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Physical activity, mortality and breast cancer risk

The Norwegian Women and Cancer Study

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“Å gå får føttene til å bevege seg, blodet beveger
seg, tankene beveger seg.
Og bevegelse er liv”

Carrie Latet

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Table of contents

Summary

An extensive amount of research has been carried out over the last decades on the effect of physical activity (PA) on several health outcomes. The population level of PA has declined over the years, and sedentary behavior is a threat to health and longevity. The aim of this thesis was to validate a PA questionnaire (Paper I), to assess the effect of PA on all-cause, cardiovascular and cancer mortality (Paper II), and on the risk of breast cancer overall and according to estrogen (ER) and progesterone (PR) receptor status (Paper III) in Norway.

The Norwegian Women and Cancer (NOWAC) Study is a large national prospective cohort study, which was initiated in 1991 and consists of more than 172,000 women living in different parts of Norway. Participants were randomly selected from the National Population Register, Statistics Norway, and answered extensive questionnaires containing information on lifestyle habits and reproductive factors. Data on vital status, cancer incidence and mortality were obtained by record linkages to Statistics Norway and the Cancer Registry of Norway. The study on the validation of the PA questionnaire (Paper I) included a random selection of women from the National Population Register living in Tromsø in the same age groups as the participants in the NOWAC study. The participants of the validation study were asked to answer a similar questionnaire on PA as women in the NOWAC study and were then fitted with a combined heart rate and movement sensor, on two different occasions approximately 5 months apart. The women wore the monitors for 4 consecutive days, including nights.

The PA measure used in the NOWAC study was sufficient to rank PA level in the Norwegian female population, with limitations to differentiate the intensity, duration and frequency of PA (Paper I). Very low and low PA levels were associated with an increased risk of all-cause mortality, compared to moderate PA levels. The associations were stronger for cardiovascular than for cancer mortality. The population attributable risk for low PA was 11.5% for all-cause mortality, 11.3% for cardiovascular mortality and 7.8% for cancer mortality (Paper II). Low PA levels assessed at age 30 years, compared to moderate PA levels at the same age, was associated with an increased risk of ER and PR receptor positive breast tumors; however, there were no other association between PA levels at age 30 or at cohort enrollment (i.e. 34-70) and risk of overall breast cancer or other subtypes of breast cancer classified according to ER and PR status. In contrast, participants who were at low PA levels at age 14 and remained at low PA levels through age 30 and cohort enrollment had a 20% significant reduced risk of overall breast cancer and ER and PR positive breast tumors compared with participants who were moderately active at age 14 and remained active throughout adulthood (Paper III).

In conclusion, our findings using the NOWAC study valid questionnaire for ranking PA indicate that there is a dose-response relationship between increasing levels of PA and decreasing all-cause, cardiovascular and cancer mortality. The study on breast cancer incidence indicated inconsistent associations between levels of PA in different periods of life and risk of overall breast cancer and ER and PR breast tumors. The study also highlights the need to assess PA over a woman's lifetime, and to considering hormone receptor status in breast cancer studies.

Sammendrag

Forskning over de siste tiårene viser at fysisk aktivitet har en forebyggende effekt på flere ulike sykdommer og tilstander. Aktivitetsnivået i befolkningen har gått ned i løpet av de siste ti årene, og sedat atferd er en trussel for god helse og lang levetid. Hovedmålet med denne doktorgradsavhandlingen var å validere et spørreskjema på fysisk aktivitet (artikkel I), og å undersøke effekt av fysisk aktivitet på total dødelighet, hjerte-kar og kreft dødelighet (artikkel II), og risikoen for brystkreft, total og i henhold til østrogen og progesteron reseptor status (artikkel III) i en norsk kvinnelig befolkning med lang oppfølging.

Den nasjonale befolkningsundersøkelsen Kvinner og Kreft, som startet i 1991, har inkludert nærmere 172.000 norske kvinner i alderen 30-70 år over hele landet. Deltagerne er tilfeldig valgt fra Personregisteret ved Statistisk Sentralbyrå, og har besvart spørreskjemaer med spørsmål om livsstilsvaner og faktorer knyttet til reproduksjon. Data på vital status og kreft ble gitt gjennom kobling til Personregisteret og Kreftregisteret i Norge. I valideringsstudien av spørreskjemaet om fysisk aktivitet ble kvinner med adresse i Tromsø kommune, og i samme aldersgruppe som kvinnene som deltar i Kvinner og Kreft Studien, tilfeldig utvalgt fra Personregisteret. Deltageren ble bedt om å rapportere fysisk aktivitetsnivå ved bruk av det samme spørreskjema som er brukt i Kvinner og Kreft studien, og fikk deretter en hjertefrekvens- og bevegelsessensor plassert på kroppen, ved to anledninger med 5 måneder mellom. Kvinnene hadde sensoren på i fire sammenhengende døgn.

Resultatene fra de ulike studiene viste at fysisk aktivitetsmålingen som er brukt i Kvinner og Kreft-studien er tilstrekkelig til å rangere fysisk aktivitetsnivå i en voksen kvinnelig befolkning, med begrensninger i å differensiere mellom intensitet, varighet og hyppighet av fysisk aktivitet (artikkel I). Funn fra artikkel II viste at veldig lavt og lavt fysisk aktivitetsnivå var assosiert med økt risiko for død av alle årsaker sammenlignet med moderat fysisk aktivitetsnivå, med en sterkere assosiasjon for hjerte-kar dødelighet enn for død av kreft. Populasjonens tilskrivbare risiko viste at 11.5% av total dødelighet, 11.3% av hjerte-kar død og 7.8% av all kreftdød kunne tilskrives lave fysiske aktivitetsnivå. Lavt fysisk aktivitetsnivå rapportert ved 30 års alder viste en økt risiko for reseptor positiv brystkreft, sammenlignet med moderat fysisk aktivitetsnivå, mens vi ikke fant noen effekt av fysisk aktivitet rapportert ved 30 års alder eller ved inklusjonstidspunkt (alder fra 34-70 år) på total brystkreft eller andre undergrupper av brystkreft i forhold til østrogen og progesteron reseptor status. I kontrast til disse funnene fant vi at kvinner som rapporterte lave fysiske aktivitetsnivå ved 14 års alder og beholdt et lavt aktivitetsmønster ved 30 års alder og perioden fra 34-70 år, hadde 20% statistisk signifikant redusert risiko for brystkreft og spesielt for østrogen og progesteron reseptor positiv brystkreft

sammenlignet med kvinner som hadde et moderat fysisk aktivitetsmønster den samme perioden.

Funnene viser at ved bruk av et valid instrument for rangering av fysisk aktivitet, er det en dose-respons mellom økte nivå av fysisk aktivitet med redusert risiko for total dødelighet, hjerte-kar og kreft dødelighet. Studien på brystkreft insidens viste inkonsistente resultater for fysisk aktivitet i ulike perioder av livet og risiko for total brystkreft og østrogen og progesteron reseptor brysttumorer. Studien framholder viktigheten av å ha informasjon om fysisk aktivitetsnivå gjennom hele livet og informasjon om hormonreseptor status på tumor.

List of papers

This thesis is based on the following papers, hereafter referred in the text as Papers I, II and III.

Paper I

Borch KB, Ekelund U, Brage S, Lund E. **Criterion validity of a 1-category scale for ranking physical activity in Norwegian women.** *International Journal of Behavioral Nutrition and Physical Activity* 2012; 9:2. PubMed: PMID 22260340

Paper II

Borch KB, Braaten T, Lund E, Weiderpass E. **Physical activity and mortality among Norwegian women – the Norwegian Women and Cancer Study.** *Clinical Epidemiology* 2011; 3:1-7. PubMed: PMID 21857790

Paper III

Borch KB, Lund E, Braaten T, Weiderpass E. **Physical activity and risk of postmenopausal breast cancer by hormonal receptor status - the Norwegian Women and Cancer Study.**
[*Submitted*]

List of figures and tables

Abbreviations

ANOVA	Analysis of variance
Bpm	Beat per minute
BMI	Body mass index
CI	Confidence interval
CRF	Cardiorespiratory fitness
CVD	Cardiovascular diseases
EPIC	European Prospective Investigation into Cancer and Nutrition
ER	Estrogen receptor
Her2	Human epidermal growth factor receptor 2
ICC	Intra-class correlation coefficient
IGF-1	Insulin-like growth factor 1
IGFBP-3	Insulin-like growth factor-binding protein 3
MET	Metabolic energy turnover
MRC	Medical Research Center
MVPA	Moderate-vigorous physical activity
NOWAC	The Norwegian Women and Cancer Study
NOPAQ	Norwegian physical activity questionnaire
PA	Physical activity
PAEE	Physical activity energy expenditure
PANACEA	Physical Activity, Nutrition, Alcohol, Cessation of smoking, Eating out of home And obesity
PAF	Population attributable fraction
PR	Progesterone receptor
RR	Relative risk
SHBG	Sex hormone-binding globulin
TEE	Total energy expenditure
VO2max	Maximal oxygen uptake
WCRF/AICR	World Cancer Research Fund/American Institute for Cancer Research

1 Introduction

The main topic of this thesis is physical activity (PA) and health among women in Norway. We used a large prospective cohort, the Norwegian Women and Cancer (NOWAC) Study, to assess the impact of PA on overall mortality and risk of breast cancer. This introduction will give an overview of the effect of PA on health, before moving on to how we understand the concept of PA and the methods that exist to assess it, followed by an overview of the relationship between PA and mortality and breast cancer risk.

1.1 The epidemiology of physical activity and health

The human body is adapted for movement. As far back as 460 BC, the Greek physician Hippocrates said *"If we could give every individual the right amount of exercise, not too little, and not too much, we would have found the safest way to health."* (Michels, 2002: page 486) [1]. He was one of the first to emphasize how disease occurrence and environmental factors, together with individual behavior, were interrelated. The first contemporary epidemiological study investigating the impact of PA on morbidity and mortality, was conducted in the 1950s by Morris and colleagues in the United Kingdom [2]. They discovered that drivers of London's double-decker buses were more likely to die from coronary heart disease than the more physically active bus conductors [2]. PA level was assessed by observation with the driver being obviously sedentary, whereas the bus conductor was unavoidably active. The different PA levels were then related to the main endpoints: first clinical manifestations of coronary heart disease and death [2]. Since 1950 a huge body of evidence has been amassed in the fields of epidemiology and public health on the effect of PA and other lifestyle factors on morbidity and mortality, stating that PA improves health [3-7]. Modifiable lifestyle factors such as smoking, alcohol consumption and dietary habits, together with sedentary lifestyle and PA pattern are of special importance since they are the targets of public health intervention for disease prevention. There is evidence that PA reduces the risk of some cancers (breast and colon),

cardiovascular diseases (CVD), diabetes mellitus type 2, high blood pressure, overweight and obesity, injurious falls, hip fractures, osteoporosis and depression, and can also postpone mortality [5, 8-11]. A curvilinear reduction in risk can be found for a variety of diseases and conditions across PA levels, defined as duration, frequency and intensity of PA combined, with the steepest increases in disease risk at the lowest end of the PA scale [5]. This dose-response relationship suggests that even light PA is beneficial, and that anything more than light PA is even more so [5, 6]. The Global Recommendations on Physical Activity For Health concluded that there is evidence of an inverse dose-response relationship between PA and mortality [12], and the Physical Activity Guidelines Advisory Committee published a review in 2008 suggesting that even light leisure time activity will reduced the risk of premature mortality by 20% [7]. These findings highlight the important contribution of PA to health and longevity.

In the field of PA, as in other domains of public health, large epidemiological studies give important insight into the relationship between exposures and outcomes. However, one major challenge is how to best achieve valid and reliable data on daily PA habits in diverse populations.

1.2 The concept of physical activity and assessment methods

1.2.1 What is physical activity?

Caspersen and colleagues (1985) presented this definition of PA *"any bodily movement produced by skeletal muscles that result in energy expenditure"* (Caspersen et al 1985: page 126) [13]. From this definition emerged interchangeable, and often confusing terms such as PA, exercise and physical fitness. Furthermore, 10 years later (in 1996) the definition was phrased in two different ways in the very same report by United States Surgeon General as: *"bodily movement that is produced by the contraction of skeletal muscles that*

increases energy above the basal level" and as *"bodily movement that is produced by the contraction of skeletal muscles and that substantial increases energy expenditure"* (U.S. Department of health and human services 1996: page 20-21)[14], which illustrates the fact that the definition of PA remains a challenge. PA is indeed a complex phenomenon, both in a behavioral context and in physiological terms, and can be studied from different angles and points of view. Depending on which context of PA one deals with, it is important to focus on the dimension of PA that is most likely to be associated with the outcome of interest. This field of research is also substantially complicated by the fact that there are several health-related dimensions of PA, all of which require different assessment tools.

Development of a framework that conceptualizes and structures the way we understand PA [15] has been ongoing since Morris and colleagues observed the important role of PA in preventing cardiovascular deaths. How we understand PA reflects the way we measure the phenomenon. The more experience we gain in measuring PA, the more knowledge we develop on how to measure it [16]. Despite significant contributions to determine and define the terms and concepts related to PA, this terminology is used inconsistently, and no reasonable gold standard measure exists. In 2010, Gabriel and colleagues [17] presented a conceptual framework model for PA as a complex and multidimensional behavior, with the objective to clarify how to place human movement in a system when investigating health-related outcomes (Figure 1).

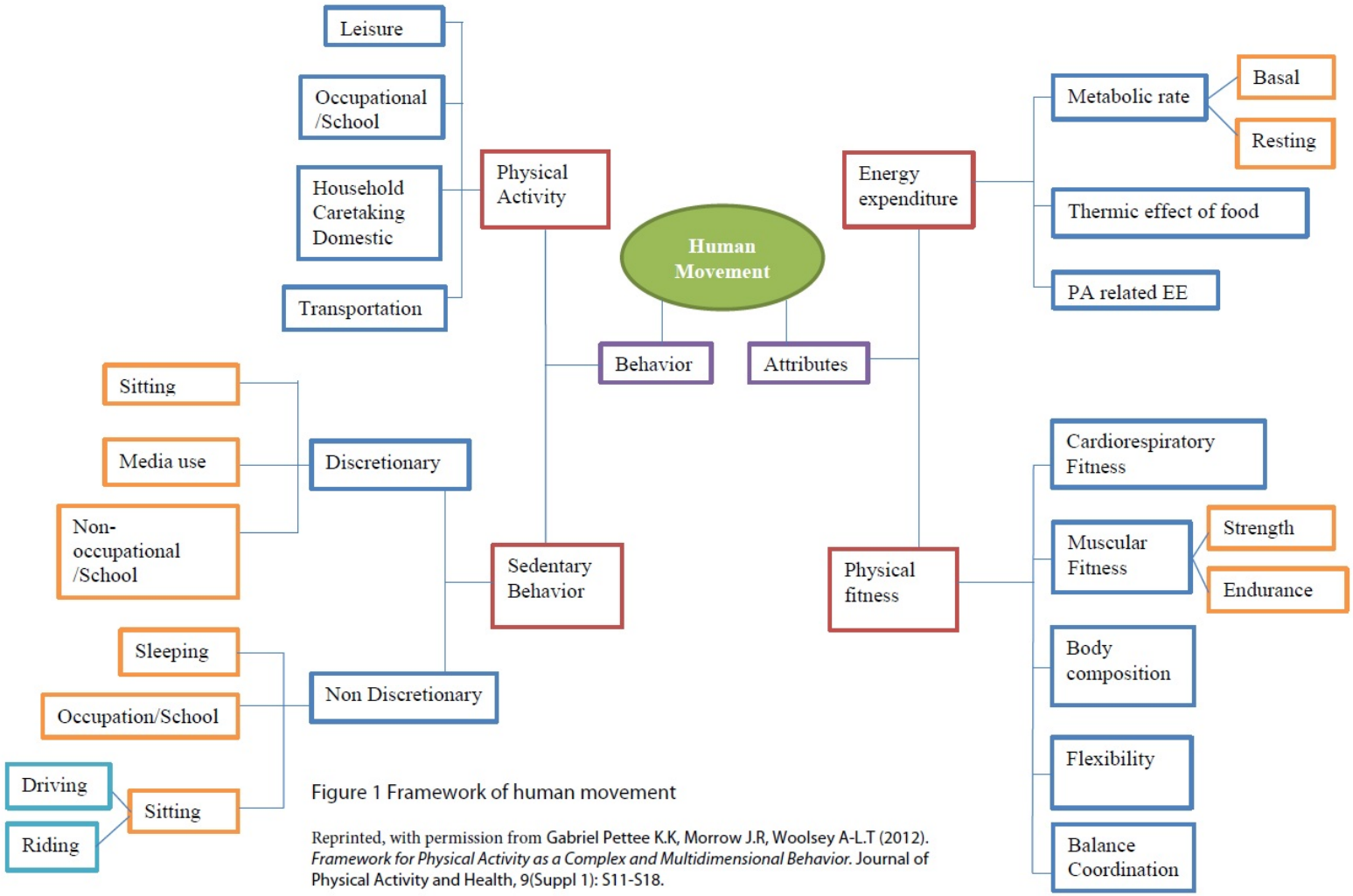


Figure 1 Framework of human movement

Reprinted, with permission from Gabriel Pettee K.K, Morrow J.R, Woolsey A-L.T (2012). *Framework for Physical Activity as a Complex and Multidimensional Behavior.* Journal of Physical Activity and Health, 9(Suppl 1): S11-S18.

In this model the global construct is human movement with a directional relationship between behavior and attributes, which are represented by the physiological consequences of PA (represented in the attributes on the right side of the framework model, figure 1). The behavioral part of human movement is classified into two categories: PA and sedentary behavior. When PA is looked at as a behavior four settings in which PA can take place are given; leisure, occupation/school, household/caretaking/ domestic and PA for transportation from place to place. Activities within these four domains are carried out with varying frequencies (how often), intensities (level of effort e.g. light, moderate, and vigorous) and durations (amount of time in a given range of intensity). The dimension of duration, frequency and intensity needed in order to gain the health benefits of PA is referred as the total volume of PA. Intensity is often quantified as metabolic energy turnover (MET) which is a multiple of resting metabolic rate. One MET for an adult corresponds to 3.5 ml of oxygen x body weight in kg^{-1} x min^{-1} when sitting at rest [18]. For example standing requires about 2 METs [18]. A light level of effort corresponds to about 1.6-2.9 METs, a moderate level to 3-5.9 METs, and a vigorous level to ≥6 METs. Exercise is part of PA behavior that most often takes place in leisure time for adults. Measuring an individual's exercise behavior consequently only captures a part of total PA behavior. Sedentary behavior according to the framework model by Gabriel and colleagues is categorized as nondiscretionary (i.e. sleeping, occupation/school and sitting, while driving or riding) or discretionary (i.e. watching television and non-work related computer and game console use). Furthermore, the model emphasizes that sedentary behavior is not the opposite of PA, as sedentary and non-sedentary behaviors can co-exist in individuals [17]. Obviously, an adult can be active, fulfilling the most updated recommendation of 150 minutes of moderate-intensity PA throughout the week [12, 19], but if the rest of the time consists mainly of sitting, sedentary behavior is still considered to be high.

The different elements presented make it of significant importance to differentiate between the physiological results of human movement, represented by cardiorespiratory fitness (CRF) and energy expenditure, and PA in a behavioral sense, as they are fundamentally different variables [13, 17, 20]. Human movement results in energy expenditure, measured as total energy expenditure (TEE) divided into resting metabolic rate, the thermic effect of feeding (ingestion, digestion, absorption, transportation and metabolism of nutrients) and physical activity energy expenditure (PAEE). TEE is the absolute intensity required for movement, whereas PAEE is the most variable component of TEE accounting for 15-30% of TEE [21]. Other physiological measures are CRF, muscular fitness, body composition, flexibility, balance and coordination. CRF is the only variable measured and emphasized in this thesis and is expressed as VO_2max, but could also be expressed as a percentage of aerobic capacity, or the percent of maximal heart rate [5].

Based on the framework model by Gabriel and colleagues a new definition of PA has been proposed: "*behavior that involves human movement, resulting in physiological attributes including increased energy expenditure and improved physical fitness"* (Gabriel et al 2012: page S15) [17].

The assessment tools available to quantify variables such as CRF, energy expenditure and PA differ greatly in precision and variability. They include highly reliable tools to measure CRF, and less reliable tools to estimate PA levels in free-living individuals, which is far more challenging. Translating PA behavior to PAEE is also problematic. Valid and accurate assessment of PA is critical when using PA as an outcome, an exposure or a confounding variable in relation to different health outcomes. The choice of a PA assessment method depends on the aspect of interest and the limitation of the derived estimates, as well as issues related to reporting, recall bias and misclassification [17, 22].

Misclassification of self-reported measurements occurs when an individual with low PA level is classified as moderately active. Non-differential misclassification is problematic because this most often reduces the overall strength of the association, meaning that the true effect of PA on the outcome may be even greater. Furthermore, the characteristics of the study, the population under study, activity characteristics and available instruments must be considered [17].

When all of above is taken into account, comparing epidemiological studies on PA and morbidity and mortality is challenging, and one needs to take into consideration which dimension of PA is measured when judging the validity and comparability of studies.

1.2.2 Physical activity assessment methods

PA behavior is difficult to measure directly, and no gold standard measurement of PA among free-living individual is yet available [23]. In large epidemiological studies, PA assessment has mainly relied on self-reported information from PA questionnaires, activity diaries or logs [24]. Indeed, PA questionnaires are most feasible in large-scale studies due to low cost and convenient administration [22]. Over the past century the contribution of self-reported PA in documenting the benefits of a physically active lifestyle has been significant [24]. PA questionnaires are practical for PA assessment in surveillance systems, for risk stratification and for the investigation of etiology in large observational studies [22]. The challenge lies in how to obtain valid and reliable measures of habitual PA in daily life through self-report, as PA questionnaires rely on an individual's ability to remember and quantify different dimensions of PA, making them prone to bias. One alternative to self-report is direct observation, but technologies available are burdensome for participants and researchers. The acute and chronic physiological consequences of human movement are that voluntarily contractions of skeletal muscles require oxygen, glucose and fat in order to release energy and to cause

bodily movement. The energy expended can therefore be measured physiologically [5]. Assessment methods, often referred to as objective methods, are physiological measurements taken in laboratory or clinical settings, like direct or indirect calorimetry or physical fitness parameters (VO_2max test), or in free-living settings as doubly-labeled water and movement (accelerometry) and/or heart rate sensors. Common features for these methods are the outcome quantified as PAEE. It is important to bear in mind when PA measures are gleaned from an objective method, it does not mean that the data, or the interpretation thereof are correct [24], as there are limitations within these methods as well. Furthermore, these methods are often used to validate self-reported instruments, as they are expensive, unpractical, burdensome to participants and not suitable in large study populations. Information on intensity, frequency and duration is also derived outcomes from movement and heart rate sensors. Movement sensors like accelerometry and pedometers have advanced technologically over the years. Accelerometry has the ability to capture activity in 3 plans/axes and to detect changes in position (standing versus sitting), which has been some of the limitations [17, 24]. Activities like cycling, water-based activity, upper-body or resistance exercise are problematic to capture by accelerometry. Heart rate sensors are limited to detecting activity of light intensity. Devices that combine movement and heart rate in one sensor have been developed over the last years, thus overcoming some of the limitations connected with each of these sensors separately [25].

Information on type of PA, where the PA takes place and in what context can best be obtained through direct observation and self-report. Doubly-labeled water gives no information of type, context, intensity or duration, but provides accurate measures of PAEE. Combination of both self-report and objective measures will complement each other and probably provide the most accurate information when it comes to habitual PA behavior. Furthermore, one must keep in mind that quantification of self-reported PA

behavior are estimates of perceived behavior, not the actual behavior [17]. In the same vein, using self-administered PA questionnaires to capture intensity generally gives perceived intensity, i.e. how hard the individual *perceives* the activity to be, which is closer to relative intensity than absolute intensity [24]. Estimates of PAEE (absolute intensity) or VO_2 max (relative intensity) are the attributes to which a self-reported instrument is compared. Furthermore, evaluations of the validity of PA questionnaires assessed in one population cannot be directly compared and used in other populations, ethnic groups or geographic areas. Comparing studies using various assessment tools is also a challenge.

