4-5 uker	7 uker eller mer
Før 10 år	☐	☐	☐	☐	☐
10-19 år	☐	☐	☐	☐	☐
20-29 år	☐	☐	☐	☐	☐
30-44 år	☐	☐	☐	☐	☐
45+ år	☐	☐	☐	☐	☐
Siste 12 mnd.	☐	☐	☐	☐	☐

Hvor mange uker pr. år soler du deg i Norge eller utenfor syden?

Alder	Aldri	1 uke	2-3 uker	4-5 uker	7 uker eller mer
Før 10 år	☐	☐	☐	☐	☐
10-19 år	☐	☐	☐	☐	☐
20-29 år	☐	☐	☐	☐	☐
30-44 år	☐	☐	☐	☐	☐
45+ år	☐	☐	☐	☐	☐
Siste 12 mnd.	☐	☐	☐	☐	☐

Hvor ofte dusjer eller bader du?

	mer enn 1 g. dagl.	1 g. dagl.	4-6 g. pr. uke	2-3 g. pr. uke	1 g. pr.	2-3 g. pr.uke	sjel-den/ aldri
Med såpe/shampo	☐	☐	☐	☐	☐	☐	☐
Uten såpe/shampo	☐	☐	☐	☐	☐	☐	☐

Når bruker du krem med solfaktor? (sett evt. flere kryss):

☐ i påsken ☐ i Norge eller utenfor syden ☐ solferie i syden ☐ aldri

Hvilken solfaktor bruker du i disse periodene?

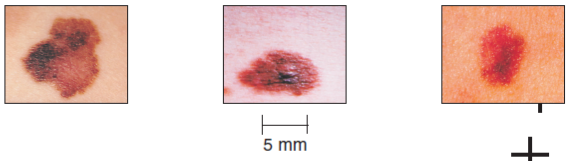
	påsken	i Norge eller utenfor syden	solferie i syden
I dag	☐☐	☐☐	☐☐
For 10 år siden	☐☐	☐☐	☐☐

Hvor ofte har du solt deg i solarium?

Alder	Aldri	Sjelden	1 gang pr. mnd.	2 ganger pr. mnd.	3-4 ganger pr. mnd	oftere enn1 gang pr. uke
Før 10 år	☐	☐	☐	☐	☐	☐
10-19 år	☐	☐	☐	☐	☐	☐
20-29 år	☐	☐	☐	☐	☐	☐
30-44 år	☐	☐	☐	☐	☐	☐
45+ år	☐	☐	☐	☐	☐	☐
Siste 12 mnd.	☐	☐	☐	☐	☐	☐

Hvor mange uregelmessige føflekker større enn 5 mm har du sammenlagt på begge bena (fra tærne til lysken)? Tre eksempler på føflekker større enn 5 mm med uregelmessig form er vist i nedenfor.

☐ 0 ☐ 1 ☐ 2-3 ☐ 4-6 ☐ 7-12 ☐ 13-24 ☐ 25+



Hvor ofte bruker du følgende hudpleiemidler?
(Sett ett kryss pr. linje)

	aldri/ sjelden	1-3 pr.mnd.	1 pr.uke	2-4 pr.uke	5-6 pr.uke	1 pr.dag	2+ pr. dag
Ansiktskrem	☐	☐	☐	☐	☐	☐	☐
Håndkrem	☐	☐	☐	☐	☐	☐	☐
Body lotion	☐	☐	☐	☐	☐	☐	☐
Parfyme	☐	☐	☐	☐	☐	☐	☐

Til slutt vil vi spørre deg om ditt samtykke til å kontakte deg på nytt pr. post. Vi vil hente adressen fra det sentrale personregister.

Ja ☐ Nei ☐

Er du villig til å avgi en blodprøve?

Ja ☐ Nei ☐

Takk for at du ville delta i undersøkelsen