Although there has been enormous strides made in the development of more sophisticated technology to measure PA objectively, most public health guidelines on PA are based on research that used self-reported PA questionnaires to investigate the relationship between PA and different health outcomes [24]. This is not to say that self-report has not been an invaluable method, and probably will continue to be so in the future, despite the lack of a gold standard PA questionnaire.

1.3 Physical activity and all-cause mortality

In 2007-2011, the age-standardized mortality rate among women in Norway was 138 per 100.000 for cancer, and 125 per 100,000 for CVD [26]. Among women in Norway in 2010, the most frequent causes of cancer mortality were lung, colorectal and breast cancer [27]. Lack of PA in daily life is considered the fourth leading cause of mortality worldwide [28]. In 2009, less than 30 % of the adult Norwegian population reported adhering to the national recommendations of 30 minutes of moderate to vigorous PA per day [29], and a recent report from a survey in North Norway concluded that only 22% of the adult population complies with the recommendations [30]. A growing body of evidence from epidemiological studies supports a strong, inverse association between PA and all-cause mortality [11, 31-35].

Furthermore, an enormous amount of information on the relationship between PA and mortality has been published between the early 1950s, when this kind of research started and the present [7, 14, 36]. As knowledge developed, the importance of habitual PA across different domains, not only occupational PA, in the inverse relationship with all-cause and disease-specific mortality became evident [3, 5, 7, 36, 37]. Sedentary behavior contributes to 9% of premature mortality worldwide, or more than 5.3 million of the 57 million deaths that occurred worldwide in 2008 [8]. In 2009, Katzmarzyk and colleagues reported that individuals who were performing moderate to vigorous PA 5 days a week, as per recommendation, but who also had an increased sitting time compared to those who reported almost no sitting time, had an increased risk of all-cause mortality [38]. Results from the Nurses' Health study showed that increased adiposity and reduced PA are strong, and independent predictors of all-cause mortality [39]. A study investigating the risk of all-cause mortality among men and women found that both self-reported PA and measured CRF were inversely related to all-cause mortality. However, the association

was strongest for the CRF measure compared to self-reported PA, and therefore the authors concluded that it was likely that the effect of PA on mortality was largely mediated by CRF [40]. Findings regarding domain-specific PA and mortality indicate inverse relationships with the risk of all-cause mortality, with reduced risk of mortality for work-related PA, leisure time PA and total PA. For CVD mortality, a reduced risk was found for work-related, household, leisure PA and total PA. For cancer a reduced risk was only found for leisure time and total PA, whereas there were no findings for transportation activity [41]. A meta-analysis of 38 different prospective studies involving 271,000 men and women aged 20-70 years, found a marked risk reduction with light and moderate PA of 24% for men and 31% for women, with only a minor additional risk reduction for vigorous PA. However, the relationship was non-linear [42]. Others have argued that there is an evident dose-response relationship between all PA levels and health-related outcomes, with no lower or upper PA thresholds for benefits [7]. Furthermore, no obvious single volume of PA is recommended [5]. Several large cohort studies in women have reported an inverse association between PA and mortality [11]. A recently published large pooled cohort analysis on leisure time PA and mortality, found that even 75 minutes of activity per week equivalent to brisk walking, resulted in a 19% reduced risk of premature mortality and corresponded to a gain of 1.8 years of life. Increasing leisure time PA to 450 minutes per week of brisk walking gained 4.5 years of life. Furthermore, the association between leisure time PA and life expectancy was evident at every level of body mass index (BMI) [6]. The dose-response relationship varies with different health conditions, most likely because the physiological and biological pathways vary, although the shapes are quite similar [5]. Figure 2 by Powell and colleagues illustrates the knowledge about PA dose, i.e. the hours per week needed to reduce the relative risk (RR) for several health outcomes [5].

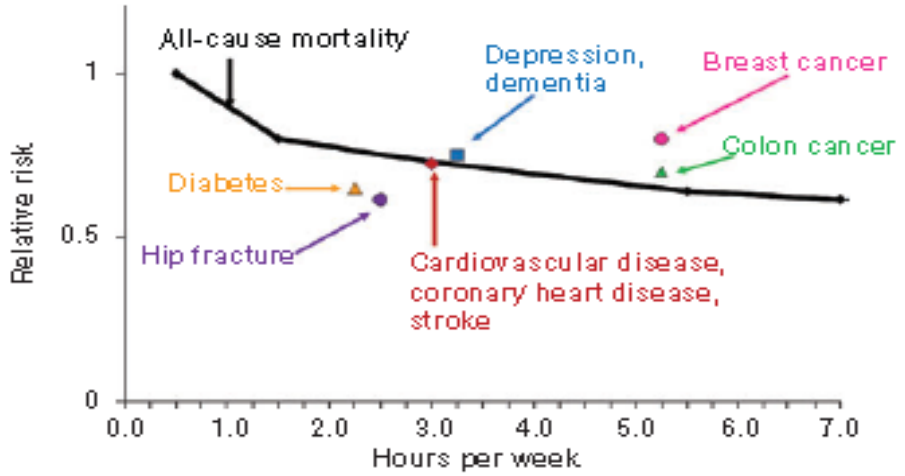


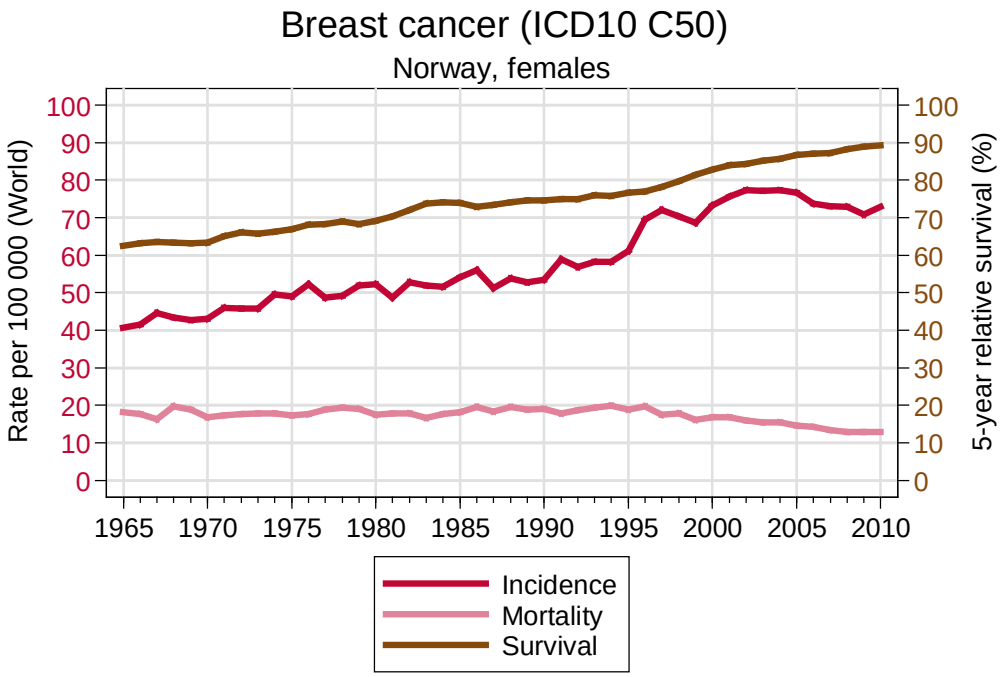
Figure 2 Risk patterns of different health events by frequency (hours/week) of moderate-vigorous physical activity. Reprinted, with permission ©Annual Reviews. *Powell KE, Paluch AE, Blair SN (2011). Physical Activity for Health: What kind? How Much? How Intense? On Top of What? Annual review of Public Health. Doi: 10.1146/annurev-publhealth-031210-101151.[17]*

Evidence suggests that the total volume of PA is most closely related to beneficial health outcomes over any one of component of PA separately [5]. The mechanisms through which PA works are characterized by multiple pathways, making it difficult to provide a single prescription for health effects in general [5]. The possible biological mechanism of all-cause, CVD and cancer mortality includes both higher CRF and energy expenditure. There is strong evidence that a sedentary lifestyle and low CRF are among the strongest predictors of mortality [14]. Higher CRF improves insulin sensitivity, blood lipid and lipoprotein profile, body composition, inflammation and blood pressure and the autonomic nervous system [43], as well as hormonal pathways through endogenous hormone levels [44]. Further details regarding biological mechanisms are beyond the scope of this thesis.

1.4 Physical activity and breast cancer

1.4.1 Occurrence of breast cancer

Breast cancer is the most frequent cancer type among women worldwide in terms of both incidence and mortality [45-49]. The global burden of breast cancer is highest in developed countries, accounting for 55% of cancers, but rapidly increasing rates in developing countries have given rise to concern [50]. Breast cancer comprises one-quarter of all incident female cancers in Norway, and in 2010 2,839 new cases of breast cancer were reported to the Cancer Register of Norway [27]. The incidence rate of breast cancer has declined by 5% in Norway between 2005 and 2010. However, the 2010 update from the Cancer Registry of Norway indicated a slight increase in incidence, as illustrated in Figure 3 (see red line) [27]. In Europe the age-specific incident rates have also been declining since 2002 in women aged 50-64 years, when the majority of breast cancer events occur [45]. In 2008 breast cancer was the major contributor to life-years lost and life-years saved of all disabilities worldwide [48]. The rise in cancer burden worldwide is mainly lifestyle related [48, 51]. On the other hand, breast cancer mortality has been declining since the early 1990s in many high-risk countries. The main reasons for this are a combination of mammographic screening, improved clinical diagnosis and advances in primary and adjuvant breast cancer treatment [50]. A recent meta-analysis that included 11 randomized trials found a reduction in RR of 20% for breast cancer mortality among women invited to mammographic screening compared to controls [52]. The Independent UK Panel on Breast Cancer Screening concluded in their recent report that some over-diagnosis occurs due to mammography screening, and that mammographic screening does reduce the incidence of invasive breast cancer and reduce the breast cancer mortality [53].



Source: Cancer In Norway 2010. Cancer Registry of Norway.

Figure 3 Trends in incidence and mortality rates and 5-years survival proportions for breast cancer. Reprinted, with permission from Cancer Registry of Norway. *Cancer in Norway 2010.* [27]

Breast cancer is a heterogeneous disease [50, 54], and hormonal factors play a clear role in its development, although detailed knowledge of the different pathways is currently lacking [55, 56]. Breast cancer can be divided into different subtypes based on clinical, histological and molecular classifications systems [57]. The clinical classification is based on the Classification of Malignant Tumors and includes stage, grade, size, affected lymph nodes and metastases [50]. Histologically, breast tumors are divided into ductal and lobular carcinomas. There are five subtypes defined by tumor marker expression: luminal A (estrogen receptor [ER]-positive and/or progesterone receptor [PR]-positive and human epidermal growth factor receptor 2 [Her2]-negative), luminal B (ER-positive and/or PR-positive and Her2-positive), Basal-like (ER-negative, PR-negative and Her2-negative), Her2-overexpressing (ER-negative, PR-negative, Her2-positive) and normal breast-like tumors [57]. In this thesis, ER and PR status of breast tumors will be

investigated, as these were the only tumor markers consistently available in the Cancer Registry of Norway database, which is the source of breast cancer diagnosis in our studies.

1.4.2 Physical activity and risk of breast cancer

In 1994 Bernstein and colleagues published breakthrough results from a case-control study of young women, investigating whether women who were exercising during reproductive age, had a reduced risk of breast cancer [58]. Findings showed that women who exercised ≥3.8 hours per week had an odds ratio of 0.42 (95% confidence limits 0.27, 0.64) compared to inactive women, and an even stronger effect was found among women who had given birth; odd ratio 0.28; (95% confidence limits 0.16, 0.50) [58]. Although there have been several studies published on this association over the years, they have resulted in conflicting evidence. Several reviews have summarized the evidence on the association between PA and breast cancer [59-62]. In the most recent review including 73 case-control and prospective studies, the author concluded that the average reduced risk for breast cancer among women engaging in PA was 25%. The association was found to be somewhat higher in case-control (30%) studies than in prospective cohort studies (20%). Furthermore, of the 73 studies in this review, 40% found a statistically significant risk reduction [62].

The study European Prospective Investigation into Cancer and Nutrition (EPIC) is a large prospective study that includes data from eight European countries. Reports from EPIC showed no association between total PA, leisure or work-related PA and breast cancer risk among postmenopausal women, but found a modest inverse association with household PA and breast cancer with risk reduction between 6% and 19% [63]. In their report from 2007, and later in updates from 2008 and 2010, the World Cancer Research Fund/American Institute for Cancer Research (WCRF/AICR) concluded that there is a probable inverse effect of PA on risk of postmenopausal breast cancer [64].

Associations between PA and breast cancer subtypes according to hormone receptor status have been investigated to a lesser extent. A recent study from EPIC investigating PA and overall breast cancer incidence by hormone receptor status found a modest inverse relationship between overall breast cancer and total PA, comparing high PA levels to low PA levels, which was similar for women diagnosed after the age of 50 years. Furthermore, analyses restricted to breast cancer subtypes found a stronger association for ER+/PR+ breast tumors and total PA, than for ER-/PR- breast tumors [65]. An earlier study investigating Norwegian women found no significant trends in leisure time and work-related PA on overall breast cancer risk in postmenopausal women, but found a modest inverse effect of PA in premenopausal women [66].

Although there are several prospective studies that support an inverse effect of PA and breast cancer risk when comparing the highest to the lowest PA levels [65, 67-79], the effect is modest. Some studies have observed a non-significant risk reduction [80, 81], whereas other studies have reported a null effect or only a borderline statistically significant risk reduction [63, 82-92], and some even found an increased risk of overall breast cancer with increasing PA level [93-95]. In cancer development the long latency period between exposure and onset makes it challenging to determine which period of life is most important for disease prevention [96]. Few studies have investigated the PA level over a women's lifetime, as most studies only have the information on PA at study enrollment, or at certain periods of life. The critical time period for PA in the etiology of cancer is therefore still unclear. However, it has been indicated that PA throughout a woman's life and especially after menopause is critical [62, 97-99]. Early investigations found that strenuous PA at age 14-22 years was associated with reduction in the risk of postmenopausal breast cancer [100], whereas others failed to detect any effect of sports at a young age [90, 101], or found only limited support for PA during adolescence [98].

(See appendix 1: Summary of the prospective studies investigating the association between of PA and risk of breast cancer in postmenopausal women published between 1987-2012)

1.4.3 Possible biological mechanism of physical activity in preventing breast cancer

The biological mechanism by which PA reduces the risk of breast cancer is still difficult to define, and likely works through a combination of complex processes. Insight into mechanisms would add biological plausibility to the association between PA and breast cancer, and are important in guiding epidemiological research, and contributing to public health recommendations [54]. Epidemiological and experimental studies have suggested different hypotheses on biological pathways, including reduction in circulating levels of, and cumulative exposure to sex hormones, reduction in insulin resistance and changes in insulin-related factors like insulin-growth factor I (IGF-1) and sex hormone-binding globulin (SHBG), reduction in leptin and adiponectin, modulation of the immune system and inflammation and reduction of body fat [51, 54, 61, 102]. Reduction of body fat through PA implies lower levels of adipokines, inflammatory markers, estrogens and testosterone (postmenopausal women) and contributes to improved insulin sensitivity and increased SHBG. The effects connected to reduced body fat are virtually the same as those of PA independent of reduced body fat, as there are demonstrated significant inverse associations between PA and breast cancer after adjusting for BMI or adiposity, and negative findings of effect modification [54]. In a review investigating the serum concentrations of sex hormones in postmenopausal women, women with high BMI had higher levels of estrogens compared to women with lower BMI [103]. The same investigation also found that SHBG level decreased with increasing BMI which could be explained by higher insulin concentrations, inhibiting SHBG synthesis in the liver [103].

It has been suggested that PA reduces insulin levels which in turn increases SHBG levels, thereby decreasing the bioavailabilities of estradiol and testosterone [54].

1.4.4 Other risk factors and breast cancer

PA is one of the modifiable risk factors with a probably role in preventing breast cancer. The other risk factors associated with breast cancer are both non-modifiable and modifiable in character, and several are related to circulating estrogen levels. Among the non-modifiable risk factors are, age, early menarche and late menopause in postmenopausal women. In Norway, as in several other Western countries, breast cancer incidence increases with age and 85% of breast cancer is diagnosed in women over the age of 50 years. The cumulative risk of breast cancer is the highest of all cancer sites, indicating that one in 12 women develop breast cancer before the age of 75, in the absence of competing risks [27]. For each 1-year delay in age at menarche, the risk decreases by approximately 5%, and the effect seems to be stronger in younger women [55], especially for ER+/PR+ breast tumors [104]. Late menopause also entails a higher risk of breast cancer, with a 3% increased risk per 1-year delay of menopause [50, 55].

Endogenous hormone levels, such as estrogens and androgens have been shown to influence breast cancer risk. Estradiol and estrone sulfate are the two most studied estrogens related to breast cancer risk. The proliferative effects of high levels of estrogens circulating in the blood, bound to SHBG, or bound to albumin or "free", may be implicated in carcinogenesis in the breast and tumor promotion [50]. An analysis from The Endogenous Hormones and Breast Cancer Collaborative Group containing nine prospective studies observed a dose-response effect of increased breast cancer risk with increasing levels of estrogens in postmenopausal women, with free estradiol showing the strongest effect [105]. These results have been confirmed in several other studies [50]. Similar associations have also been observed for high levels of androgens and breast

cancer in postmenopausal women, with the strongest association seen for testosterone [106, 107]. There is limited research related to high levels of progesterone, and one case-control study observed no relationship between progesterone levels and breast cancer in postmenopausal women [108]. With respect to breast cancer and IGF-1, a peptide growth hormone and the binding protein IGFBP-3, the research findings are inconsistent; lack of association, null associations and modest positive associations have all been reported [50]. In 2009, Gunter and colleagues reported on a large analysis of postmenopausal women that showed a 1.21-fold increased RR for women in the highest quintile of circulating IGF-1 concentration, though it was not significant [109]. Overall, higher blood concentrations of estrogen and androgens rank among the strongest risk factors for postmenopausal breast cancer [50].

Of breast cancer that arises in women with a family history of breast cancer, 5%-10% can be directly attributed to heredity. It is assumed that familial breast cancer is attributable to a small number of high-penetrance susceptibility genes, such as breast cancer susceptibility genes 1 and 2, commonly known as BRCA1 and BRCA2 [50].

Reproductive history is also important in breast cancer development. Nulliparous women and women with late age, i.e. 35 years, at first childbirth have an increased risk of breast cancer compared to women who had their first childbirth before age 20 years [50, 104]. Compared with nulliparous women, women with at least one childbirth reduce their risk of breast cancer by around 25%, and the risk decreases further with increasing number of births [55]. Studies on the effect of parity on breast cancer mortality in Norwegian women showed a decreased risk of death from breast cancer with increasing parity [110]. There are also findings stating that longer duration of breast feeding (i.e. ≥12 months) is correlated with a reduced risk of breast cancer [104, 111, 112].

Anthropometric factors are also related to breast cancer risk [113]. Attained height is considered a proxy measure of early-life nutrition, regulated by growth hormones, and is established as a risk factor for breast cancer [50]. Indeed, studies have shown that taller people have an increased risk of postmenopausal breast cancer [55, 113-115]. A large prospective study among women in the United Kingdom showed an increased risk of 16% for every 10 cm of increased height [115]. Furthermore, the relationship between BMI and the risk of breast cancer has been investigated extensively, and main findings show that the role of BMI differs by menopausal status. The risk of premenopausal breast cancer is reduced in women high BMI, whereas the opposite is true for postmenopausal breast cancer [113]. Studies have also observed that use of hormone replacement therapy is an effect modifier in this relationship, as there was no effect of high BMI on breast cancer risk in users of hormone replacement therapy [116]. Studies focusing on weight gain in women have reported a 5% increased risk per 5 kg of weight gained in adulthood [113], and that hormone replacement therapy acts as an effect modifier in the association with weight gain as well [50].

The association between oral contraceptive use and breast cancer risk has been investigated and findings suggest an increased risk in current users [55]. The NOWAC study has generated findings suggesting an increased risk of breast cancer associated with long-term use of oral contraceptive of any type [117, 118]. There are also several studies that found no relationship with duration of oral contraceptive use, but there is consistent evidence that recent use of oral contraceptive increases the risk of breast cancer in premenopausal women [50]. Observational studies and clinical trials have demonstrated an increased risk of breast cancer is associated with use of hormone replacement therapy [119, 120]. This has also been confirmed in the NOWAC study, in which a strongly increased risk of breast cancer was found among current users of hormone replacement therapy [121]. Several studies reported a consistent increased risk of ER+/PR+ breast

tumors subtypes related to use of hormone replacement therapy, but no association with ER-/PR-breast tumors [50].

Observational studies have shown that alcohol consumption increases the risk of breast cancer [122-125], and WCRF/AICR concludes that the evidence is convincing [113]. The risk increases around 10% per 10 grams of alcohol consumed per day and there seems to be a linear dose-response relationship, i.e. a consumption of around 30 grams per day increases the risk by 30% [123]. The effect of smoking on breast cancer risk has been shown to be limited. Some recent studies have shown an increased risk of breast cancer among ever smokers compared to never smokers, and that high quantity (pack-years), younger age at smoking initiation, and smoking duration before first childbirth increase the risk [126, 127].

2 Aims of the thesis

The aims of this thesis are to study the association between PA and all-cause mortality and breast cancer risk according to hormone receptor status of breast tumors in Norway. To do so, we used the NOWAC study. We validated the original assessment of PA used in the NOWAC study, hereafter named the NOPAQ, which was done using a questionnaire.

Thus, the specific aims were to:

1. Investigate the criterion validity of the PA questionnaire, NOPAQ, when compared to PA measured with a combined heart and movement sensor.
2. Explore prospectively the association between PA and all-cause, CVD and cancer mortality among Norwegian women in the NOWAC study and calculate population attributable fraction (PAF) of PA on mortality.
3. To study the effect of PA in different periods of life and the risk of postmenopausal breast cancer overall and classified by ER and PR status of breast tumors in the NOWAC study.

3 Material and methods

The study participants included in Paper I, which investigated the criterion validity of the questionnaire on PA in the NOWAC study were Norwegian women randomly selected from the National Population Register, Statistics Norway. The study participants in Papers II and III are participants of the NOWAC study.

3.1 Paper I - The NOPAQ validation study

In order to better understand the design rationale for the validation NOPAQ study, a glance into the international collaboration behind the NOWAC study is essential. The NOWAC study is part of EPIC, which was designed to investigate the relationship between nutrition and cancer and comprises more than 500,000 participants from 10 European countries [128]. The short PA questionnaire used in EPIC is the same as that used in the InterAct and Physical Activity, Nutrition, Alcohol, Cessation of smoking, Eating out of home And obesity (PANACEA) studies, which are based on the EPIC cohort. The InterAct study aimed to validate EPIC's short PA questionnaire, as well as two other questionnaires; the International Questionnaire of PA and Recent PA Questionnaire, and included 200 participants from each of 10 European countries. The criterion instrument was a combined heart rate and movement sensor. The Norwegian center of EPIC, represented by the NOWAC study, became part of EPIC in 1998, and thus did not use the EPIC short PA questionnaire. The participants of the NOWAC study were asked to report their PA using a 10-category scale in the 4-to 8-pages questionnaires used in the study. We therefore aimed to validate the NOPAQ in a sub study of the InterAct validation study. Therefore the NOPAQ validation study consisted of the same Norwegian sub sample and followed the same design and protocol as the InterAct validation study [129]. To assure a 200-participants study sample a random sample of 600 women aged 40-55 years living in Tromsø was drawn in 2007 from the National

Population Register, Statistics Norway. Due to emigration and unknown addresses, 589 women were found to be eligible and were invited to participate in the study. The participants had to live in the same municipality as the investigation premises at the University of Tromsø, and had to match the age of the original sample in the NOWAC study.

A total of 221 women agreed to participate; however 23 women did not come to the first clinical visit, resulting in an initial study sample of 198 women (overall response rate 33.6%). Following the two clinical visits complete data was available for 177 women: four did not provide sufficient free-living data at visit 1 and a further 17 had missing data from visit 2 (Figure 4). Exclusion criteria were conditions that had led to mobility limitations, which made walking unaided impossible. To determine whether the participants were able to perform the sub-maximal PA calibration test (step-test) they completed a general questionnaire on chest pain and safety of exercising based on the Rose Angina Questionnaire [130] and the Physical Activity Readiness Questionnaire [131]. Participants taking medications that affected heart rate (use of beta blockers, 50% or more of maximum dose, n=1) were excluded from the step-test, but were included in all other parts of the study.

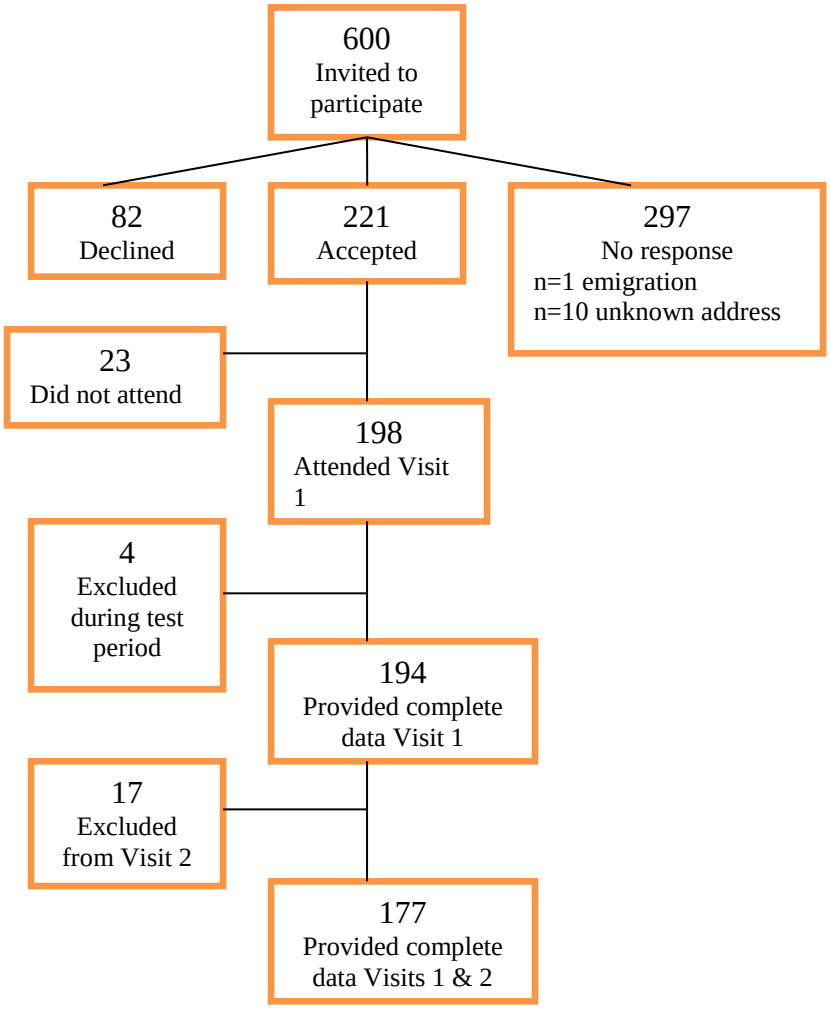


Figure 4 Flow chart for inclusion in the NOPAQ validation study.

Prior to the clinical visits all study staff attended a training seminar at the MRC Cambridge to standardize the procedures. The participants attended two clinical visits approximately 4-6 months apart in 2007-2008 (Figure 5). At each visit, the women completed the NOPAQ (Figure 6), rating their overall PA level on a 10-category scale (1 being a *"very low"* and 10 being a *"very high"* PA level) and were fitted with a heart rate and movement sensor (Actiheart, Cambridge Neurotechnology, Ltd.), which was attached to the chest via two standard electrocardiography electrodes. Height, weight,

waist and hip circumferences were also measured, and an 8-minute step-test was performed to estimate CRF (VO_2max) and to determine the relationship between heart rate and workload. The step height was 200 mm (similar to that in 'the Modified Canadian Aerobic Fitness Test' [132]). The step pattern was up-up-down-down (=1 body lift), and started at 60 beats per minute (bpm) (15 body lifts per min) for 1 min, increased by Δ0.15 bpm every second (by a ramped increase in step frequency) for a total of 8 minutes (to a frequency of 125 bpm) or until volunteer wanted to stop or was unable to keep the pace. During the step-test heart rate was monitored with a Polar heart rate monitor (F4™ Black Thunder, Polar Electro Oy, Kempele, Finland). The criteria for stopping the step-test were as follows; the participant wanted to stop, the participant reached 90% of the age-predicted maximal heart rate, or the participant had been exercising at or above 80% of age-predicted maximal heart rate for more than 3 minutes. After 2 minutes of recovery immediately after the step-test, the Actiheart sensor was initialized for long-term recording summarized into 1-minutes epochs, for 4 consecutive days of free-living.

All data collected by the Actiheart sensor were cleaned and processed at the MRC Epidemiology Unit, Cambridge, United Kingdom, which included estimation of activity intensity (J/min/kg) for each time point by acceleration [133]. The equation for the relationship between PAEE and heart rate from the step test was as follows; PAEE [J/min/kg] = (6.22 - 0.003 * age + 0.28 * sex - 0.0062 * sleeping heart rate * heart rate above sleeping heart rate + 0.21 * age + 3.9 * sex - 0.97 * sleeping heart rate - 31.8 (age in years, sex coded as 1 for men and 0 for women) [129]. The heart rate trace was processed using a robust Gaussian Process regression method to handle potential measurement noise [134]. For each time point the activity intensity (J/min/kg) was estimated from the combination of movement registration and individually calibrated heart rate [133] using a branched equation framework [135]. In order to detect periods of non-wear the

combination of non-physiological heart rate and prolonged periods of inactivity was identified. The movement sensor provided activity counts which were converted into units of acceleration ($m/s^2/d$) as recommended in the literature [136, 137]. The intensity time-series were summarized into time spent in moderate to vigorous PA (%time/day) or sedentary time (%time/day) which were presented as hours/day in Paper I.

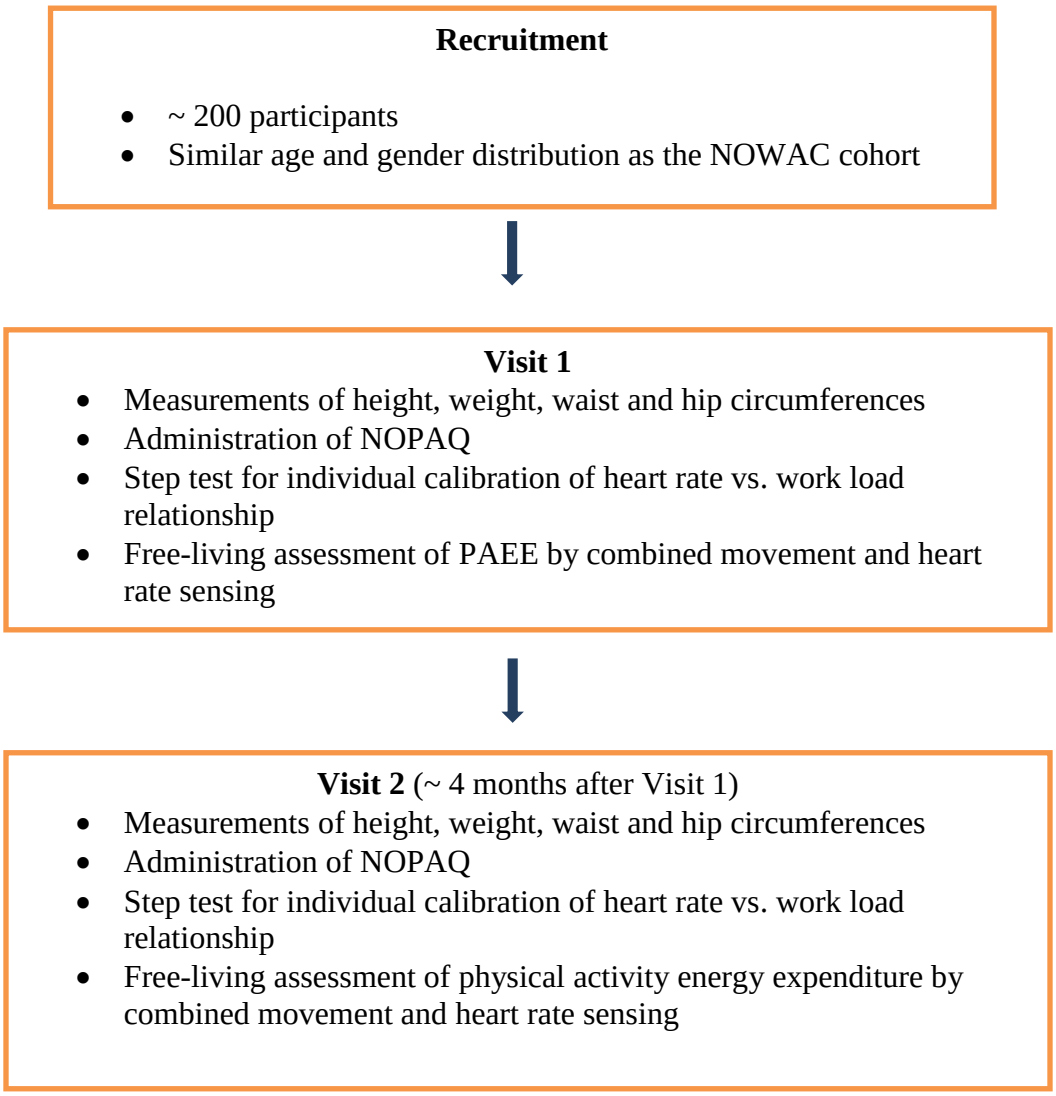


Figure 5 Study design of the NOPAQ validation study (the figure is based on the InterAct validation study design in Peters et al [129])

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

Figure 6 the question on PA (NOPAQ) in the NOWAC study.

(See appendix 2. Letter of invitation to the validation study, appendix 3. Consent of participation in the validation study, appendix 4. Procedures first visit, appendix 5. Procedures second visit and appendix 6. Actiheart instructions to the participants)

3.2 The NOWAC study

The NOWAC study is a national, population-based cohort study which was initiated in 1991[138]. Details of the NOWAC study, the scientific rationale, and its design and baseline characteristics have been published elsewhere [138, 139]. The primary aim of this large cohort study was to investigate the association between oral contraceptive use and breast cancer risk, and was further expanded to other outcomes and risk factors. The study was based on sampling from the National Population Register of Norway to ensure representativeness and external validity to estimate RRs and population attributable fractions, as these estimates have important implications for planning public health strategies [138, 139]. All women of Norwegian citizenship have an 11-digit national personal identification number, which is assigned at birth and registered in the National

Population Register. This number is used in all official registers in Norway. Statistics Norway has a drawing register linked to the National Population Register, which enabled to draw a random sample of adult women born between the years 1943-1957 and replace their personal number with a serial number for depersonalized data. Repeated measurements of exposure information every 5-7 years is also made possible by using the national registers.

Participants born in 1927-1957 were enrolled in three main waves in a stepwise manner, mainly due to practical administration reasons, limited financial support, and the performance of methodological sub-studies. The first participants were enrolled in 10 mailing series in 1991. The second wave of enrollment took place in 1995-1997, mailing series 17-24, and the third wave in 2003-2007, mailing series 35-36, 40, 41, 43-45 (Figure 7 the NOWAC study enrollment, red boxes). In the period 1998-2002 those in the first 24 mailing series were invited to answer a second questionnaire, mailing series 25-29 (Figure 7 the NOWAC study enrollment, green boxes). Lastly, a third questionnaire was sent in 2004-2005 (Figure 7 the NOWAC study enrollment, yellow boxes). Written reminders were sent twice within each series.

A total of 179,388 women were invited to participate in the first and second wave in 1991-1997, among whom 102,540 completed the questionnaire. Sixty women refused to participate in the record linkage and were excluded, thus the total number of women in the NOWAC study was 102,480, representing series 1-24. The overall response rate in the NOWAC study was 57.5% [139]. The third wave (series 35-36, 40-41 and 43-45) occurred between the years 2003-2007, and 148,088 women were invited to participate and 70,081 responded positively. The response rate was 48% after correction for ineligible women due to emigration, death and unknown addresses. For the second questionnaire, series 25-29, the response rate was 81% (corrected for death and emigration).

The participants answered a detailed four-page questionnaire including questions on use of oral contraceptives and hormone replacement therapy, reproductive history, age at menarche and menopause, smoking habits, PA, alcohol consumption, anthropometric measures (height/weight), socioeconomic status, breast cancer screening, and family history of breast cancer, sun bathing habits and pigmentation, and self-reported diseases. Furthermore, a large proportion of the questionnaires contained an additional four pages on dietary habits. Thus, the questionnaires varied slightly with regard to length (2-8 pages) and type of questions. This thesis comprises data only from series 1-10, 11-16, 25-29, and 35-36 only (Figure 7). (See appendix 7. Letter of invitation and information to the NOWAC study first questionnaire, series 35, appendix 8. Reminder, series 35, appendix 9. Pamphlets on oral contraceptives and hormone replacement therapy, series 35, appendix 10. Questionnaire series 35, appendix 11. Letter of invitation and information to the NOWAC study regarding the second questionnaire, series 26, appendix 12. Questionnaire series 26)

3.2.1 **Paper II: Study sample**

In Paper II we collected baseline information from the women who answered the first mailing (series 11-16 and 19-24) in 1996-1997 (37,899 women), and those who answered a second mailing (series 25-29) in 1998 (46,965 women) for a total of 84,864 women (Figure 7). The rationale for including the second mailing as the baseline was the availability of information on dietary habits as this information was not included in the first mailing in 1991-1992. This gave the opportunity to adjust for total energy intake. The second mailing was also collected closer in time to the first mailing in 1996-1997.

We excluded 53 women with a reported date of emigration or death that was before the date of recruitment. We further excluded 8,137 (9.6%) women with missing information

on PA level at cohort enrollment and another 10,538 women due to lack of information on other covariates adjusted for in the analyses. Hence 66,136 NOWAC participants were eligible for inclusion in Paper II.

3.2.2 **Paper III: Study sample**

From the initial NOWAC cohort 122,857 women were included in this study sample, which included 22 series from the first mailing in the first wave and two series (35 and 36) from the second wave of first mailing (Figure 7). The rationale for this was to include all participants with baseline information available independent of information on dietary habits and total energy intake, as this did not show any association in our earlier (preliminary) analysis of interest. The follow-up time was then expanded to increase the power for cancer-specific analyses. In addition, we used information from the second mailing for those who responded to the first mailing series 1-10, to complete information about age at menopausal and PA level at age 14 and age 30 if available.

We excluded all women with prevalent cancer (n=4,620) at enrollment and those who died within the first year of follow-up (n=265), as they may suffered from a disease when answering the questionnaire at enrollment. After these exclusions 117,972 women remained in the cohort. Further, we excluded those women with missing information on PA status at enrollment (n=12,313), leaving a study sample consisting of 105,659 women. We aimed to analyze women who were postmenopausal at enrollment and those who became postmenopausal during follow-up, which left a study sample of 93,424 postmenopausal women. Finally, we excluded participants with missing information on covariates. The proportions of missing data on covariates ranged between 0.1%-6.6%, and were lowest for age at first childbirth and highest for alcohol consumption. This left a final analytic study sample of 80,202 postmenopausal women with complete information on PA at enrollment. Of the analytic study sample, 3.2% of participants had missing

information on PA at age 14 and 2.2% had missing at age 30, therefore the number of participants included in the analyses using PA level at age 14 and 30 were 77,623 and 78,477 respectively.

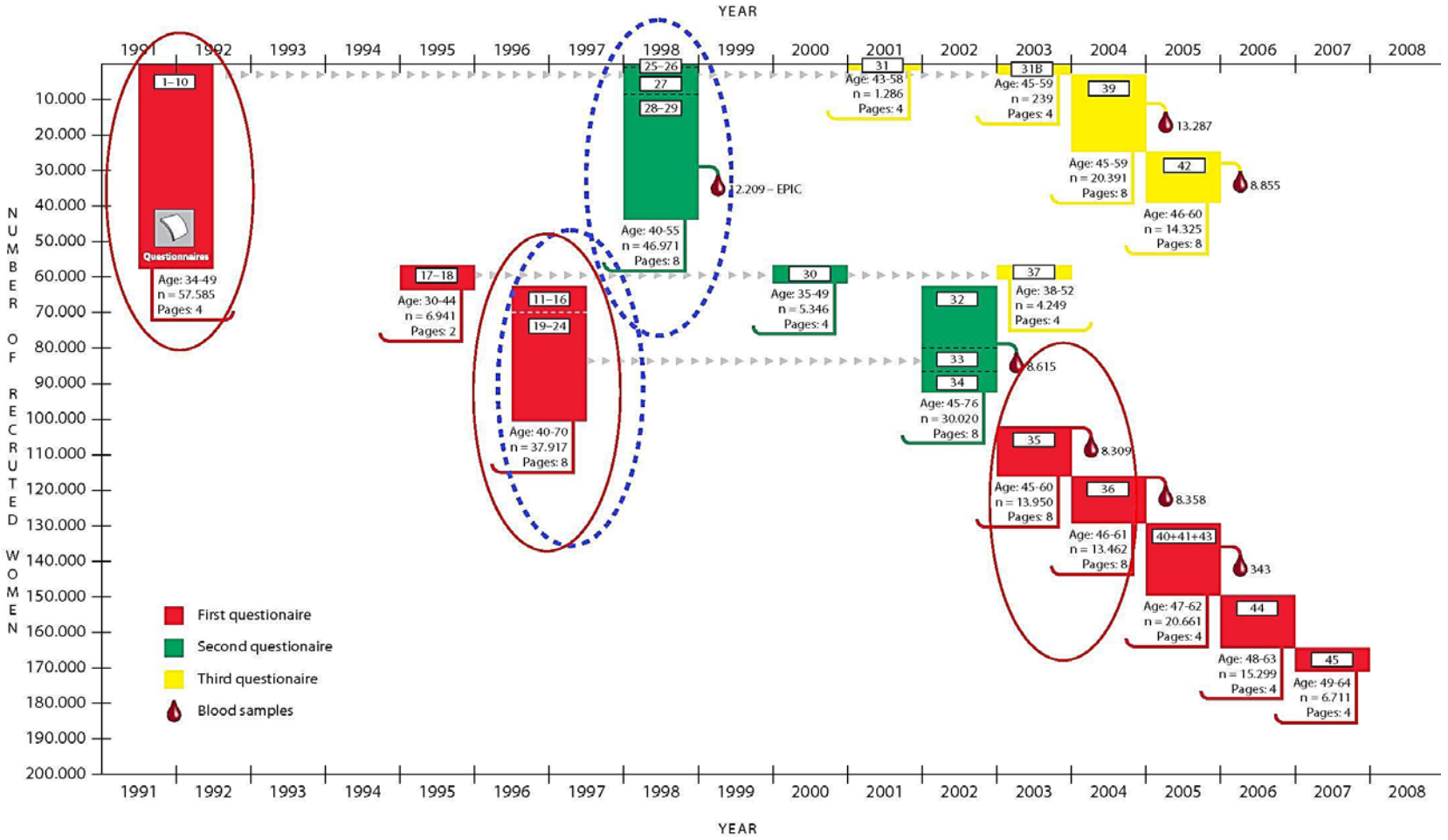


Figure 7 Cohort enrollment in the NOWAC Study (Paper II: blue, stippled circles. Paper III: red circles.

3.3 Ethics

The Regional Ethical Committee of North-Norway and the Norwegian Data Inspectorate approved the NOPAQ validation study and the NOWAC study. Written informed consent was obtained from each participant in the NOPAQ validation study. The women included in NOWAC study were asked if they consent to participate and marked this in the questionnaire, and were informed about later linkages to the Cancer Registry of Norway and the Cause of Death Register in Statistics Norway. The NOWAC study has a legal exemption from confidentiality rules for linkages to these registries.

3.4 Identification of cancer, vital status and emigration

Complete follow-up of cancer, death and emigration was performed through linkages to national registers using each individual's unique 11-digit personal identification number. The National Population Register keeps records of vital status (from the Cause of Death Register) and emigration in Norway, and the data is processed by Statistics Norway. Regular requests are sent to Statistics Norway to update the vital status of all the participants, and to confirm that they are still residing in Norway. For cancer status Statistics Norway links with the Cancer Registry of Norway to obtain information about date of diagnosis, cancer site and stage, and the hormone receptor status of tumors.

3.5 Statistical analyses

Analyses were conducted using STATA version 11.0 and 12.0, special edition (StataCorp, College Station, Texas, USA), with all statistical tests two-sided and conducted at the 0.05 significance level. Descriptive characteristics of the study population in each paper were presented as mean and standard deviations or frequency (%) or median with interquartile range. Paper I relied on the analysis of relative agreement between visits examined by a single-measure intra-class correlation coefficient (ICC) [140], and analysed with Analysis of variance (ANOVA) to check whether time between assessments influenced the ICCs. Spearman's rank correlation was used as a measure of criterion validity between the

NOPAQ and the different outcomes from the movement and heart rate sensor (PAEE, moderate to vigorous PA, accelerometry and VO_2max and zPAEE. We combined the VO_2max and PAEE by averaging their z-scores into a new variable zPAEE. In addition, linear regression analysis was used to examine the PAEE and zPAFIT at three levels of adjustments (unadjusted, adjusted for age and BMI, and with additional adjustment for VO_2max in the model for PAEE). The normality assumption of linear regression was examined by the Shapiro-Wilk test [141].

In Papers II and III the association between PA and outcome (all-cause, CVD and cancer mortality and breast cancer incidence, overall and by ER and PR status) were examined using Cox proportional hazards regression analyses to calculate hazard ratios, interpreted as estimates of RR. The precision of the estimates was assessed based on the 95% confidence intervals (CI). In Paper II follow-up time was assigned from the date of study entry to the date of outcome (all-cause, CVD (I00-I99) and cancer (C00-C97) mortality), emigration, death or end of follow-up (31 December 2008), whichever occurred first. In paper III follow-up were calculated from age at study entry for postmenopausal women and age at menopause for women who changed status from premenopausal to postmenopausal during follow-up to the date of breast cancer diagnosis, death or end of follow-up (31 December 2009), whichever occurred first. Breast cancer was defined as incidence of invasive breast cancer (C50), characterized according to ER and PR status, combined as follows: ER+/PR+, ER+/PR-, ER-/PR+, ER-/PR- and unknown status. The Cox proportional hazard assumption was checked using Schoenfeld residuals and Kaplan-Meier plots, which suggested no evidence of deviations from proportionality [142].

PA level and outcomes in Papers II and III were examined in age adjusted models, and then in multiple analyses models which included relevant and available confounders. PA

was treated as a 10-category exposure in Paper II, and included only the baseline measure of PA level. In Paper III the 10-category PA level used in Paper II was collapsed into five: very low (PA levels 1 and 2), low (PA levels 3 and 4), moderate (PA levels 5 and 6), high (PA levels 7 and 8) and very high (PA levels 9 and 10) PA levels. PA levels at age 14 years, 30 years and at study enrollment were examined separately, and also across periods to investigate the effect of changing PA levels. We dichotomized PA levels as inactive (PA levels 1-4) and active (PA levels 5-10) for each time point. We compared PA levels between ages 14 and 30, age 14 and enrollment, and between age 30 and enrollment. This led to four categories of PA: those who remained inactive, those who remained active, those who were active and became inactive, and those who were inactive and became active. Tests for trend were estimated using either the 10 (Paper II) or the 5 (Paper III) level scales and entered as a continuous term in the Cox proportional hazards regression models. Stratified analyses were conducted for subgroups of age, BMI, history of CVD, diabetes mellitus or cancer in Paper II, and for BMI and use of hormone replacement therapy in Paper III. Sensitivity analyses were conducted in both Papers II and III using Wald statistics [142] to test homogeneity.

In Paper II we calculated the PAF which was interpreted as the proportional reduction in the average population mortality risk that would occur if low PA levels were eliminated from the population, assuming the distribution of the adjustment variables remained unchanged. Following equation was used: PAF= (P_e (RR-1)/1+P_e (RR-1)), where P_e is the proportion of the exposed population and RR is the relative risk estimate for the exposed compared to the unexposed population in the final multivariate model [143]. The cut-off point *a priori* for the exposed population was set at a PA level ≤4, which divided the study population in two; exposed (PA level 1-4) and unexposed (PA level 5-10).

4 Results – summary of papers

4.1 Paper I: Criterion validity of a 10-category scale for ranking physical activity in Norwegian women

In this study we compared the self-administered PA questionnaire from the NOWAC study with a criterion method in middle-aged Norwegian women. A sample of 177 randomly recruited healthy women attended two clinical visits approximately 4-6 months apart. At each visit, the women completed the NOPAQ, rating their overall PA level on a 10-category scale (1 being a *"very low"* and 10 being a *"very high"* PA level) and performed an 8-minute step-test to estimate VO_2max. After each visit, the women wore a combined heart rate and movement sensor for 4 consecutive days of free-living. Measures of PA obtained from the combined heart rate and movement sensor, which were used as criterion, included individually calibrated PAEE, acceleration, and hours/day of moderate to vigorous PA. These were averaged between visits and compared to NOPAQ scores at Visit 2. The results showed ICCs for objective measures from both free-living periods were in the range of 0.65-0.87 (P<0.001), compared to 0.62 (P<0.001) for NOPAQ. There was a moderate Spearman's rank correlation coefficient in the range of 0.36-0.46 (P<0.001) between NOPAQ and objective measures of PA. Linear trends for the association between the NOPAQ rating scale with PAEE, hours/day of moderate to vigorous PA and VO_2max *(*P<0.001) were also demonstrated.

The conclusion of the study was that self-reported PA level measured on a 10-category scale is valid to rank PA in a female Norwegian population.

4.2 Paper II: Physical activity and mortality among Norwegian women – the NOWAC study

The objective of this study was to investigate what impact PA levels had on all-cause mortality in middle-aged women. We specified the RRs estimates of death due to CVD and cancer, and calculated the PAF of all-cause, CVD and cancer mortality associated with PA among Norwegian women. The results showed that PA levels 1-4 were associated with a significantly increased risk of all-cause mortality (level 1 RR=2.35; 95% CI: 1.94-2.84, level 2 RR=1.71; 95% CI: 1.45-2.00, level 3 RR=1.30; 95% CI: 1.14-1.49, level 4 RR=1.07; 95% CI: 0.95-1.22), compared with PA level 5. CVD mortality risk increased in PA levels 1-3 (level 1 RR=3.50; 95% CI: 2.41-5.10, level 2 RR=1.50; 95% CI: 0.99-2.25, level 3 RR=1.12; 95% CI: 0.79-1.60) as did cancer mortality risk (RR=1.32; 95% CI: 0.96-1.81, RR=1.48; 95% CI: 1.19-1.84, RR=1.26; 95% CI: 1.06-1.50, respectively). The magnitude of the associations was consistent across strata of age, smoking, and BMI. The PAFs for PA levels defined as inactive were: all-cause mortality, 11.5%; CVD mortality, 11.3%; cancer mortality, 7.8%.

In conclusion there was a significant trend of increased risk of all-cause, CVD and cancer mortality in relation to low PA levels among Norwegian women.

4.3 Paper III: Physical Activity and risk of Postmenopausal breast cancer – The NOWAC study

The objective of the third paper was to investigate the relationship between PA from age 14 years to adulthood and the risk of breast cancer overall and by ER and PR status. Among 80,202 postmenopausal women, 1,767 invasive breast cancer cases were identified during 8.2 years of median follow-up. Data on ER and PR status were available for 80% of the cases. In crude and multivariate adjusted models, breast cancer risk (overall and ER/PR status) was not associated with PA level at cohort enrollment. For PA levels assessed at age 30, an increased risk of ER+/PR+ (*P for trend*=0.04) breast tumors was observed with low PA level compared to moderate PA level, but not for overall breast cancer. In contrast, participants who were inactive at age 14 years and remained inactive in adulthood had a 20% significantly reduced risk of overall breast cancer, ER+/PR+ and ER+/PR- breast tumors compared with participants who were active in adolescence and remained active in adulthood. The findings were consistent over strata of BMI and use of hormone replacement therapy. Although the effect of low PA levels in adolescence and adulthood unexpectedly reduced the risk of postmenopausal breast cancer, there was also an inverse effect of PA levels in adulthood on the risk of ER+/PR+ breast tumors. Study results confirmed an inconsistency in the relationship between breast cancer and PA and highlighted the need to assess PA over a woman's lifetime.

5 Discussion of methodological considerations

The summary of the main outcomes of this work comprise a validation study of PA assessment indicating that the NOPAQ instrument is sufficient in ranking the PA level of Norwegian women, with limitation in differentiate between the different dimensions of PA, e.g. intensity, duration, frequency and type. Furthermore, we found that PA even at low levels would reduce the risk of early all-cause, CVD and cancer mortality in women. PA in different periods of a woman's life revealed inconsistent associations with risk of postmenopausal overall breast cancer and with ER and PR status of breast tumors, with a modest inverse association of PA at age 30 on ER+/PR+ breast tumors. Simultaneously, findings also suggested a decreased postmenopausal breast cancer risk in women who were inactive at age 14 and remained inactive over time compared to active women. Lastly, the risk of postmenopausal overall breast cancer or ER and PR breast tumors was not associated with PA level at study enrollment (i.e. 34-70 years).

Epidemiological studies present considerable opportunities for errors, which could take place in any step of the research process. The conclusions drawn from any analysis could, therefore, be limited. When looking at this question, one must consider the internal validity, i.e. whether the study provide unbiased estimates, and external validity, i.e. generalizability beyond the source population to one or more target populations [144].

Internal validity implies that the observed differences between the comparison groups on the dependent variables (in the case of this thesis all-cause mortality, CVD and cancer mortality and or risk of postmenopausal breast cancer) under study may be attributed only to the hypothesized effect of exposure under investigation (PA) [145].Internal validity is threatened by chance (random error), bias (systematic errors) and confounding [146]. Bias is often grouped into selection bias and information bias [144]. Under paragraph 5.1 the possible selection bias regarding study samples in Papers I, II and III

are discussed. Further, under paragraph 5.2 we are discussing the possible effect of information bias regarding the validity of outcome in PA assessment methods and the statistical analyses in Paper I (5.2.1). Followed by discussions about the validity of endpoints in Papers II and III (5.2.2), and validity of the statistical analyses and confounding factors in Papers II and III.

5.1 Selection bias

Selection bias in a cohort study can result from the procedures used to select participants, from factors that influence participation in the study and whether the participants in the exposed and unexposed groups display systematic differences in important aspects besides the investigated exposure [144]. Selection bias can distort the estimated effect of the exposure on the outcome.

5.1.1 **The validity of the NOPAQ (Paper I)**

In Paper I the initial sample of 600 women was randomly selected from the National Population Register, Statistics Norway. Due to death, emigration and wrong addresses, 589 women were invited, of whom 198 participated (33.6% response rate). The random selection of participants suggests a reasonable external validity, however the response rate was low, and therefore there is the possibility that the responders differ from the non-responders. Unfortunately, we have no information available for those who chose not to participate, as the Medical Research Ethics Committee in Norway does not allow information to be collected regarding non-responders. The important question is whether the responders differ from the source population, in this case the NOWAC study participants, who completed the NOPAQ in the framework of that study. We considered several factors in this regard. The City of Tromsø covers a large geographical area, and some of the eligible women could have been hindered from participation due to long travel distances. However, the residence of actual responders was distributed across the

entire municipality. The NOPAQ scale showed a normal distribution of PA level, suggesting that the study sample did not suffer from a skewed distribution in favor of more physically active women. The distribution of PA level was also comparable to that of the original NOWAC study population, as was the median of PA level. The mean age and BMI of the study sample were comparable to the NOWAC study population as well. Thus, it is unlikely that our analytic population suffers from severe selection bias, and we therefore assume that selection bias does not affect the ability to generalize our results to the NOWAC study population, although we cannot rule out the possibility entirely.

5.1.2 The NOWAC study (Papers II and III)

In prospectively designed cohort studies selection bias is less probable than in other epidemiological study designs (such as case-control studies), since the outcome is not known at the time of recruitment [147]. In this design, however, it could become a problem if participants in one exposure category are less often followed up than those in another group, and if the reasons for loss to follow-up are associated with the outcome of interest [147]. The NOWAC study has been constructed over the years to create a representative, population-based prospective study cohort with minimal loss to follow-up. In the study samples of Papers II and III, we reported a follow-up of more than 99%, which clearly strengthens our estimates.

With respect to non-response bias, the response rate in NOWAC was investigated at the time the study was initiated [148] in order to describe the responders versus the non-responders. The results showed that recruitment decreased with age, and that the highest response was in North Norway and for shorter questionnaires. Validation studies within NOWAC have also shown that the distribution of exposures is independent of response rate [148]. The healthy volunteer effect could be a source of bias, as volunteers are often characterized as healthier than the general population [149]. Earlier studies of the

NOWAC cohort have shown that responders are not significantly different from non-responders when it comes to number of children, use of oral contraceptives and number of years of education [139]. However, when comparing responders with a random sample of Norwegian women from Statistics Norway, the responders were younger, had a higher age at first childbirth, fewer were nulliparous or uniparous, but comparable if three or more children, and a larger proportion of women had slightly more than 12 years of education. The inconsistency regarding these results are probably caused by the small sample size in the study of responders versus non-responders, causing no significant differences [139]. The reasons given for not participating were lack of time, lack of interest, worries about confidentiality, or having forgotten to fill in the questionnaire. More than 99.5% of eligible women received the invitation due to the high quality of data in the National Population Register in Norway and of the postal service. There has also been a study on the selection of participants between the first and second mailing, and almost no differences were uncovered, except that women responding to the second mailing were slightly younger and more educated [138]. This supports our decision to use the second mailing in Paper II as a baseline measure, as there is only a minimal possible selection of participants.

The proportion of women with missing information on PA level in the study samples in Papers II and III was 9.6% and 10.4% respectively. PA information comprised the highest proportion of missing information in the NOWAC data. The exclusion of all women with missing PA information could lead to item non-response bias if participants with missing PA were significantly different from the eligible participants in the NOWAC cohort, or from the participants with PA information present. One approach is to investigate if those included in the final analytical cohort in Papers II and III differ from all the eligible participants included in the NOWAC cohort. Sensitivity analyses were carried out comparing the distribution of available covariate information and are presented in Tables

1 and 2 for Papers II and III, respectively. The results suggest no significant differences between populations. However, this will not show whether the estimated effect measures were distorted, merely that the levels of measures were not characteristic of large differences.

Table 1 Characteristics of included versus eligible participants according to PA level in Paper II

Characteristics	N*	Included	N	Eligible
Age, mean (years)	76,727	51.0 (6.8)	84,864	51.3 (7.0)
Duration of education, mean (years)	72,962	11.9 (3.4)	79,993	11.7 (3.4)
Height (cm)	76,220	166.1 (5.6)	84,026	166.0 (5.7)
Weight (kg)	75,577	67.8 (11.3)	83,266	67.8 (11.3)
BMI (kg/m^2)	75,387	24.6 (3.9)	82,970	24.6 (3.9)
Current smoker (%)	76,222	31.4	84,023	31.4
Alcohol consumption mean (g/day)	70,644	3.2 (4.0)	77,916	3.1 (3.9)
Kcal intake, mean (Kcal/day)	61,526	1629 (441.5)	68,510	1608 (454.7)
Nulliparous (%)	76,727	8.5	84,864	8.5
Age first childbirth, mean (years)	70,182	23.9 (4.3)	77,549	23.9 (4.3)
Ever hormone replacement therapy use (%)	74,470	31.8	81,991	31.6
Postmenopausal (%)	59,504	55.5	66,335	57.5
CVD (%)	76,727	2.2	84,864	2.4
Diabetes mellitus (%)	76,727	2.0	84,864	2.2
Cancer (%)	76,727	4.32	84,864	4.4

*Women eligible for analyses were 84,864; 8,137 (9.6%) were excluded due to missing information on PA.

Table 2 Characteristics of included versus eligible participants according to PA level in Paper III

Characteristics	N*	Included	N	Eligible
Age, mean (years)	80,202	48.3 (7.9)	122,857	48.3 (8.6)
Height (cm)	80,202	166.2 (5.6)	121,598	166.1 (5.7)
Weight (kg)	80,202	66.3 (11.1)	120,380	66.4 (11.2)
BMI (kg/m^2)	80,202	24.0 (3.8)	119,921	24.0 (3.9)
Current smoker (yes)	80,202	32.1	120,771	32.5
Alcohol consumption , mean (g/day)	80,202	3.4 (5.0)	114,943	3.3 (5.6)
Nulliparous (%)	80,202	8.37	122,857	9.3
Age at first childbirth, mean (years)	80,202	23.9 (4.3)	122,742	23.8 (4.3)
Oral contraceptive use (%)	80,202	45.2	118,327	45.8
Ever hormone replacement therapy use (%)	80,202	22.2	120,590	21.0
Age at menopause, mean (years)	80,202	53.3 (4.8)[1]	29,781	48.3 (4.8)[2]
CVD (%)	80,202	4.5	122,857	4.9
Diabetes mellitus (%)	80,202	1.4	122,857	1.6

*Women eligible for analyses were 122,857; 12,313 (10.4%) were excluded due to missing information on PA.

[1]Menopausal age for all participants based on first questionnaire, second questionnaire and cut off age 53 years

[2]Menopausal age available only for participants menopausal at study enrolment (46,981)

Based on the information that is available, we can also compare the observed incidence rates of breast cancer from the NOWAC study with the expected rates from the Cancer Registry of Norway (Figure 8). The cumulative incident rate of breast cancer in the period 2005-2009 in the NOWAC study follows the shape of the national trend, arguing for the presence of severe selection bias. However, in Paper III we acknowledge that 21% of the participants diagnosed with breast cancer had unknown ER and PR status, and this could threaten the validity of that study due to possible selection bias, as receptor status was only available from the Cancer Registry of Norway for women who had undergone breast cancer mammographic screening. Participation in the breast cancer mammographic

screening progame is voluntarily, and those women who chose to be screened, could differ from those who chose not.

In conclusion, based on the material available and earlier investigations in the NOWAC cohort, suggesting a slightly higher education level among responders versus non-responders, we do not suspect that selection bias had a substantial effect on the RR estimates.

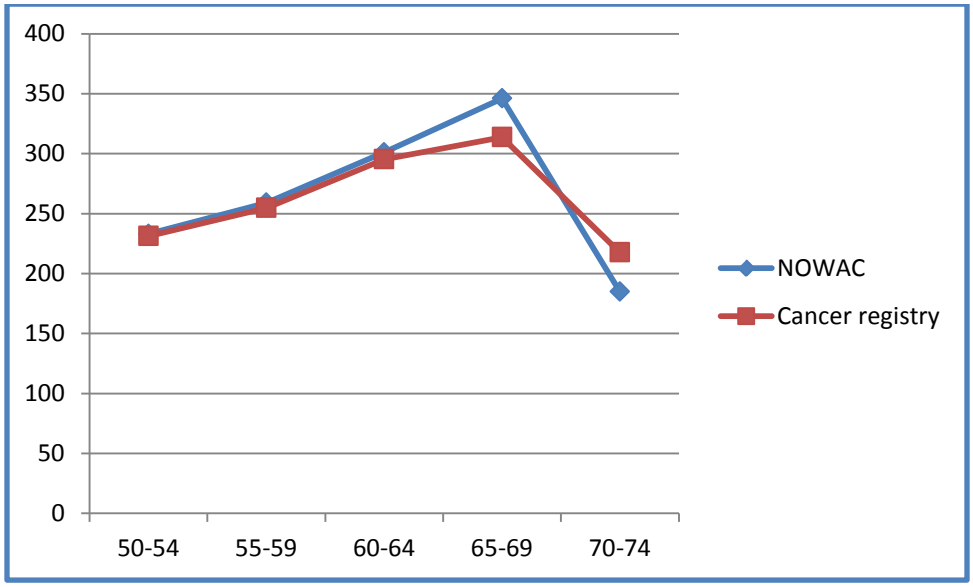


Figure 8 Cumulative age-specific breast cancer incident rates per 100,000 person year (2005-2009) in the NOWAC cohort and from the Cancer Registry of Norway.

5.2 Information bias

Measurements of exposure data in the NOWAC study were mainly based on self-administered questionnaires. Inaccurate exposure measurements are one of the main sources of information bias. The true exposure is often not measurable, and the way to operationalize the exposure is essential [150]. We therefore aimed to validate the measurement of the exposure of interest (PA) prior to the study of all-cause mortality and breast cancer. Below the possible measurement bias will be discussed.

5.2.1 Validity of physical activity assessment methods and statistical analysis in Paper I

Paper I investigated the criterion validity of the NOPAQ scale. Criterion validity is defined as "*the extent to which the measurement correlates with an external criterion of the phenomenon under study*" (Porta, 2008: page 252) [151]. Furthermore, we were interested in the concurrent validity, as one of the aspects of criterion validity, which implies that the NOPAQ and the criterion refer to the same point in time. The main aim of this validation study was therefore to evaluate the concurrent criterion validity of the self-reported instrument, the NOPAQ, in a cross-sectional design. The choice of concurrency omitted the possibility to investigate the measure properties of PA level at age 14 and 30 years, which was also included in the NOPAQ. The study protocol was similar to a standardized protocol used in a large validation study in 10 European countries [129].

The women were fitted with a combined heart rate and movement sensor, which was attached to the chest via standard electrocardiogram electrodes. The participants wore the sensor for 24 hours over 4 consecutive days over two different periods, which clearly measured all activity during this time, including sleeping. The ability to wear the device non-stop made it less vulnerable than waist-belt monitors, which need to be removed in

the evening, running the risk that the participant will forget to put it back on the next day. In addition, as the monitor was water resistant, we avoided the exclusion of water-based activities, again making non-wear time less of an issue.

The validation study was designed with two visits that took place 4-5 months apart, which allowed us to capture a wide range of habitual PA patterns over that time period. The number of days the device was worn is considered sufficient to derive reliable PAEE estimates [152]. However, considering daily variability in PA, and particularly differences across weekdays and weekends, a full week of monitoring would have been preferable. In addition, although the measurement was repeated once, and therefore reflects habitual PA more accurately than a single measure, due to seasonal variation it may have been preferable to repeat the measurement over a year in order to capture any eventual seasonal variation in PA level [153]. On the other hand, PA levels can be mediated by other factors as much as by seasonal influences [154]. The agreement the PA measurement between the clinical visits, expressed as ICC, was moderate to good, and this is supported by the fact that ICCs for the sensor-based measures were similar. Some of the differences could be explained by seasonal variations.

The criterion method used in this study was a heart rate and movement sensor (the Actiheart sensor), which has been previously successfully validated against indirect calorimetry and doubly-labeled water estimating PAEE [155-158]. One of the strengths using the combined heart rate and movement sensor is that heart rate and accelerometry are individually calibrated. Furthermore, a combined heart rate and movement sensor in a repeated measurement design and will most likely give a more robust estimate of the PA level, as compared to a single measure. The study participants preformed an 8- minute step-test to determine the individual relationship between heart rate and workload [129, 133]. Additionally, the parameters made it possible to estimate VO_2-max (mL/kg/min) by

extrapolating each individual's sub-maximal heart rate-PAEE relationship to an age-predicted maximum heart rate [159] and adding an estimate of resting metabolic rate [160]. The validity of the step-test has not yet been determined against a gold standard, but The Canadian Home Fitness Test, which is similar, correlates strongly (r=0.88) with directly measured oxygen uptake [161].The individual calibration of heart rate response to exercise strengthens the precision of estimation of PAEE [133, 158]. However, there are also limitations to using sensors that measure heart rate or accelerometry separately. Heart rate monitoring is less valid to measure PAEE during sedentary and light PA because it is influenced by factors other than body movement, e.g. temperature and emotional stress [162]. Accelerometry attached to the hip or trunk is less accurate in measuring activities such as cycling, swimming or other upper-body movements. The combined heart rate and movement sensor overcomes some of these mentioned limitations, and is considered a valid criterion method in quantifying PAEE [129].

For proper administration of the criterion instrument (the Actiheart) all staff was trained in a 2-day workshop by the Medical Research Center (MRC) Epidemiological Unit, Cambridge, which was responsible for the coordination of the InterAct validation study. Detailed training was given in use of the sensor, which included setting up the sensor before placing it on the participants, and downloading the raw data and transferring it back to the MRC Epidemiological Unit, where the data were prepared for analysis. Anthropometric measures of height and weight were taken by trained personnel using a standard protocol. Measures of height were assumed to be the same over a time period of 4-5 months in adults, and this was confirmed by the identical measures we found. Weight can change during a period of 4-5 months, but these measures were also comparable between the two visits (mean weight Visit 1 was 71.0 kg, standard deviation (10.8) versus 71.4 kg standard deviation (11.1) at Visit 2).

The statistical analyses were carried out using ICC to investigate the relative agreement between the Visit 1 and Visit 2. ICC is a general measurement of the strength of agreement for continuous variables, and expresses proportions of variance. The advantage of ICC is that it is adjusted for the effects of the scale of measurements [140]. Time between assessments could introduce a source of between-subjects variance into the data. Therefore sensitivity analyses using ANOVA were carried out, and indicated that there were no biased estimates due to different length of time between visits. The criterion validity was examined by Spearman's rank correlation coefficient (rho), which is an appropriate method for measurements taken from ordinal scales. The creation of the zPAEE variable was justified by the fact that intensity bias can distort the self-reported level of PA. We chose to use NOPAQ information collected at Visit 2 in the analyses. To ensure that this would not differ significantly from using NOPAQ scores from Visit1, we performed the same analysis and found that estimates did not differ statistically significant. Finally, linear regression was used to examine relationships between the PAEE and zPAEE measures and the NOPAQ, treated as a continuous variable, at three levels of adjustment. One limitation was that we were not able to adjust for other putative confounding variables, as they were not assessed. The statistical methods were considered appropriate to investigate the criterion validity of the NOPAQ. The sample size was considered acceptable for a validation study.

Overall, there were no important systematic errors in the information obtained from participants in this study. The results of the validity of NOPAQ as a self-report instrument will be further discussed in section 6.

5.2.2 **Validity of vital status and cancer assessment in Papers II and III**

In Papers II and III all-cause mortality (divided into CVD deaths and cancer deaths) and breast cancers (overall and categorized by ER and PR receptor status in breast tumors) were the endpoints of interest. In a cohort study information about endpoints should be obtained in the same manner, regardless of exposure [163]. Information on vital status and cause of deaths was obtained from Statistics Norway. The cause of death statistics are classified and coded according to the World Health Organization's International Statistical Classification of Diseases and Related Health Problems, 10th revision, and the Automated Classification of Medical Entities [164]. The potential source of error from vital statistics is mainly uncertainty regarding the cause of death by the physician filling in the death certificate. There is, however, subsequent contact with physicians to ensure the quality of the information on cause of death. Death notification is mandatory in Norway and the registration is valid [164], therefore our mortality outcomes in Paper II can be considered valid.

Information on breast cancer and ER and PR status of breast tumor was obtained from the Cancer Registry of Norway, which is considered to be one of the most complete cancer registries in the world [165]. Mandatory notification of cancer cases from hospitals, pathological laboratories and general practitioners is a matter of law in Norway, which is unique. Informed consent of the patient is not required, which is an important premise. As all persons residing in Norway can be identified with a unique 11-digit personal identification number, which provides a reliable means of tracking people and keeps the potential for duplicate to a minimum [165]. Still, there is always the potential for uncertainty, which may arise when filling in the notifications, together with the fact that notifications are sent retrospectively and delayed reporting by clinicians could degrade the quality. However, the data comes from different sources and delays are often

discovered by notifications from pathologists, death certificates (Statistics Norway) and the Norwegian Patient Register, whereas the clinical information is missing. The Cancer Registry of Norway sends reminders three times per years to all physicians and hospitals that have failed to report new cases, or given insufficient information for registration [165]. Studies have reported an overall completeness of over 95% for the Cancer Registry of Norway [165]. In 2008 the quality of the Cancer Registry of Norway was evaluated, and showed a high degree of comparability, completeness, accuracy and timeliness, with specific precision for breast cancer [165].

Breast tumors are classified by the Cancer Registry of Norway according to sensitivity to ER and PR binding. The classification is based on the proportion of ER and PR positive cells and is as follows: ER: positive test (positive > 50%), weak positive test (positive ≥ 10% and < 50%), negative test (negative < 10% and positive ≥ 1% and < 10%). For PR: positive test (positive > 50%), weak positive test (positive ≥ 10% and < 50%), negative test (negative < 10%). We had 21% of participants with unknown ER and PR status in breast tumors. This is due to the fact that the Cancer Registry of Norway has not registered this information for women diagnosed outside the breast cancer screening program until recently. The group of weak positive hormone receptor status (positive ≥ 10 % and < 50 %) represents a challenge how to treat this in the statistical analyses. From a clinical point of view, patients with ≥ 1% and < 50% positive cells would be considered as positive and treated with hormones [166]. In the statistical analyses we chose to do sensitivity analyses prior to the main analyses in the group of ER+ breast tumors, with weakly positive cases included and not included. If there was a difference in the effect of PA for breast tumors with strongly positive hormone receptor status compared to weakly positive tumors, it could distort the estimates of effect. The results of these pre-analyses showed that there was no significant difference in the RR estimates between the two different approaches. Therefore, we chose to add cases classified as weakly positive to the

group of breast tumors with positive hormone receptor status. Overall, we judge that the outcome according to the hormone receptor status of breast tumors in Paper III is valid.

5.2.3 Validity of statistical analyses and including confounding factors in Papers II and III

We adjusted for lifestyle factors in the multivariate analysis based on self-reported measures. In large epidemiological studies the advantage of using self-reported measure is practicality, low cost and easy administration [167]. To adjust adequately for confounders it is essential that these measures are valid. The internal validity of the NOWAC study has been previously investigated for this purpose, and was validated for specific items in the questionnaire, such as use of oral contraceptives, number of children, years of education [139], menopausal status and use of hormone replacement therapy [168, 169], and dietary habits [170-172]. The conclusions regarding these factors are considered valid in this cohort.

Other measures may be subject to measurement error due to misclassification, i.e. when the participant is classified into the wrong category. Misclassification was considered non-differential in Papers II and III, due to equal questionnaire measures and the fact that they are unrelated to any outcome at time of cohort enrollment. BMI is one of the important factors to consider in the relationship between PA and mortality and risk of breast cancer, as it is related to both. Increased body weight has been associated with mortality and morbidity in general [167], and also specifically associated with an increased risk of breast cancer in postmenopausal women [51]. Since PA helps maintain an energy balance and reduces body fat [51], these mechanism may influence each other and must be controlled for in the examined relations. Self-reported weight and height are well known to be underestimated (weight) and overestimated (height) due to recall bias

and/or social desirability bias [167, 173]. Thus, the calculation of BMI is prone to error, which could lead to misclassification. The tendency is toward underestimating, especially as BMI increases, but subjects within the normal range of BMI have been found to report these variables more accurately [167, 173]. A limited sample of women participating in the NOWAC study have information available on both self-reported height and weight, as well as weight and height measures that have been taken directly by medical staff. The results of this comparison are yet to be published, but suggests relatively small differences in self-reported versus directly measured weight (1.5 kg in mean difference) and height (<1 cm in mean difference) (personal communication Dr. Eiliv Lund and Mrs. Nicolle Mode, University of Tromsø, Norway), suggesting that the information on BMI in this cohort is valid.

For certain behaviors, e.g. smoking and alcohol habits, it can also be a challenge to capture accurate measures of "usual levels". Additionally, sensitive questions are prone to social desirability bias causing people to misreport (most likely under-report) their actual behavior [150]. Furthermore, studies investigating the association between alcohol consumption and breast cancer risk suggest that there is a modest, consistently positive relationship due to ethanol *per se,* regardless of type of beverage [174], with a moderate risk increase with increasing alcohol consumption when compared to non-drinkers [50]. We therefore adjusted for alcohol consumption in grams per day divided into four categories (none, 0.1-3.9, 4.0-10.0 and >10 grams/day) independently of type of beverage.

Participants with self-reported information on CVD and diabetes mellitus and information from the Cancer Registry of Norway on prevalent cancer had a lower PA level than who reported no disease. Similar findings were observed for participants excluded from the analyses due to missing information on PA; they reported a higher proportion of CVD and diabetes mellitus. CVD and diabetes mellitus or preliminary

stages of cancer may limit an individual's ability to remain physically active and therefore may distort the estimates for the effect of PA on breast cancer. Still, we chose to include those with CVD, diabetes mellitus and prevalent cancer in the analysis of all-cause mortality, and adjusted for self-reported disease in the models. We conducted sensitivity analysis in order to investigate whether this affected the risk estimates, compared to results obtained when after exclusion of these participants. The effect of PA on mortality remained consistent both in sensitivity analyses and stratified analyses. In Paper III we excluded participants with prevalent cancer, but we adjusted for other self-reported diseases as CVD and diabetes mellitus.

In Paper III we included participants that changed menopausal status from premenopausal to postmenopausal during follow-up. Women with missing information on age at menopause, age 53 years were used as a proxy for age at menopause. Women who reached 53 years or reported their age at menopause during follow-up (available from second questionnaire for some of the study women) were categorized as postmenopausal. One possible weakness with this approach is that we are modeling with information on PA and covariates (BMI, smoking habits, alcohol consumption, use of hormone replacement therapy, self-reported CVD and diabetes mellitus) measured at cohort enrollment, and do not take into consideration that the exposure level may have changed in the years after enrollment.

The statistical approach of using Cox proportional hazards regression analysis to investigate the associations of early mortality and incidence of breast cancer with PA, were considered appropriate to answer the research questions in Papers II and III. Additionally we calculated the PAF in Paper II based on adjusted RRs as the NOWAC cohort is representative of the adult Norwegian female population in the age group 30-70 years (see 5.3). The hazard ratio comparing any two specifications of predictors is

assumed to be constant over time (i.e. the hazard for one individual is proportional to the hazard for any other individual, where the proportionality constant is independent of time) [142], and was tested and fulfilled in our analysis. The multivariate modeling allowed adjusting for confounding factors. In Paper II we chose to build the multivariate model in a backward stepwise manner by manually removing the confounding factors that did not contribute statistically significant to the model. This was done attempting to model as sparsely as possible. In this way information regarding years of education and total energy intake were excluded from the final multivariate models after adjustments for other confounders, as these factors did not contributed in a statistically significant manner. This consideration was also based on earlier analyses of the association between breast cancer and socioeconomic status in the NOWAC study, where education did not have any effect on the incidence of breast cancer after adjustment for established breast cancer risk factors [175]. In model fitting we also investigated the association with total energy intake separately as a background analysis and found no statistical association, nor did this information contributed significantly in the multivariate modeling process. Therefore we removed it from the final model in Paper II. These two covariates were not included in the models presented in Paper III partly based on the investigation done in Paper II and because we did not have information on total energy intake for women recruited in the first 10 series.

For Paper III we chose to set the menopausal age as the time variable when modeling for Cox proportional hazards regression. We aimed to investigate only postmenopausal breast cancer risk associated with PA; therefore we included both those who reported a menopausal age at enrollment and those who became postmenopausal during follow-up. We thereby strengthened the power of the analyses by increasing the number of event. To do so we collected information about menopausal age from the questionnaire, in which women gave information about age at menopause if applicable. We then updated

information on age at menopause from the second questionnaire, if it was available. Lastly those women with unknown age at menopause who were ≥53 years old were classified as postmenopausal, as about 90% of the women above 52 years that had answered the questions about age at menopause reported that their menstrual periods had stopped by that age.

In Paper II we analyzed the association between PA and all-cause mortality, taking PA level at study enrollment into consideration. We could have also analyzed PA levels at different ages and changes in PA levels over time.

PA and other lifestyle factors are interrelated, as are several lifestyle factors related to the outcome of interest in this thesis. We therefore sought to adjust the models for known risk factors, however as sparse models as possible, despite the large sample size in both Papers II and III as mentioned above. Covariates collected in continuous format were grouped into categorical variables, if the sample size was sufficient to obtain stable risk estimates in each subcategory. For a few covariates, we chose to group information from several variables into one variable: for example age at first childbirth and number of children were combined into one variable, as was smoking status, age at smoking initiation and duration, resulting in one single smoking variable with five categories. We considered it essential to adjust for smoking, age at initiation smoking, duration and dose of smoking in the association between PA and risk of breast cancer [127]. We used ten categories of PA levels in Paper II, which was justified by the importance to identify those at the bottom end of the scale, i.e. PA levels 1 and 2, in order to visualize the difference in the effect on mortality outcome even at very low PA levels. In Paper III we analyzed PA in five categories, collapsing the original 10 levels two by two, into very low, low, moderate, high and very high, as this sufficiently visualized the effect and made the results easier to interpret. Moreover, we used different levels of PA exposure over three different time

points and changing PA levels combined with several outcomes according to different ER and PR statuses of breast tumor. Furthermore, we chose moderate PA level as the reference category in both Papers II and III, as this was the largest group and represented the women at lowest expected risk level in regard to PA.

In Paper II we adjusted for age, BMI, height, smoking status, pack-years of smoking, smoking duration and age at smoking initiation, alcohol consumption, menopausal status, and age at first birth, parity, use of hormone replacement therapy, prevalent cancer and self-reported CVD and diabetes mellitus. We further adjusted for reproductive covariates based on the results of the cancer mortality analysis. In Paper III we were able to adjust for almost all known risk factors for breast cancer, including reproductive factors such as age at menarche and menopause, parity and age at first childbirth, use of oral contraceptives and use of hormone replacement therapy, BMI, height, alcohol consumption, cigarette smoking, duration of smoking, age at smoking initiation and self-reported diseases as CVD and diabetes mellitus, and if the women's mother had a history of breast cancer.

In Paper II the PAF was calculated to estimate the effect of low PA levels on all-cause mortality, and separately for CVD and cancer mortality. The underlying RR used for this calculation was based on the adjusted models as these were judged to be the most correct estimates considering the possible effect of confounders [143].

In summary, despite certain limitations, the results in Papers II and III do not suffer from serious information bias that would distort the effect estimates.

5.3 Generalizability (external validity in NOWAC)

Selection bias must be distinguished from the selection of subjects, which potentially can affect the external validity [176], i.e. whether the results apply to a wider population than that included in the study , but that the study does not claim to estimate [151]. The participants of the NOWAC study were drawn randomly from the general female population of Norway according to age. Thereby the external validity has to a large extent been secured [138, 139]; together with the relatively high response rates, this suggests that our results can be generalized to the population of Norwegian women. Furthermore, as described under 5.1.2, a comparison of the cumulative age-specific breast cancer incidence rate for the period 2005-2009 in the NOWAC cohort and the national numbers from the Cancer Registry of Norway showed no marked differences, indicating the NOWAC study's representativeness for the female population of Norway (Figure 8).

6 Discussion of main results

The main results are discussed in details in the respective Papers I, II and III. In this section, the discussion will concentrate on how to interpret the results in the context of the international scientific literature. The methodological discussions above pointed out to some limitations in the three studies that should be considered when interpreting the findings. Still, the findings of the three papers hopefully comprise important contributions to the field of PA and health.

6.1 Assessment of physical activity

Self-reported on PA is widely used in large epidemiological studies, despite the known limitations of this methodology. The major challenge in the domain of PA and health is how to obtain valid and reliable data on habitual PA behavior in free-living in the populations of interest [24]. The operationalization of PA and determining the appropriate method of PA assessment depends on which facet of PA is relevant to the outcome. Indeed, the main objective is to measure PA as accurately as possible, with minimal participant burden and study costs. The choices made by researchers prior to study entry have important consequences that imply meeting some constructs of PA while omitting others. Important considerations in the NOWAC study, which was initiated in 1991, include the study's main aim to investigate the relationship between oral contraceptives and breast cancer, adjusting for other confounders in this relationship. In this context a global questionnaire consisting of a 10 point scale to discriminate levels of PA was considered sufficient to elicit information on current PA level, to differentiate physically active versus less physically active individuals at a population level. A ten-point scale was assumed to discriminate among PA levels to a higher extent than a five-point scale. As the cancer might develop after several years of exposure to potential carcinogenetic substances or risk factors (such as PA), it was important to gather

information over a longer time frame, so PA levels were recorded at age 14 and 30 years. Lastly, practical reasons and the length of the total questionnaire limited the space for each question included. In order to consider these factors, a global ranking scale was used to differentiate between levels of PA in the population of women as a secondary variable of interest. In large study populations there are several factors that can influence the measure of PA like age, cognitive function, cultural norms, highest attained education level, and general health status [17]. In the NOWAC study age ranged from 30 to 70 year at study enrollment, in which the woman's age may give a different apprehension of the NOPAQ scale. However, a global scale may be less cognitively demanding than more complex PA questionnaires. We relied upon recall of PA levels in the distant past. For the oldest participants it may have been a problem to recall PA levels at age 14 and age 30, and therefore past PA could suffer from a greater degree of misclassification. The main challenge is that different individuals may use different frames of reference to define their PA as behavior, and may also "translate" this into a number very differently. These references may differ based on recent events and experiences, life changes in a long-term perspective, and the acknowledgement that PA levels are not constant over life.

The results from Paper I confirmed that the NOPAQ provides a global assessment of ranking PA levels on a 10-point scale in adult women. Furthermore, the NOPAQ can be used to discriminate between different PA levels when estimating effect on outcome such as disease and mortality in an adult female Norwegian population. Despite the shortcomings of using a simple scale, the correlation between NOPAQ and PAEE, moderate to vigorous PA, acceleration and VO_2max derived from the criterion measure was moderate, with the strongest correlation for accelerometry (Spearman's rho=0.46). Self-reported PA also contributed significantly to explaining the variance in PAEE at all levels of adjustment, but the precision of the measure was limited. The results also suggested that the NOPAQ cannot provide differentiation of intensity, duration and

frequency as separate dimensions of PA, other than the total volume. Overall, our correlation coefficients are in accordance with results from other validation studies of self-report instruments [22].

CRF and PA are related to each other and physical fitness reflects an individual's recent activity pattern [20]. In our study we found a positive correlation between self-reported PA and VO_2max of Spearman's rho=0.36, with an increasing fitness level associated with increasing self-reported PA level. However, these variables are fundamentally different, whereas CRF describes a physiological condition, assessed by VO_2max in our study; the self-reported PA level in NOWAC is described as a behavior, and depends on how the participants perceive their PA level. The fitness level could be perceived by the participant in the way that it interferes with the reported PA levels, causing an intensity bias [177]. In the additional analysis we operated with the zPAFIT variable to account for this possibility by creating a composite outcome of PAEE and VO_2max. This resulted in only minor improvements in the correlation with NOPAQ suggesting that the NOPAQ does not suffer severely from any bias by VO_2max level.

The majority of validation studies of self-reported PA questionnaires indicate poor to moderate correlation when Pearson or Spearman's correlation coefficients are used, which suggest that most PA questionnaires are valid to rank PA levels, whereas their absolute validity is limited to quantifying PA as true behavior [22, 177]. This demonstrates the challenges of assessing free-living PA by self-report. Our study on all-cause mortality demonstrated the face validity of the NOPAQ scale in the relationship between PA level and CVD and cancer death, in which low PA levels convincingly suggested an increased risk of mortality compared to moderate PA levels. Our results in Paper I indicate that focusing of the total volume of activity in one global measure is sufficient to discriminate PA levels. Interestingly, our global measure of PA does not have

priority over other self-reported PA measures regarding the magnitude of the correlations estimates [22]. However, investigating specific diseases, such as the risk of breast cancer in relation to PA is perhaps more challenging. The dose-response effect of PA on breast cancer was inconsistent, and an inverse effect was found mostly when comparing the highest versus the lowest PA levels [62].The total volume of PA needed to reduce the risk of breast cancer has been suggested to be larger than for other diseases [5, 69], and is likely to comprise more than the current Norwegian recommendations of 30 minutes of moderate-intensity PA daily [178]. The WCRF/AICR has described the overall evidence of lack of PA as probably carcinogenic [113], which is regarded as sufficient evidence to issue PA recommendations and guidelines. For this reason it would be preferable to separate the total volume of PA into the duration, intensity and frequency, especially since the findings suggest that PA level higher than the existing recommendations is needed. Also, crude measures of PA may lead to false-negative results in addition to inconsistent results for the association of PA and disease risk [179].

As discussed above, PA was not the primary variable of interest in the NOWAC study and the use of self-report explains the rationale for a global scale. Paper I contributes with the exploration of the criterion validity of the NOPAQ used in the NOWAC study, which is necessary to evaluate the validity of the effect estimates of PA related to several health outcomes. Although there are limitations to using self-reported information, the results of the present validation study and Papers II and III in fact provide an overall insight into the role of PA in a Norwegian female population. When it comes to the need for more precision and accuracy regarding the intensity, frequency and duration of PA, other assessment methods, including self-report, must be considered. Self-report will remain an adequate method in large study populations and efforts must be made to develop valid and reliable self-reported PA questionnaires covering the PA dimensions of interest, and these questionnaires must be sensitive to changes in behavior.

6.2 Physical activity and all-cause mortality

In Paper II we found a significant trend that PA was inversely related to deaths caused by CVD, and a weaker but also statistically significant inverse relationship with cancer mortality, indicating that the all-cause mortality estimates were mainly driven by CVD deaths. Research suggests that there is no lower threshold for benefits of PA on health outcomes as early death, CVD, diabetes mellitus type 2, breast and colon cancer, and furthermore that the risk reduction is greatest at the lower end of the PA scale [5, 6]. Our results on all-cause mortality, CVD and cancer mortality confirmed both these suggestions; however, we found an upper threshold of effect of PA indicated that there is not much gain in increasing PA beyond the moderate level, which is in conflict with the established dose-response effect [5]. In contrast, in two recent meta-analyses of all-cause mortality [34, 42] the authors found a dose-response effect only from sedentary behavior to moderate PA, with only a limited additional effect beyond moderate PA levels. This is in concordance with our findings of a non-linear curve in the relationship between PA and all-cause mortality. A longitudinal study found inverse relationship between leisure time PA and overall cancer mortality, however non-significant, and further restricting the analysis to individuals without prevalent cancer did not change the results [180]. In contrast, our results showed a significant trend also for cancer mortality. However, we included total PA, not only leisure time PA.

Research on mortality shows that individuals with high levels of PA and CRF have been consistently associated with lower mortality, and that this association is consistent whether or not a chronic condition such as CVD is present [20]. This support our findings in Paper II arguing to include participants with self-reported diseases, despite their lower PA levels compared to their more physically active counterparts, and adjust for this in the multivariate models.

We have sparse information on type of PA, however it seems reasonable to assume that the main type of PA among women in the NOWAC cohort is walking, as evidenced by studies showing that walking is indeed the most common form of PA among Norwegian women [178]. We also have a PA question in the NOWAC study that was given to a limited sample of women who responded to a second follow-up questionnaire, asking particularly about type of PA. Unpublished results indicate that the main PA type is walking (personal communication Dr. Eiliv Lund, University of Tromsø, Norway). As pointed out earlier, we cannot examine intensity, frequency or duration of PA separately using our PA measure. However, in the relationship with all-cause mortality, the total activity volume seemed to be the most important measure [5].

The PAF represents the proportion of cases that would be eliminated if the whole population moved into a low-risk category while the other factors were held constant [143]. In calculation of PAF there was a difference between CVD and cancer of 11.3% versus 7.8%, respectively. Our PAF calculations may be underestimated as the prevalence of low PA levels included self-report, which probably underestimates the true prevalence. Furthermore, PAF estimates are dependent on the cut-off points set for the exposure [181]. We let the categories very low and low PA levels represent the exposed population, and this must be considered when interpreting and comparing the estimates. The proportions of the Norwegian population that does not adhere to the national recommendation of 30 minutes of moderate activity on a daily basis is around 50% [182], and in a surveillance study of 3,000 Norwegian men and women this proportion was estimated to 30% [178]. Thus, to what extent low PA levels can be eliminated from a Norwegian female population is debatable. Nevertheless, it is important to know the effect of potential risk factors might have in population-based strategies to shift the distribution of those same risk factors. Our results have shown that there is a

considerable gain in longevity to be had even when increasing PA levels from very low to low. Another Norwegian study found an inverse association between PA and mortality, among people with metabolic syndrome, and even low levels of PA reduced mortality [183]. A recent large pooled analysis found positive effects at very low levels of PA, i.e. 0,1-3,5 MET [6]. Although research findings suggest that there are beneficial effects even at light levels of PA, it is important to highlight that the total volume of PA needed to create beneficial effects against other diseases may demand a higher volume of PA, as we have indicated with our results in this work on the risk of breast cancer. We need to consider this when developing guidelines for PA and health for different target populations. Physical inactivity is considered the fourth leading cause of death worldwide [184], and the reduction, or removal of sedentary behavior could improve health substantially [8]. Our results together with the extensive body of research supporting an inverse relationship between PA and mortality from several diseases, give important contributions to public health strategies. Non-communicable diseases like CVD, cancers, chronic respiratory diseases and diabetes mellitus represent a leading health threat, and are estimated to cause 60% of all deaths globally [28]. Tobacco use, unhealthy diet, sedentary behavior and alcohol abuse are all modifiable lifestyle factors that increasing the risk of mortality, and eliminating these risk factors could lower the mortality burden for all these non-communicable diseases substantially [28].

6.3 Physical activity and breast cancer

The third paper aimed to investigate the association between total PA and breast cancer overall and by ER and PR status. Our results showed inconsistent findings, with an modest inverse association between ER+/PR+ breast tumors, and simultaneously found a preventive effect of low PA levels at age 14 in relation to breast cancer overall and ER+/PR+ breast tumors. The reasons for this can only be speculated. Since the risk estimates are derived from self-reported PA they may be underestimated in general, and a non-differential misclassification could attenuate the effect estimates toward the null. Another explanation could be that the weak association is in fact the true effect. However, this is in contradiction with the results from several former studies [62]. Among the women participating in the NOWAC study, independent of year of study entry, a large majority was born in the period 1943-1957 and was 14 years old in the period 1957-1971. The fact that this generation of women probably had a more physically active pattern in daily life compared to today, would suggest that the reported PA level may suffer from a larger extent of underestimation at this age in the women's life, thereby attenuated the association. Studies on Norwegian children show that sedentary behavior, such as sitting has more than doubled in the last 20 years [29], indicating that daily PA levels in general have declined.

On the other hand, when comparing our results to those of other studies, there is obviously conflicting evidence. Previous findings range from a modest relationship between PA and breast cancer, to no effect of PA, to a borderline statistical effect and non-significant effect of PA. This demonstrated how complex this relationship is. The biological mechanisms of PA in breast cancer carcinogenesis are not known in detail and the assessments of PA vary across different populations. Therefore, the variability in the study design and questionnaires makes reviewing the literature and comparing results

quite challenging. At the same time, it is of significant importance to investigate this relationship in different populations using a variety of assessment methods in order to prove a consistent protective effect, as consistency is one of Hills criteria of causation [151].

Hills criteria of causation is a widely used guideline when judging evidence [151]. One of the criteria is the strength of association. A strong association is more likely to account for causality and plausible biological explanations, and is unlikely to be explained by bias. Furthermore, associations described as RRs have a zone of potential bias and confounding with thresholds in cohort studies with RRs ≥ 2 or ≤ 0.5, with a more conservative threshold suggested relative risks ≥ 3 or ≤ 0.33 [185]. If this is applied to the association between PA and breast cancer, none of the studies published to-date, including our own, report RRs that shows strong associations, instead they show only weak or modest associations. Thus, cautious interpretation is required. The fact that the results are likely to be attributable to bias should be considered, and Grimes (2012) argues that no clinical decisions should be based on such results [185]. Furthermore, judging the evidence as strong implicates a dose-response relation. Several of the studies published have found an association when comparing the lowest PA level with the highest PA level, which reveals only two levels and is argued as moderate evidence [186]. However, plausible biological pathways through which PA may act have been hypothesized in relation to breast cancer prevention.

The WCRF/AICR has concluded in its most recent evaluation of the evidence that PA of all types (occupational, household, transport and recreational) probably protects against postmenopausal breast cancer. For premenopausal breast cancer, the WCRF/AICR considers that the evidence for PA in decreasing breast cancer risk is limited-suggestive. Given the other benefits of PA on health, including convincing protection against colon

cancer, the WCRF/AICR recommends to the general public to be physically active as part of everyday life [113]. It has been demonstrated that healthy life-long dietary habits, and a sedentary or active routine and other environmental factors contribute much more than genetic to the onset of tumors [113]. Furthermore, Colditz and colleagues [96] pointed out the need to apply what we know to accelerate cancer prevention. He highlights the fact that emphasis on environment and life-style factors will significantly reduce the incidence of cancer. This will also contribute to reducing the burden of other chronic diseases, and not only among high-risk individuals [8, 96]. Furthermore, we should promote changes in the population distribution of modifiable risk factors, as we already know that more than half of cancers all over can be prevented [96]. Paper III is the first to explore the relationship between PA and hormone receptor status in breast tumors in a Norwegian female population. In spite of limitations in quantifying PA level beyond the total volume of PA, and the modest inverse associations, we believe that our results contribute to the complex field of PA and breast cancer. Although the results regarding the role of PA in breast cancer are inconsistent, and many details remain to be explained, there is overall sufficient evidence to inform the public and contribute to immediate recommendations encouraging women to engage in an active lifestyle pattern throughout their life in order to maintain good health.

7 Conclusions and further perspectives

The aims of this thesis was to study the association between PA and all-cause mortality and breast cancer risk overall and according to hormone receptor status of breast tumors in the Norway study. We also aimed to investigate the criterion validity of the original assessment of PA which has been used in the NOWAC study.

7.1 Conclusions

Main conclusion 1: The NOPAQ is sufficient to rank PA levels in a female Norwegian population.

- The agreement between two free-living periods was comparable.
- There were moderate correlations between the criterion and the NOPAQ.
- There were significant linear trends in the relationship between self-reported PA levels and measures of PA derived from a heart rate and movement sensor.

Main conclusion 2: PA is inversely associated with all-cause, CVD and cancer mortality in adult women.

- There was a positive dose-response relationship shown from the very low PA level to the moderate PA level; there was only a limited benefit beyond more than moderately physically active on all-cause, CVD and cancer mortality in adult women.
- The RR of CVD mortality was 3.5 fold at the very low PA level compared to the moderate PA level.
- There was a significant trend of decreasing cancer mortality with increasing PA levels.

- If low PA levels were eliminated from the Norwegian female population 11.5% of all deaths could be postponed, as well as 11.3% of CVD deaths and 7.8% of all cancer deaths.

Main conclusion 3: PA in different periods of life is inconsistently associated with breast cancer, overall and classified according to ER and PR status.

- Women who reported very low PA levels at age 30 years had a weak increased risk of ER+/PR+ breast tumors compared to women who were physically active at moderate level.
- There was no effect of PA on the risk of overall breast cancer or breast tumors with negative receptor status.
- Women who were inactive at age 14 and remained inactive in adulthood seemed to have a protective effect of 20%, both on overall breast cancer and on ER+/PR+ breast tumors.

7.2 Further perspectives

Several studies have investigated the relationship between PA and different health outcomes and mortality. However, gaps in the knowledge still exist, especially regarding the role of PA in breast cancer, and fewer studies have addressed the impact on subtypes of breast cancer and life-long PA, making future prospective studies a necessity. Although randomized controlled trials and intervention studies are ideal study designs to examine the dose and intensity of PA needed to prevent breast cancer, the large sample size needed, and the cost of such studies limits their feasibility. However, given the magnitude of the impact of PA on health, support for moving toward for this level of evidence is warranted [187].

To further develop the field of PA assessment, one needs to consider PA as a complex and multidimensional behavior when making decisions on how to measure PA, which self-report tool to use, and how it will be perceived by the responders. Efforts need to be invested in developing technological devices that can provide more reliable and valid PA assessments, also in large study populations. At the same time, a gold standard for self-report is still needed for use in large populations, as this will complement information that may be provided by use of technological devices. Moreover, information on sedentary behavior itself (such as sitting time) is needed to complete future studies on PA and health, as there is increasing evidence suggesting that sedentary behavior seem to influence both morbidity and mortality independently of PA. The recommendation of at least 30 minutes of moderate intensity PA every day, or at least 150 minutes per week, but also the impact of reducing sedentary behavior such as sitting time, must be included in public recommendations.

Our findings emphasize the need to perform further studies that investigate the impact of PA in different periods of life on cancer risk. As the number of events increase with longer follow-up, we will eventually have the possibility to investigate the association of PA on different health outcomes using repeated PA measurements in the NOWAC study. Moreover, it would also be of great interest to investigate the effect of PA and on breast cancer survival in our cohort. The number of cancer survivors has increased substantially during recent decades partly due to improved diagnosis and treatment methods. Research into the effects of PA and cancer survival is in an early stage, and for this reason the evidence is so far inconclusive [113]. PA on a regular basis may prevent recurrence and increase survival of some cancers and improve quality of life. As PA is a modifiable factor, it may be possible to utilize it to gain general health benefits and to help prevent certain diseases. In the NOWAC study, lifestyle-related factors have already been collected with repeated measurements at different time points (both pre- and post-diagnostic

information), which would allow the study of cancer survival. However, pre-diagnostic information on PA is probably more reliable and accurate than information on PA after a breast cancer diagnosis, as women with a breast cancer diagnosis may somewhat misreport what can be perceived a risk factor (recall bias). Combining information both PA before and after cancer diagnosis should provide important information in examining the impact of changing PA patterns on breast cancer survival.

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PAPER I

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PAPER II

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PAPER III

Borch KB, Lund E, Braaten T, Weiderpass E.

Physical activity and risk of postmenopausal breast cancer by hormonal receptor status
- the Norwegian Women and Cancer Study.

[*Submitted*]

APPENDICES

1. Summary of the prospective studies investigating the association between of PA and risk of breast cancer in postmenopausal women published between 1987-2012
2. Letter of invitation to the validation study
3. Consent of participation in the validation study
4. Procedures first visit in the validation study
5. Procedures second visit in the validation study
6. Actiheart instructions to the participants in the validation study
7. Letter of invitation and information to the NOWAC study first questionnaire (series 35)
8. Reminder first questionnaire (series 35)
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10. Questionnaire (series 35)
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12. Questionnaire (series 26)

APPENDIX 1

Prospective studies published in the period 1987-2012 on the association between physical activity and postmenopausal breast cancer.

Author/year	N	Study population	PA assessment	Outcome	Results	Comments
Dorgan et al.1994	2,321 Pre/post-menopausal	Framingham Heart Study United States	Interview by physicians at enrollment, recent PA. Hours spent on different activity: Total PA, summary score 25-28 (ref) vs. 33-54	BC	RR =1.6 (95% CI 0.9, 3.0) Non-significant increased risk being in high activity. Test for trend P=0.6	Few cases and non-cases
Margolis et al. 2005	99,504 Pre/post-menopausal	Norwegian-Swedish Women's Lifestyle an Health cohort Norway and Sweden	Self-reported PA at enrollment None (ref) vs. vigorous	BC	HR= 1.24 (95% CI 0.85, 1.82) No effect of PA in premenopausal women. A trend of lower risk among physically active postmenopausal women	Very few postmenopausal women (6.9 %) in the study
Schnohr et al. 2005	13,216 Post-menopausal	The Copenhagen Centre for Prospective Population Studies Denmark	Self-reported PA at study enrollment, recent Leisure time Low (ref) vs. moderate and vigorous	BC	Non-significant effect of PA in postmenopausal women Moderate PA RR=1.01 (95% CI 0.79-1.30). Vigorous PA RR=1.12 (95% CI 0.83-1.53). Test for trend p=0.45	

Paffenbarger et al. 1987	4,706 Pre/post-menopausal	College Alumni Study United States	Self-reported sports activities >5 hrs./week	BC	No association for sport PA for pre and postmenopausal. RR = 0.96	No CI reported
Albanes et al. 1989	7,407 Pre/post-menopausal	NHANES I and NHEFS United States	Self-reported non-recreational PA and recreational as exercise Very active (ref) vs. quite inactive Much exercise vs. little or no exercise	BC	No association found RR=1.1 (95% CI 0.6, 2.0) RR=1.0 (95% CI 0.6, 1.6)	
Steenland et al. 1995	14,407 men and women Pre/post-menopausal	NHANES I United States	Self-report of recreational and work PA. Little Moderate	BC	No association for recreational or work PA.	No information on number of women or differentiation between pre/post-menopausal
Rockhill et al. 1998	116,671 Pre/post-menopausal	Nurses' Health Study II United States	Self-reported strenuous PA in high school and between the ages 18-22 At least twice a week None (ref) and	BC	No association between PA in late adolescence RR 1.1 (95% CI 0.8, 1.5) RR 1.1 (95% CI 0.8–1.5)	

			>7 hours of activity/ week relative to <1 hour/week			
Moore et al. 2000	37,105 Postmenopausal	Iowa Women's Health Study United States	Self-reported leisure PA levels and hrs./week, at study enrolment. Low (ref) vs. high	BC	HR = 0.95 (95% CI 0.83, 1.10) No effect of PA in the postmenopausal period of life on the risk of breast cancer. No effect in subgroups either.	
Luoto et al. 2000	30,548 pre/post-menopausal	Finnish Adult Health Behavior Study Finland	Self-report PA leisure and commuting to work.	BC	No significant trend, increased PA gave non-significant reduced risk of BC leisure and commuting to work, RR=1.01 (95% CI 0.72, 1.42) and RR=0.87 (95% CI 0.62, 1.24).	
Lee IM et al. 2001	39,322 Pre/post-menopausal women (mainly nurses)	The Women's Health Study United States	Self-reported PA. KJ/week expended on recreational PA the last year. <840 KJ/week (ref) 840-2519 KJ/week 2520-6299 KJ/week ≥6300 KJ/week	BC ER/PR	Results for postmenopausal women: Significant inverse trend for BC RR=0.67 (95% CI 0.44, 1.02) Unrelated to ER/PR breast cancers. PA >=6METs No associations Not uniformly associated.	Limited statistical power to detect small effects.
Bardia et al. 2006	36,363 Post-menopausal	Iowa Women's Health study United States	Self-reported recreational PA, frequency and type of moderate and	BC ER/PR	High PA BC overall: RR=0.86 (95% CI 0.78, 0.96) ER+/PR+: RR=0.87 (95% CI 0.75,	One of the first studies reporting on postmenopausal

			vigorous PA, rest as low PA: Low (ref) vs. high		1.00) ER+/PR-: RR=0.67 (95% CI 0.47, 0.96) No effect other subtypes PAF: 10.9 % BC 7.9 % ER+/PR+ 28.9 % ER+/PR- 21.9 % ER-/PR-	and ER/PR breast cancer tumors
Mertens et al. 2006	7,994 Pre/post-menopausal	ARIC United States	Self-report PA in leisure, sport an work Modified Baecke PAQ Low (ref) to high, 5 categories	BC	Postmenopausal: No association for leisure, sport or work PA.	
Silvera et al. 2006	40,318	NBSS Canada	Self-report last month of vigorous (sport and housework) PA min/per day None (ref) vs. 0-30, 30-60, >60	BC	Postmenopausal: No association for recreational or housework PA.	
Lahmann et al. 2007	218,169 Pre/post-menopausal	EPIC 9 European countries	Self-report and interviews. Leisure, work and household PA, last year. MET hrs./week Inactive (ref) vs. Active	BC	Postmenopausal: Total PA: RR= 0.92 (95% CI 0.76, 1.12) Test for trend P=0.06 Recreational and household PA: RR=0.83(95% CI 0.73, 0.95) Test for trend p=0.002.	

Howard et al. 2009	45,631 Pre/Post-menopausal	US Radiologic Technologist cohort United States	Self-reported PA recent year, hours spent, MET hrs./week total PA score: Strenuous, walking/hiking for exercise, walking at home/work	BC	No significant trends of reduced risk with increasing METs.	
McTiernan et al. 2003	74,171 Post-menopausal	Women's Health Initiative Cohort Study United States	Self-report PA at study enrollment, 18, 35 and 50 years of age. Hrs. per week of strenuous PA, daily walking frequency, duration and intensity. None vs. 7.0+ hrs./week	BC ER+	Total strenuous PA 35 years: RR=0.86 (95% CI 0.78, 0.95) 50 years: no sign effect 18 years: no sign effect Total PA: test for trend p=0.03 ER+: same results as for BC BMI: stronger association among leaner women Total energy intake, MHT, age, parity: no modifiable effect	Short follow-up (4.7 years)
Patel et al. 2003	72,608 Post-menopausal	Cancer Prevention Study II Nutrition Cohort United States	Self-report recreational PA last year. MET hrs. per week >0-7.0 MET hrs./week vs. 42+ MET hrs./week	BC	Three different time periods At enrolment RR=0.71 (95% CI 0.49, 1.02) At 40 years RR=0.79 (95% CI 0.61, 1.03) 10 year before study enrolment: RR=0.87 (95% CI 0.68, 1.13)	
Leitzman et al. 2008	32,269 Post-	Breast Cancer Detection	Self-report PA last year,	BC ER/PR	No inverse effect of PA on BC (RR 0.87 (95% CI 0.74, 1.02)) or	

	menopausal	Demonstration Project United States	hrs./week/weekend in moderate/vigorous PA. Total weekly MET-hour score, 5 quintiles, low (ref) vs. high.		ER/PR subtypes, no significant trend in multivariate analysis. No effect of MHT. Weak risk reduction among normal BMI women (significant trend), but not overweight women.	
Chang et al. 2006	27,544 Post-menopausal	Prostate, Lung, Colorectal and Ovarian Screening (PLCO) Trial United States	Self-reported PA recreational, hour per week of vigorous PA 0 (ref) vs. ≥ 4	BC	No significant trend RR=0.81 (95%CI 0.63, 1.05) No effect of less PA levels.	
Fraser and Shavlik 1997	20,341 Pre/post-menopausal	Adventist Health Study United States	Self-report of vigorous work and leisure PA, combined into High (ref) vs. low	BC	Overall: Low level of exercise RR=1.46 (95% CI 1.11-1.92) 21 % decreased lifetime risk (P < 0.09) and delay of 6.6 years in age of diagnosis (P < 0.003) associated with higher exercise levels.	Mainly post-menopausal BC cases (74.3 %)
Thune et al. 1997	25,624 Pre/post-menopausal	National Health Screening Service Norway	Self-reported leisure and work PA Sedentary (ref) vs. regular exercise sedentary work vs. heavy manual labor	BC	Overall Pre/post-menopausal: Leisure: Test for trend P=0.04 RR 0.63 (95% CI 0.42, 0.95) Work: Test for trend P=0.02 RR=0.48 (95% CI 0.25, 0.92) Mainly driven by premenopausal Postmenopausal: No effect of	Few cases: Regular exercise 36 cases Heavy manual labor 11 cases

					leisure time and work PA BMI, energy intake and fat intake did not modify the association.	
Sesso et al. 1998	1,566 Pre/post-menopausal	College Alumni Health Study United States	Self-report of study enrollment PA as sports and stairs climbing < 500 Kcal/week (ref) vs. 1000+ Kcal/week	BC	Pre/post-menopausal: HR= 0.73 (95% CI 0.46, 1.14), test for trend P=0.17 Postmenopausal: HR=0.49 (95% CI 0.28, 0.86), test for trend P=0.015 BMI, MHT and age did not modify the association	
Cerhan et al. 1998	1,806 Post-menopausal	Iowa 65+ Rural Health Study United States	Self-reported PA and physically capable based on the Rosow-Breslau Functional Health Scale Disability Inactive Moderate Highly active Inactive(ref) vs. High Inactive vs. disability	BC	RR=0.2 (95% CI 0.05, 1.00), Test for trend P=0.006 For women reporting any disability: RR=0.4 (95% CI 0.2, 0.4) – reduced risk of BC also in disabled women	Few cases: 46
Rockhill et al. 1999	85,364 Pre/post-menopausal	The Nurses' Health Study United States	Self-report over more life periods of hours/week moderate/vigorous	BC	Pre/post-menopausal: RR=0.82 (95% CI 0.70, 0.97) MVPA: test for trend P=0.004 No evidence of variation across	

			recreational PA < 1 hrs./week (ref) vs. ≥ 7 hrs./week		subgroups of BMI, weight change, parity, MHT and family history of cancer.	
Wyshak and Frisch 2000	3,940 Pre/post-menopausal	College Alumnae United States	Self-report of walking, jogging, running etc.	BC	All ages: OR=0.605 (95% CI 0.44, 0.84) P=0.0023 The risk of BC is significantly lower in former athletes compared to non-athletes.	Retrospective cohort study Athletes compared to non-athletes
Moradi et al. 2000	982,270 Post-menopausal	Swedish Cancer-Environment Register III Sweden	Self-reported work PA Sedentary High + Very high (ref) vs. sedentary	BC	Standardized Incidence Ratio 1960 and 1970: SIR 1.35 (95% CI 1.29-1.41). RR=1.3 (95%CI 1.2-1.3)	
Wyrwich and Wolinsky 2000	3,131 Post-menopausal	Longitudinal Study on Aging (LSOA) United States	Self-reported PA and physically capable based on the Rosow-Breslau Functional Health Scale Disability Inactive Moderate Highly active Inactive (ref) vs. high Inactive vs. disability	BC	RR=0.42 (95% CI 0.19, 0.95), weaker association compared to Cerhan et al 1998. For women reporting any disability: RR=0.78 (95%CI 0.41, 1.50) – No significant reduced risk of BC in disabled women	Replication of Cerhan et al 1998 with additional classification of disability Few cases: 77

Breslow et al. 2001	6,160 Pre/post-menopausal	NHANES I United States	Self-reported recreational PA, recent. Consistently low (ref) vs. consistently high	BC	≥50 years of age: RR=0.33 (95% CI 0.14, 0.87) Test for trend 0.026 Not modified by BMI	Few participants, only 138 cases in total and 96 cases in women ≥50 years of age.
Dirx et al. 2001	62,573 Post-menopausal	The Netherlands Cohort Study Netherlands	Self-reported Recreational History sports participation Work PA Hours per week and METs 5+ hrs./week (ref) vs. < 1hrs/week	BC	Recreational: RR=0.76 (95% CI 0.58, 0.99) Sports: RR=1.13 (95% CI 0.94, 1.37) Work: RR=0.83 (0.51, 1.34) BMI/weight loss: No interaction	
Tehard et al. 2006	90,509 Pre/post-menopausal	E3N Cohort (mainly teachers) (also part in EPIC) France	Self-reported leisure and household, walking, flight stairs PA, total MET hrs./week: <28.3 (ref) vs. ≥57.8	BC	Overall: RR=0.90 (95% CI 0.80, 1.02), test for trend p<0.05. BMI, family history of cancer, MHT and nulliparity did not modify the association	Adjusted for menopausal status
Suzuki et al. 2011	53,578 Pre/post-menopausal	Japan Health Center-based Prospective Study Japan	Self-reported leisure and work PA METs hrs./day Leisure: ≥3days/week (ref) vs. ≤3 days/month	BC ER/PR	Pre/post-menopausal overall: RR=0.73 (95% CI 0.54, 1.00), test for trend P=0.037 ER+/PR+: RR=0.43 (95% CI 0.19, 1.00), test for trend P=0.022 Postmenopausal: overall RR=0.78 (95% CI 0.52, 1.17), test	

					for trend p=0.21 ER+/PR+: RR=0.25 (95% CI 0.06, 1.06), test for trend P=0.041 BMI did modify the association with decreased risk if overweight.	
Peters et al. 2009	182,862 Post-menopausal	NIH-AARP Diet and Health Study United States	Self-report at enrollment PA, frequency of past years PA at work, home, leisure per week. Inactive (ref) vs. ≥5 times a week	BC ER/PR	BC: RR=0.87 (95% CI 0.81, 0.95) ER+: RR= 0.97 (95% CI 0.84, 1.12) ER-: RR=0.75 (95% CI 0.54, 1.04). No association for any of the combinations of ER/PR Effect of BMI for lean women and those never users MHT.	
Peters et al. 2009	118,899 Post-menopausal	NIH-AARP Diet and Health Study United States	Self-reported PA of light and MVPA intensity during 4 periods of life. Past 10 years: Inactivity (ref) vs. > 7 hrs./week MVPA	BC ER/PR	RR=0.84 (95% CI 0.76, 0.93) No association with other time periods or by tumor characteristic for any period of life. BMI did not modify the association.	
Eliassen et al. 2010	95,396 Post-menopausal	The Nurses' Health Study United States	Self-reported, total PA, recent and during follow-up period. METs hrs./week	BC ER/PR	Baseline: RR=0.91 (95% CI 0.83, 1.01 Test for trend P=0.21 Most recent update : RR=0,85 (95% CI 0.78-0.93)	

			<3 MET-hrs./week (ref) vs. ≥27 MET-hrs./week		Test for trend P<0.001 Cumulative average: RR= 0.88 (95% CI 0.79-0.98) Test for trend P=0.003 No differences by receptor subtypes BMI, MHT did not modify the association	
Phipps et al. 2011	155,723 Post-menopausal	Women's Health Initiative United States	Self-reported current recreational exercise, frequency, duration, intensity METs hrs./week Total recreational PA: No activity (ref) vs. ≥ 16.5 MET-hrs./week Moderate recreational PA: No activity (ref) vs. ≥ 5.75 MET-hrs./week	BC ER+ Triple-negative	ER+: RR=0.85 (95% CI 0.74, 0.98) Test for trend P<0.01 RR0.88 (95% CI 0.79-0.98) Test for trend P=0.01 No effect with strenuous PA. Increased BMI indicated a 1.39 fold increased risk for ER+, not sign for triple negative BC. Interaction by current MHT use in BMI and waist/hip circumference for ER+.	
Steindorf et al. 2012	257,805 Pre/post-menopausal	EPIC 9 European countries	Either self-reported or interview, total PA (work, household, recreational) MET hours/week	BC ER/PR	Overall: RR=0.87 (95% CI 0.79, 0.97), test for trend P<0.01 >50 years: RR=0.86 (95% CI 0.77, 0.97), test for trend P<0.01	

			Inactive Moderately inactive Moderately active Active Inactive (ref) vs. active		ER+/PR+ tumors: RR=0.84 (95% CI 0.74, 0.96), test for trend P=0.02, Other subtypes: non-significant BMI did not modify the association.	

ARIC=the Atherosclerosis Risk in Communities Study
BC=breast cancer
BMI=body mass index
CI=confidence interval
EPIC= the European Prospective Investigation into Cancer and Nutrition
ER=estrogen receptor
NBSS=Canadian National Breast Screening Study
NHANES I= National Health and Nutrition Survey I
NIH-AARP =American Association of Retired Persons Diet and Health Study
MET=metabolic energy turnover
MHT=menopausal hormone therapy
PA=physical activity
PR=progesterone receptor
RR=relative risk

Forespørsel om å delta i forskningsprosjektet Kvinner, Kreft og Fysisk Aktivitet.

Det er for tiden stor interesse for sammenhengen mellom fysisk aktivitet og ulike kreftformer. Institutt for samfunnsmedisin, Universitetet i Tromsø ønsker å finne ut hvordan svarene fra våre spørsmål om aktivitet samsvarer med andre målemetoder for fysisk aktivitet, nemlig pulsmålinger og bevegelsessensorer. Til dette trenger vi 200 kvinner i alderen 41-55 år som er villige til å delta i en valideringsstudie, og vi spør om du vil delta. Ved hjelp av det sentrale personregisteret ved Statistisk Sentralbyrå har du blitt trukket ut tilfeldig blant kvinner i Tromsø i aldersgruppa.

Kvinner og kreft-studien ved Institutt for samfunnsmedisin ved Universitetet i Tromsø har i flere år samlet inn opplysninger om fysisk aktivitet og andre helse- og livsstilsfaktorer som kan påvirke kreftutvikling. Om du ikke har deltatt i Kvinner og kreft tidligere kan du likevel delta i denne studien.

Siden studien innebærer at du kommer til oss og blir testet kan den ikke foregå anonymt. Identiteten din vil være kjent for tre av våre prosjektmedarbeidere. Alle opplysninger vil bli behandlet konfidensielt. Studien er tilrådd av Regional komité for medisinsk forskningsetikk Nord-Norge og Norsk samfunnsvitenskaplig datatjeneste. Data vil bli lagret i sikret nettverk. Navnelister vil bli holdt atskilt fra innsamlede opplysninger. Etter at datainnsamlingen er ferdig, og kvalitetskontroller utført vil alle opplysninger bli anonymisert. Vi vil analysere og skrive artikler ut fra de anonymiserte dataene. Studien er del av en større internasjonal studie, og avidentifiserte opplysninger vil bli sendt til studiekoordinator ved universitetet i Cambridge i England. Disse vil også bli anonymisert så snart kvalitetskontrollene er gjennomført. Studien er i sin helhet finansiert av offentlige midler. Deltagere vil være forsikret gjennom Universitetet i Tromsø, samt Pasientskadeerstatningsordningen.

Studien vil foregå over to perioder à fire dager, en i april-august og en i september-desember. Vi vil avtale et tidspunkt når du kan komme til oss for å få målt høyde, midje- og hofteomkrets og vekt. Du vil i tillegg bli bedt om å svare på et spørreskjema om fysisk aktivitet. Deretter gjennomføres en steptest. Steptesten gjennomføres med bevegelsessensorer og pulsmåler på, og gjør at vi får mer nøyaktige opplysninger om aktivitet. Testen tar ca 8 minutter. Deretter beholder du sensorene på i fire dager før de returneres til oss. Hele prosedyren gjentas til høsten. Ved andre besøk ber vi deg svare på spørreskjemaer om fysisk aktivitet.

Steptesten er ikke en test av maksimalt aktivitetsnivå, og vil bli stoppet dersom du nærmer deg maksimal puls, eller dersom du ønsker det. Deltakere som bruker medikamenter som påvirker hjerterytmen (f. eks. betablokkere) eller har kjent hjertesykdom eller andre medisinske lidelser som begrenser muligheten til å delta i steptesten kan likevel delta i resten av studien. Sensorene veier ca 10 gram. Det er ikke forventet at studien skal føre til ubehag av noe slag, men man vil bli litt svett av steptesten. Elektrodetape kan gi hudirritasjoner ved sensitiv hud.

DET MEDISINSKE FAKULTET
INSTITUTT FOR SAMFUNNSMEDISIN
Universitetet i Tromsø, N-9037 Tromsø, Telefon 77 64 48 16, Telefaks 77 64 48 31

Hvis du vil delta i forskningsprosjektet ber vi om at du fyller ut samtykkeerklæringene og sender ett eksemplar tilbake i den ferdigfrankerte svarkonvolutten og beholder den andre selv. Det er frivillig å være med i studien. Du kan når som helst og uten begrunnelse trekke deg, uten at det vil få noen konsekvenser for deg. Opplysningene du har gitt kan du be om å få slettet, dersom du trekker deg før data blir anonymisert, ved prosjektslutt i 2008. Når studien er ferdig kan de som ønsker det få tilbakemelding om noen av sine måleresultater. Ut over dette vil du ikke ha noen personlig nytte av å delta i prosjektet.

Professor Eiliv Lund er leder for prosjektet og ansvarlig for studien. Ønsker du flere opplysninger, vennligst kontakt Kristin Benjaminsen Borch på telefon 77 64 54 43 eller kristinbenjaminsen.borch@ism.uit.no eller Bente Augdal på telefon 77 64 66 38 eller bente.augdal@ism.uit.no.

Vennlig hilsen

Kristin Benjaminsen Borch prosjektmedarbeider	Bente A. Augdal prosjektmedarbeider	Eiliv Lund professor dr.med

Du kan finne mer informasjon om Kvinner, kreft og fysisk aktivitet-studien her: www.kvinnerogkreft.no

---

SAMTYKKEERKLÆRING (BEHOLDES AV DELTAGER)

☐ Ja, jeg vil delta i studien Kvinner, kreft og fysisk aktivitet (KKFA).

☐ Ja, jeg samtykker i at KKFA kan kontakte meg på telefon for å avtale oppmøte til steptesten. Jeg treffes lettest på telefon/mobil…….. på tidspunkt mellom ……..

☐ Ja, jeg samtykker til å svare på spørreskjemaer om fysisk aktivitet.

☐ Nei, jeg ønsker ikke å delta i studien Kvinner, kreft og fysisk aktivitet. (Kryss her for å unngå å få påminning)

Dato Signatur

……..

DET MEDISINSKE FAKULTET
INSTITUTT FOR SAMFUNNSMEDISIN
Universitetet i Tromsø, N-9037 Tromsø, Telefon 77 64 48 16, Telefaks 77 64 48 31

Kvinner og kreft, InterAct valideringsstudie, Fysisk aktivitet.

Deltager id-nummer:

Navn på prosjektleder: Professor Eiliv Lund, ISM, Universitetet i Tromsø

1. Jeg bekrefter at jeg har lest og forstått informasjonen i invitasjonsbrevet om studien datert …./…/2007, og har muligheten til å stille spørsmål.

2. Jeg er inneforstått med at min deltagelse er frivillig og at jeg kan trekke meg på et hvilket som helst tidspunkt fra studien uten å oppgi årsak.

3. Jeg samtykker til å delta i studien.

……	……	……
Navn Deltager (Blokkbokstaver)	Dato	Signatur

……	……	……
Prosjektmedarbeider	Dato	Signatur

Dato:

Kvinner, Kreft
Og
Fysisk aktivitet

Deltager
ID

Generelle spørsmål og måleskjema

DET MEDISINSKE FAKULTET
INSTITUTT FOR SAMFUNNSMEDISIN
Universitetet i Tromsø, N-9037 Tromsø, Telefon 77 64 48 16, Telefaks 77 64 48 31

Kvinner, kreft - Fysisk aktivitet

Deltager id-nummer:

Navn på prosjektleder: Professor Eiliv Lund, ISM, Universitetet i Tromsø

☐ Jeg bekrefter at jeg har lest og forstått informasjonen i invitasjonsbrevet om studien datert ...../...../2007, og har hatt muligheten til å stille spørsmål.

☐ Jeg er inneforstått med at min deltagelse er frivillig og at jeg kan trekke meg på et hvilket som helst tidspunkt fra studien uten å oppgi årsak.

☐ Jeg samtykker til å delta i studien.

.....	.....	.....
Navn Deltager (Blokkbokstaver)	Dato	Signatur
.....	.....	.....
Prosjektmedarbeider	Dato	Signatur

Generelle helsespørsmål

Deltager ID

- Bruker du noe medisin for øyeblikket?

  ☐Ja ☐Nei

- Hvilke medisiner tar du og hvorfor?

Navn på medisin	Dose	Årsak til bruk av medisin	

Deltager ID

	Ja	Nei
1. Har legen din fortalt deg noen gang at du har hjerteproblemer?		
2. Har du noen ganger hatt smerter eller ubehag i brystet? Hvis nei, fortsett på spm 7 Hvis ja, svar neste spørsmål		
3. Opplever du ubehag når du går i motbakker eller i høyt tempo?		
4. Opplever du ubehag når du går i et vanlig tempo og i flatt terreng?		
5. Hva gjør du når du kjenner ubehag?	Stopper/senker tempo	Fortsetter
6. Hvis du stopper, hva skjer med ubehag?	Opphører	Fortsetter
7. Opplever du noen gang svimmelhet eller å ville besvime?		
8. Har legen din noen fortalt deg at du har høyt blodtrykk?		
9. Hvis du har høyt blodtrykk, får du behandling for det?		
10. Har legen din noen ganger fortalt deg at du har problemer med skjelett/ledd, slik som for eksempel gikt, som blir utløst under aktivitet eller verre under aktivitet?		
11. Er du gravid?		
12. Er det noen grunn til at du ikke skulle følge et aktivitetsprogram selv om du ønsker det?		
Hvis ja - spesifiser		

Eksklusjon sjekkliste

Deltager ID

A. Eksklusjon basert på selvrapporterte tilstander tidligere forekommet i henhold til generelle helsespørsmål (fra spørsmålet om du tidligere har opplevd hjertetrøbbel):

1. Aorta aneurisme
2. Aorta stenose
3. Ustabil angina
4. Tidligere hjerteinfarkt (de siste 3 mnd eller hvor deltageren ikke ennå har blitt vurdert i forhold til fysisk aktivitet)
5. Myoarditt (også kalt hjerteinfeksjon)
6. Lungeemboli eller systemisk emboli siste 4 uker
7. Cardiomyophati (også kalt stort hjerte)
8. Medikamentbruk: Beta-blokkere mer enn halvparten av den maksimale mulige dosen vil ekskludere fra steptesten, men kan delta på resten.

Tabell: Vanlige beta –blokkere

Generisk navn	Salgsnavn	Max daglig dose	Dose for EST
Propranolol			
Atenolol			
Bisoporol			
Carvedilol			
Labetolol			
Metoprolol			
Nebivolol			
Sotalol			

B. Ekslusjon basert på nåværende tilstand

1. Graviditet
2. Pusteproblemer som begrenser trappegang eller gange uten hjelp på flatt underlag i 10 minutter. Dette vil også gjelde pusteproblemer pga kronisk lungesykdom eller uspesifikk lungeproblemer.

Deltager eksludert:

☐ Ja ☐ Nei

Hvis ja, oppgi årsak:

Prosedyreskjema for kliniske mål:

Deltager ID

Antropometriske mål:

Hofte og midjeomkrets:
Deltager skal ha på seg lette klær. Fjern eventuelle belter og innhold i lommene. Deltager skal stå med vekten likt fordelt på begge bein, og armene hengende løst langs siden.

Målingene gjøres på slutten av et rolig utpust, som gir minimalt press på buken. Bruk speil for å sikre at målbåndet ligger i en rett horisontal linje hele veien rundt. Målbåndet skal ligge tett, men ikke stramme.

Målingene skal gjøres to ganger, og hvis de to første målinger har større differanse enn 3 cm, mål en tredje gang. Oppgi målene i nærmeste 0,1 cm.

Hofteomkrets:
Måles i nivå med trochanter major. Få deltager til å rotere hele beinet fram og tilbake og finn punktet etter der hvor "kulen" er mest uttalt. Dette vil være i samme nivå der hvor setemuskulatur er størst. Be deltager plassere en finger på punktet mens du finner det på den andre siden, og få deltager til å plassere en finger der også.

1. □□□.□ cm 2. □□□.□ cm 3. □□□.□. cm

Midjeomkrets:
Måles midt mellom bekkenkammen (spina iliaca superior kanten) og nederste ribbe.

1. □□□.□ cm 2. □□□.□ cm 3. □□□.□. cm

Vekt og høyde
Deltager skal stå med ryggen mot vektens display. Hodet i rett posisjon, i Frankfort horisontalt plan, avslappet i skuldrene, armene hengende langs siden.

Høyde □□□.□ cm

Vekt □□□.□ kg

Målene utført av:

Actiheart Informasjon

Deltager ID

Alder:

Max HR (hjertefrekvens) (100%):

90% HR:

80% HR:

Før oppsett av monitorer må deltager ha hvilepuls

Actiheart nummer

Topp plassering:

Bunnplassering:

Step test

Hjertefrekvens før step test start:	
Protokoll tid (minutter)	Hjertefrekvens (HR) Polar pulsmåler
02.00	
04.00	
06.00	
08.00	
10.00	

<u>Kriterier for å stoppe step test:</u>

Hvis en eller flere av følgende kriterier oppstår vil testen stoppe tidligere beregnet:

1. Deltager ønsker selv å stoppe.
2. Deltager når 90% av max HR (220-alder)
3. Deltager har nådd 80% eller mer av max HR i 3 minutter eller mer.
4. Deltager rapporterer: brystsmerter (føler tranghet eller press), tungpustet, svimmel eller besvimer, opplever leggsmerter eller annen smerte.

Måle sjekkliste:

Deltager ID

	Kryss av når utført
Samtykkeskjema fylt ut	
Gjennomgått eksklusjon og helsepørsmål	
Årsak:	Hvis ekskludert:
Høyde/vekt	
Midje- og hoftemål	
Step-test	
4 dagers måling	

2. BESØK Dato:
Generelle helsespørsmål

Deltager ID

- Bruker du noe medisin for øyeblikket?

  ☐Ja ☐Nei

- Hvilke medisiner tar du og hvorfor?

Navn på medisin	Dose	Årsak til bruk av medisin	

DET MEDISINSKE FAKULTET
INSTITUTT FOR SAMFUNNSMEDISIN
Universitetet i Tromsø, N-9037 Tromsø, Telefon 77 64 48 16, Telefaks 77 64 48 31

Deltager ID

	Ja	Nei
1. Har legen din fortalt deg noen gang at du har hjerteproblemer?		
2. Har du noen ganger hatt smerter eller ubehag i brystet? Hvis nei, fortsett på spm 7 Hvis ja, svar neste spørsmål		
3. Opplever du ubehag når du går i motbakker eller i høyt tempo?		
4. Opplever du ubehag når du går i et vanlig tempo og i flatt terreng?		
5. Hva gjør du når du kjenner ubehag?	Stopper/senker tempo	Fortsetter
6. Hvis du stopper, hva skjer med ubehag?	Opphører	Fortsetter
7. Opplever du noen gang svimmelhet eller å ville besvime?		
8. Har legen din noen fortalt deg at du har høyt blodtrykk?		
9. Hvis du har høyt blodtrykk, får du behandling for det?		
10. Har legen din noen ganger fortalt deg at du har problemer med skjelett/ledd, slik som for eksempel gikt, som blir utløst under aktivitet eller verre under aktivitet?		
11. Er du gravid?		
12. Er det noen grunn til at du ikke skulle følge et aktivitetsprogram selv om du ønsker det?		
Hvis ja - spesifiser		

Eksklusjon sjekkliste

Deltager ID

A. Eksklusjon basert på selvrapporterte tilstander tidligere forekommet i henhold til generelle helsespørsmål (fra spørsmålet om du tidligere har opplevd hjertetrøbbel):

1. Aorta aneurisme
2. Aorta stenose
3. Ustabil angina
4. Tidligere hjerteinfarkt (de siste 3 mnd eller hvor deltageren ikke ennå har blitt vurdert i forhold til fysisk aktivitet)
5. Myoarditt (også kalt hjerteinfeksjon)
6. Lungeemboli eller systemisk emboli siste 4 uker
7. Cardiomyophati (også kalt stort hjerte)
8. Medikamentbruk: Beta-blokkere mer enn halvparten av den maksimale mulige dosen vil ekskludere fra steptesten, men kan delta på resten.

Tabell: Vanlige beta –blokkere

Generisk navn	Salgsnavn	Max daglig dose	Dose for EST
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Atenolol			
Bisoporol			
Carvedilol			
Labetolol			
Metoprolol			
Nebivolol			
Sotalol			

B. Ekslusjon basert på nåværende tilstand

1. Graviditet
2. Pusteproblemer som begrenser trappegang eller gange uten hjelp på flatt underlag i 10 minutter. Dette vil også gjelde pusteproblemer pga kronisk lungesykdom eller uspesifikk lungeproblemer.

Deltager eksludert:

☐ Ja ☐ Nei

Hvis ja, oppgi årsak:

Prosedyreskjema for kliniske mål:

Deltager ID

Antropometriske mål:

Hofte og midjeomkrets:

Hofteomkrets: (I høyde med Trochanter major)

1. □□□.□ cm 2. □□□.□ cm 3. □□□.□. cm

Midjeomkrets:
Måles midt mellom bekkenkammen (spina iliaca superior kanten) og nederste ribbe.

1. □□□.□ cm 2. □□□.□ cm 3. □□□.□. cm

Vekt og høyde
Deltager skal stå med ryggen mot vektens display. Hodet i rett posisjon, i Frankfort horisontalt plan, avslappet i skuldrene, armene hengende langs siden.

Høyde □□□.□ cm

Vekt □□□.□ kg

Målene utført av:

Actiheart Informasjon

Deltager ID

Alder: Fødelsmnd/år:

Max HR (hjertefrekvens) (100%):

90% HR:

80% HR:

Før oppsett av monitorer må deltager ha hvilepuls

Actiheart nummer

Topp plassering:

Bunnplassering:

Step test

Hjertefrekvens før step test start:	
Protokoll tid (minutter)	Hjertefrekvens (HR) Polar pulsmåler
02.00	
04.00	
06.00	
08.00	
10.00	

Kriterier for å stoppe step test:

Hvis en eller flere av følgende kriterier oppstår vil testen stoppe tidligere beregnet:

1. Deltager ønsker selv å stoppe.
2. Deltager når 90% av max HR (220-alder)
3. Deltager har nådd 80% eller mer av max HR i 3 minutter eller mer.
4. Deltager rapporterer: brystsmerter (føler tranghet eller press), tungpustet, svimmel eller besvimer, opplever leggsmerter eller annen smerte.

ACTIHEART INSTRUKSJON

Actiheart sensoren du nå har fått på deg skal du ha på i 4 dager og netter. Gjennom denne tiden skal du holde på med alle dine vanlige aktiviteter i ditt daglige miljø (ingen lange reiser i denne perioden). Hvis du av en eller annen grunn må ta av deg Actiheart sensoren, så er det fint om du kan sette den på deg så snart du kan.

Actiheart sensoren er en kombinert hjertefrekvens- og bevegelsessensor. Fra hovedknappen går en wire til den lille knappen, disse to festes til EKG-elektroden som du får festet på huden. Sensoren og elektroden tåler vann, så du kan også ha den på når du dusjer og svømmer.

Actiheart sensoren holdes på plass av elektrodene som har tape på baksiden, slik at de ikke faller av. Disse vil bli plassert på venstre side av brystkassen mens du er inne til step testen. Skulle de av en eller annen grunn falle av, får du med deg nye elektroder som du må plassere på samme sted der de forrige satt. Før du setter de på må du vaske huden og deretter tørke godt med et håndkle. Ikke bruk hud lotion der hvor elektrodene skal festes, da vil de ikke feste seg. For å plassere Actiheart sensoren på elektrodene må du trykke den lille knappen inn idet du setter de på. Pass på at ledningen ikke er helt stram, men har en liten slakk slik at de tillater at du beveger deg.

Actiheart sensoren har et lite lys som blinker hvert 5 minutt. Dette indikerer at den fortsatt virker, så hvis du oppdager at den ikke har lyst på lang tid, eller at du har andre problemer eller spørsmål, vennligst ring: Kristin B Borch, 776 45443/ mob 91604690.

Dagbok for Actiheart:

	Dag 1	Dag 2	Dag 3	Dag 4	Tidspunkt Actiheart ble tatt av
Tid tatt av					Dag: Kl.slett:
Tid satt på plass					
Annet					

INSTITUTT FOR SAMFUNNSMEDISIN
UNIVERSITETET I TROMSØ
9037 TROMSØ
Telefon 77 64 48 16/77 64 66 38

Appendix 7

KVINNER OG KREFT

Institutt for samfunnsmedisin ved Universitetet i Tromsø gjennomfører en spørreundersøkelse om levesett og kreft blant norske kvinner. En slik undersøkelse gir et verdifullt grunnlag for å studere mulige sammenhenger mellom f.eks. kosthold, barnefødsler, p-piller, solvaner og utviklingen av kreft. Resultatet vil bli publisert i dagspressen og i internasjonale fagtidsskrifter. Ansvarlig for undersøkelsen er professor Eiliv Lund.

Du forespørres hermed om å delta i undersøkelsen. Alle som blir forespurt er trukket ut tilfeldig. Statistisk Sentralbyrå har trukket utvalget og står for utsending av spørreskjemaene.

Med noen års mellomrom fram til 2033 ønsker vi å sammenholde opplysningene som er gitt i undersøkelsen mot opplysninger fra Kreftregisteret, Mammografiregistrert og Dødsårsaksregisteret. Samtykket fra deg for dette vil være ensbetydende med returnering av spørreskjemaet.
Alle opplysninger fra undersøkelsen og fra registrene vil bli behandlet konfidensielt og etter regler Datatilsynet har gitt i sin tillatelse, samt tillatelse fra Sosial- og helsedirektoratet. På spørreskjemaet er navn og fødselsnummer erstattet med et løpenummer slik at ingen av de som mottar og tar hånd om skjemaene vil kjenne din identitet. Undersøkelsen er tilrådd av Regional komite for medisinsk forskningsetikk i Nord-Norge.

Hvis du vil delta i undersøkelsen, ber vi deg om å besvare det vedlagte spørreskjemaet så riktig som mulig. Dersom ingen av de oppgitte svaralternativ dekker din situasjon, sett kryss for det alternativet som ligger nærmest. Gi eventuelle tilleggsopplysninger i skjemaet.
Du behøver ikke svare på alle spørsmål.

Det vil senere bli aktuelt å samle inn blodprøver fra noen av deltakerne.
Dette vil skje hos nærmeste lege, og vil være gratis. Det vil også bli aktuelt å spørre noen av deltakerne om å være med på et kostholdsintervju over telefon. Bare de av deltakerne som på forhånd har krysset av for at de er villig til å bli kontaktet på nytt og/eller til å bli spurt om å avgi blodprøve, vil få henvendelse om dette. Det vil da bli gitt nærmere informasjon og innhentet samtykke til dette.

Det er frivillig om du vil være med i undersøkelsen. Det er også adgang til å trekke seg senere, hvis du skulle ønske det. Du kan få slettet dine opplysninger hvis du krever det. De innsamlete opplysninger vil bli anonymisert 31.12.2033.

Ditt bidrag til undersøkelsen vil være å svare på spørsmålene i spørreskjemaet.
For spørsmål om hormoner og p-pille bruk finner du bilder i denne brosjyren som skal være et hjelpemiddel til å svare riktig (brosjyren skal ikke returneres). Spørreskjemaet returneres i vedlagte konvolutt med betalt svarporto.

Med vennlig hilsen

Eiliv Lund
professor dr.med.

Bente A. Augdal
prosjektmedarbeider

Du kan finne mer informasjon om "Kvinner og kreft" og om forskningsresultatene på våre nettsider: www.ism.uit.no/kk/

Appendix 8

Undersøkelsen
"KVINNER OG KREFT"

Vi minner om at vi nylig har sendt deg et spørreskjema som vi håper du tar deg tid til å svare på. Ditt svar er et viktig bidrag for oss, fordi slutningene vi kan trekke ut fra undersøkelsen vil være mer pålitelige dersom mange har svart.

Vi ønsker at resultatene fra undersøkelsen skal komme deg og andre kvinner til gode. Du velger likevel selv om du vil delta i undersøkelsen.

Hvis du nylig har returnert skjemaet, ber vi deg se bort fra denne hendvendelsen. Vi takker for verdifull bistand.

Alle opplysninger fra undersøkelsen behandles konfidensielt og etter Datatilsynets regler.

Har du spørsmål om undersøkelsen, eller trenger du et nytt spørreskjema, kan du kontakte Institutt for samfunnsmedisin, Universitetet i Tromsø, 9037 Tromsø,
Bente A. Augdal tlf. 77 64 66 38

Med vennlig hilsen

Eiliv Lund
professor dr.med.

LUNDBLAD MEDIA AS, TROMSØ – 032163

INSTITUTT FOR SAMFUNNSMEDISIN
UNIVERSITETET I TROMSØ
9037 TROMSØ
Telefon 77 64 48 16

Appendix 9

Bilder av hormoner til bruk i og etter overgangsalderen (østrogen)

Denne brosjyren er et hjelpemiddel for å huske riktig navn på de hormontabletter/plaster du har brukt.
Under bildene er det oppgitt hvilke år disse var i salg. For noen hormontabletter/plaster finnes det esker med samme utseende, men med ulik styrke av hormonene. Vi ber deg tenke nøye gjennom navnet på de hormon-tabletter/plaster du har brukt. Eldre avregistrerte preparater er ikke gjengitt med bilder, det gjelder:

Nr. 104 **Etifollin** 50 mcg tabletter, solgt fra 1953-2000
Nr. 121 **Menorest** 37,5 mcg/24t plaster, solgt fra 1996-2002
Nr. 122 **Menorest** 50 mcg/24t plaster, solgt fra 1996-2002
Nr. 123 **Menorest** 75 mcg/24t plaster, solgt fra 1996-2002
Nr. 124 **Menorest** 100 mcg/24t plaster, solgt fra 1996-2002
Nr. 196 **Primolut** tabletter, solgt fra 1958-
Nr. 197 **Perlutex** tabletter, solgt fra 1960-
Nr. 199 **Provera** 5 og 10 mg tabletter, solgt fra 1964-
Nr. 202 **Diethylstilbøstrol** 0,1 mg tabletter solgt fra1980-85
Nr. 204 **Primodos** tabletter solgt fra 1961-74
Nr. 205 **Østriol** 1 mg tabletter solgt fra 1975-95
Nr. 206 **Østriol** 0,25 mg tabletter solgt fra 1961-83

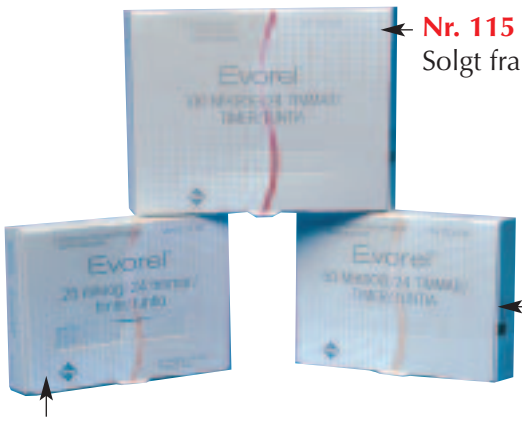
Nr. 110 Solgt fra 1994-2002

Nr. 111 Solgt fra 1971

Nr. 112 Solgt fra 1989

Nr. 113 Solgt fra 1983

Nr. 114 Solgt fra 1984



Nr. 115 Solgt fra 1995

Nr. 117 Solgt fra 1994

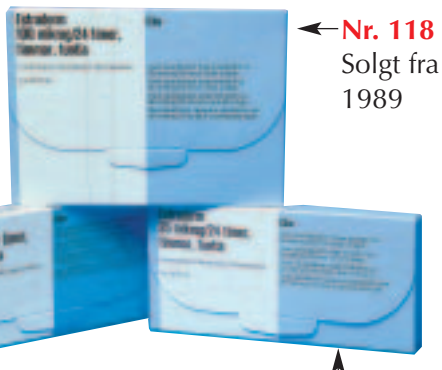
Nr. 116 Solgt fra 1995

Nr. 101 Solgt fra 1978

Nr. 102 Solgt fra 1978

Nr. 103 Solgt fra 1978

Nr. 105 Solgt fra 1988



Nr. 118 Solgt fra 1989

Nr. 119 Solgt fra 1989

Nr. 120 Solgt fra 1989

Nr. 107 (2mg) Solgt fra 1967

Nr. 106 (1mg) Solgt fra 1970

Nr. 125
Solgt fra 1996.

Nr. 136 Vagifem
Solgt fra 2000

Nr. 126
Solgt fra 1997.

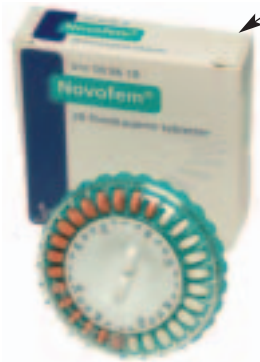
Nr. 127
Solgt fra 1997.

Nr. 138
Climodien
Solgt fra 2001

Nr. 140 Oestriol
Solgt fra 1999

Nr. 128
Livial
Solgt fra 1999

Nr. 141
Novofem
Solgt fra 2002



Nr. 143
Estradot 50 mg

Nr. 142
Estradot
37,5 mg

Nr. 144
Estradot 75 mg

Solgt fra 2002

Nr. 145
Estradot 100 mg

Nr. 130
Indivina 1mg/2,5 mg Solgt fra 2001

Nr. 132
Indivina 2mg/5 mg
Solgt fra 2001

Nr. 131
Indivina 1mg/5 mg
Solgt fra 2001

Nr. 146
Estalis
Solgt fra 2002

Nr. 147
Estalis Sekvens
Solgt fra 2003

Nr. 133
Diviseq
Solgt fra 2001

Nr. 134
Climen
Solgt fra 1999

Nr. 135 Activelle
Solgt fra 1999

Nr. 148
Totelle Sekvens
Solgt fra 2003

Bilder av P-pille merker i salg 1965-2003

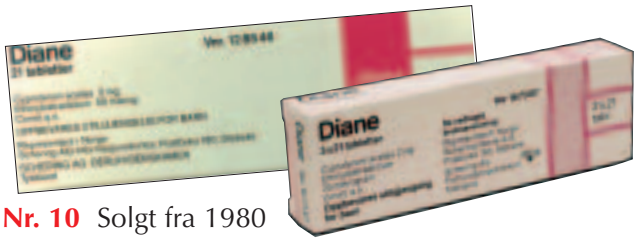
Denne brosjyren er et hjelpemiddel for å huske riktig navn på de p-piller du har brukt. Under bildene er det oppgitt hvilke år p-pillene var i salg. For noen p-piller finnes det esker med samme utseende, men med ulik størrelse, anhengig av om de inneholder p-piller for en eller flere måneder. Vi ber deg tenke nøye gjennom navnet på de p-pillene du har brukt. Av noen p-piller/ merker har vi ikke bilder, det gjelder:

Nr. 1. **Follistrel,** solgt fra 1973–76
Nr. 2. **Menokvens,** solgt fra 1971–72
Nr. 3. **Novokvens,** solgt fra 1969–70
Nr. 5. **Anovlar Mite,** solgt fra 1967–69
Nr. 8. **Consan,** solgt fra 1968–70
Nr. 9. **Delpregnin,** solgt fra 1968–71
Nr. 14. **Kombikvens,** solgt fra 1971–75
Nr. 20. **Micronor,** solgt fra 1971–79
Nr. 22. **Norlestrin,** solgt fra 1965–80
Nr. 23. **Nyo-Kon,** solgt fra 1968–70
Nr. 26. **Ortho-Novin Mite,** solgt fra 1968–72
Nr. 39. **Implanon,** solgt fra 2002-

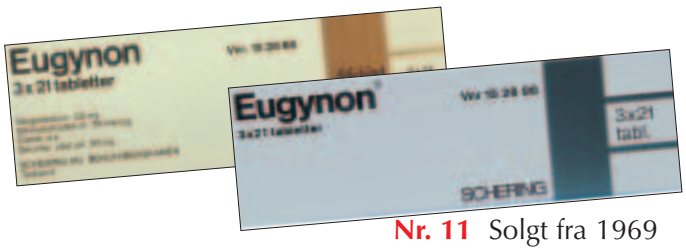
Nr. 4 Solgt fra 1965-68

Nr. 6. Solgt fra 1980

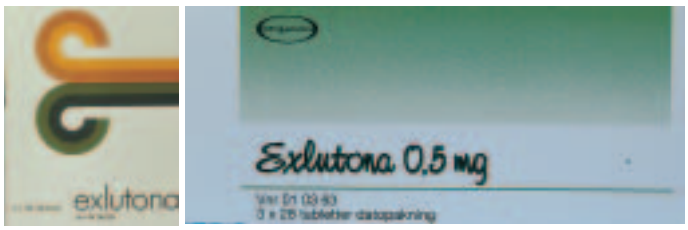
Nr. 7 Solgt fra 1971



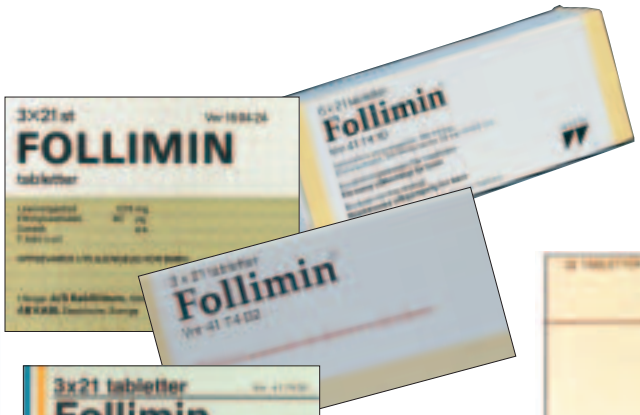
Nr. 10 Solgt fra 1980



Nr. 11 Solgt fra 1969



Nr. 12 Solgt fra 1973



Nr. 13 Solgt fra 1978

Nr. 15 Solgt fra 1966-72

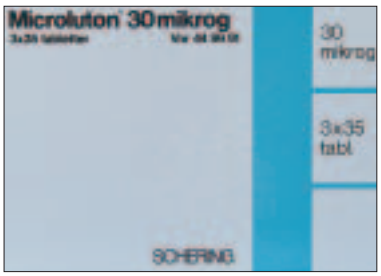
Nr. 16 Solgt fra 1965

Nr. 17 Solgt fra 1985

Nr. 18 Solgt fra 1975

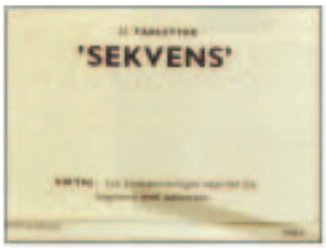
Nr. 29 Solgt fra 1973-82

Nr. 30 Solgt fra 1968-84

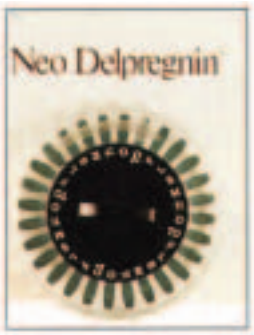


Nr. 19 Solgt fra 1973

Nr. 31 Solgt fra 1977

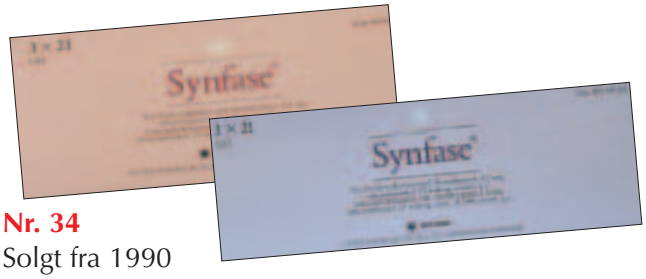


Nr. 32 Solgt fra 1969-70



Nr. 21 Solgt fra 1971-79

Nr. 33 Solgt fra 1967-69



Nr. 34
Solgt fra 1990

Nr. 24 Solgt fra 1971-81

Nr. 35
Solgt fra 1981

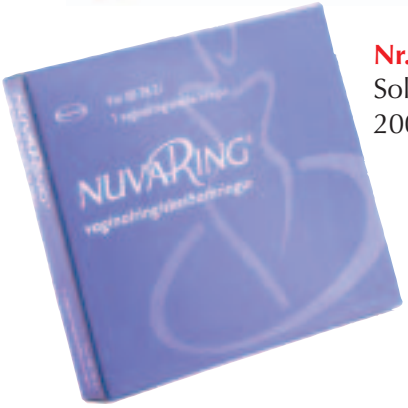
Nr. 36 Solgt fra 1981

Nr. 25 Solgt fra 1966-69

Nr. 37
Solgt fra 2001

Nr. 38 Solgt fra 2002

Nr. 27 Solgt fra 1965-71



Nr. 40
Solgt fra 2003

Nr. 28 Solgt fra 1970

TAKK FOR INNSATSEN!

Høst 2003

KVINNER OG KREFT

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? ☐☐

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? ☐☐

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? ..... ☐☐

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

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	☐	☐	☐	☐	☐	☐	☐
Grønnsakblanding (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 ☐

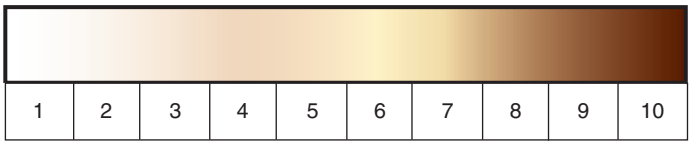
Hvilken øyefarge har du? (sett ett kryss)

☐ 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?

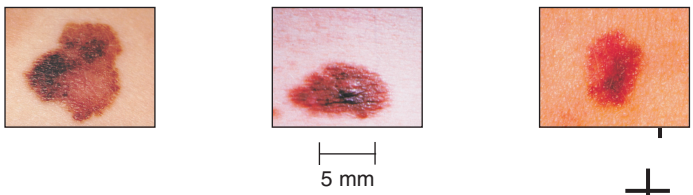
	påsken	i Norge eller utenfor syden	solferie i syden
I dag	☐☐	☐☐	☐☐
For 10 år siden	☐☐	☐☐	☐☐

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 beina (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

INSTITUTT FOR SAMFUNNSMEDISIN
UNIVERSITETET I TROMSØ
9037 TROMSØ
Telefon 77 64 48 16

Appendix 11

KVINNER OG KREFT

Orientering om undersøkelsen

Du samtykket i 1991/1992 til å fylle ut et fire siders spørreskjema som du mottok i posten. Spørreskjemaet tok opp en rekke forhold knyttet til ditt liv som barnefødsler, p-pille bruk, kosthold, røking og sosiale forhold. Formålet med undersøkelsen var å se om disse forhold har betydning for utvikling av kreft hos kvinner. Resultatene vil bli publisert i dagspressen og i internasjonale fagtidsskrifter. Ansvarlig for undersøkelsen er professor Eiliv Lund.

Vi retter nå en ny forespørsel til deg om du nok en gang vil besvare det vedlagte spørreskjema. Begrunnelsen for å kontakte deg på ny er at mange av de spørsmålene du besvarte sist gjaldt levevaner som vi vet endrer seg med alderen. De fleste spørsmålene vil dreie seg om årene siden siste utfylling. Vi vil i tillegg spørre om du i løpet av de siste 6-7 år har fått enkelte andre sykdommer enn kreft.

Undersøkelsen er tilrådd av Regional komite for medisinsk forskningsetikk i Nord-Norge. Adressen din henter vi fra det sentrale personregister ved hjelp av Statistisk Sentralbyrå. Som forrige gang inneholder spørreskjemaet kun løpenummer uten annen identifikasjon, for derved å gi dine opplysninger et bedre personvern.

Med noen års mellomrom frem til år 2018 vil vi sammenholde opplysningene som du har gitt i undersøkelsen med opplysninger fra Kreftregisteret og Dødsårsaksregisteret. Ved å studere materialet på nytt, håper vi å finne ut årsakene til at noen kvinner får kreft. Alle opplysningene fra spørreskjemaene og registrene vil bli behandlet konfidensielt og etter de regler Datatilsynet har gitt i sin tillatelse.

Deltagelse i undersøkelsen medfører kun at du skal fylle ut dette spørreskjemaet. Det er frivillig om du vil være med i undersøkelsen. Du kan senere trekke deg uten begrunnelse og uten at det vil få noen konsekvenser for deg. Opplysninger du har gitt kan du be om å få slettet.

Vi vil be deg om å besvare det vedlagte spørreskjemaet så riktig som mulig. Dersom ingen av de oppgitte svaralternativ dekker din situasjon, sett kryss for det alternativet som ligger nærmest. Gi eventuelt merknader eller tilleggsopplysninger i skjemaet. Vi spør også alle som deltar om tillatelse til fornyet kontakt om noen år i form av et liknende spørreskjema.

For spørsmål om p-pille bruk og bruk av hormoner i overgangsalderen finner du bilder i denne brosjyren som skal være et hjelpemiddel (brosjyren skal ikke returneres). Spørreskjemaet sendes tilbake i vedlagte konvolutt som vi betaler svarporto for.

Med hilsen

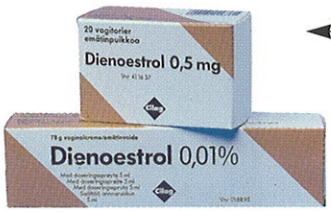
Eiliv Lund
professor dr.med.

JAN.-98

Bruk av østrogener i og etter overgangsalderen

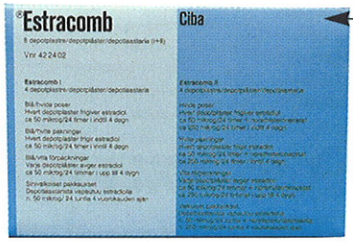
Denne brosjyren er et hjelpemiddel for å huske riktig navn på de hormontabletter/plaster/salver/stikkpiller du har brukt. Under bildene er det oppgitt hvilke år disse var i salg. For noen hormontabletter/plaster finnes det esker med samme utseende, men med ulik styrke av hormonene. Vi ber deg tenke nøye gjennom navnet på de hormon-tabletter/plaster/salver/stikkpiller du har brukt. Eldre avregistrerte preparater er ikke gjengitt med bilder, det gjelder:

Nr. 201 **Dietylstilbøstrol** 1mg stikkpiller til skjeden (1976-92)
Nr. 202 **Dietylstilbøstrol** 0,1 mg tabletter (1980-85)
Nr. 203 **Dietylstilbøstrol** 0,5 mg stikkpiller (1976-81)
Nr. 204 **Primodos** tabletter (1961-74)
Nr. 205 **Østriol** 1 mg tabletter (1975-95)
Nr. 206 **Østriol** 0,25 mg tabletter (1961-83)



Nr. 108.
Solgt fra 1976

Nr. 109.
Solgt fra 1954



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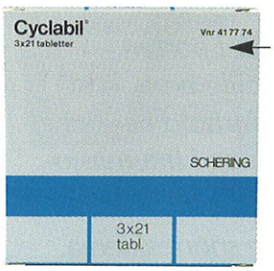
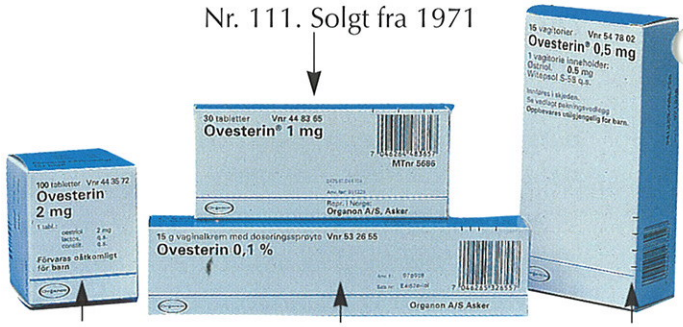


Nr. 101. Solgt fra 1978

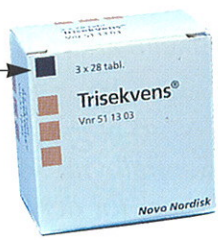
Nr. 111. Solgt fra 1971



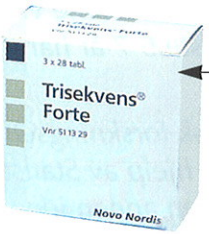
Nr. 112.
Solgt fra 1989

Nr. 113.
Solgt fra 1983

Nr. 114.
Solgt fra 1984



Nr. 102.
Solgt fra
1978

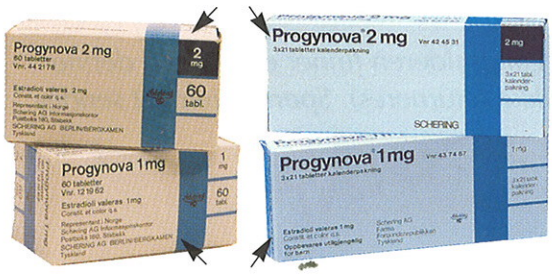


Nr. 103.
Solgt fra
1978

Nr. 104.
Solgt fra
1953

Nr. 105.
Solgt fra
1988

Nr. 107. Solgt fra 1967

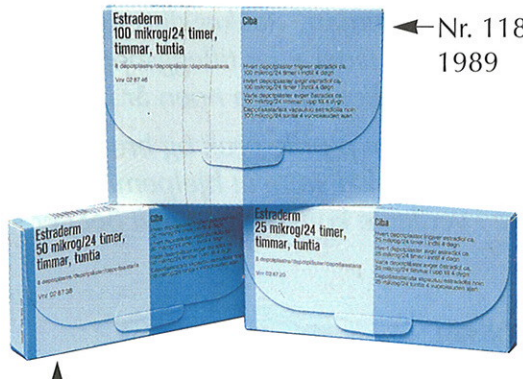


Nr. 106. Solgt fra 1970

Nr. 115. Solgt fra
1995

Nr. 117.
Solgt fra
1994

Nr. 116.Solgt fra 1995



Nr. 118. Solgt fra
1989

Nr. 120.
Solgt fra
1989

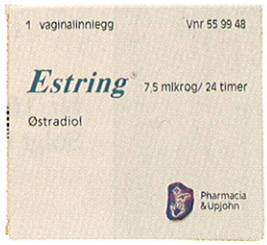
Nr. 119. Solgt fra 1989

Nr. 121
Solgt fra
1996.

Nr. 122
Solgt fra
1996.

Nr. 123
Solgt fra
1996.

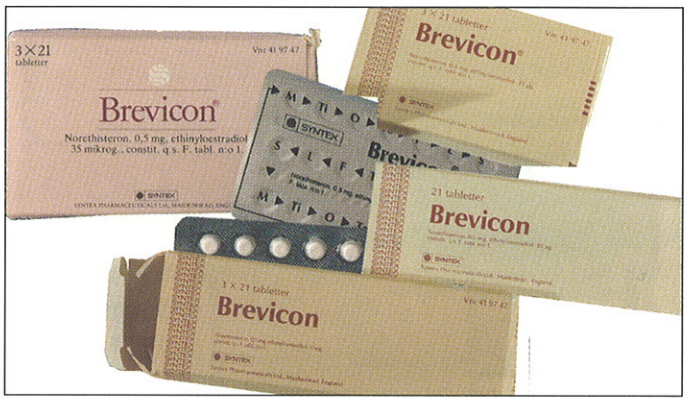
Nr. 124
Solgt fra
1996.



Nr. 125
Solgt fra 1996.

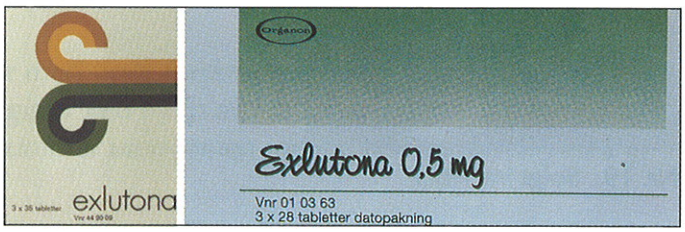
P-pille merker i salg 1991-98

Denne brosjyren er et hjelpemiddel for å huske riktig navn på de p-piller du har brukt de siste årene. Bildene er ordnet alfabetisk. Under bildene er det oppgitt hvilke år p-pillene var i salg.
For noen p-piller finnes det esker med samme utseende, men med ulik størrelse, avhengig av om de inneholder p-piller for en eller flere måneder.
Vi ber deg tenke nøye gjennom navnet på de p-pillene du har brukt.

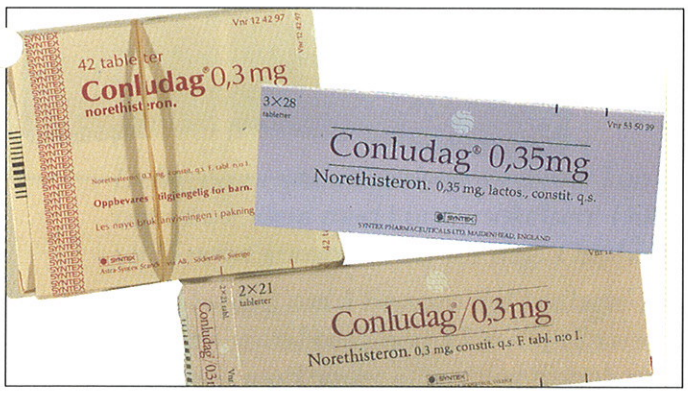


Nr. 6. Solgt fra 1980

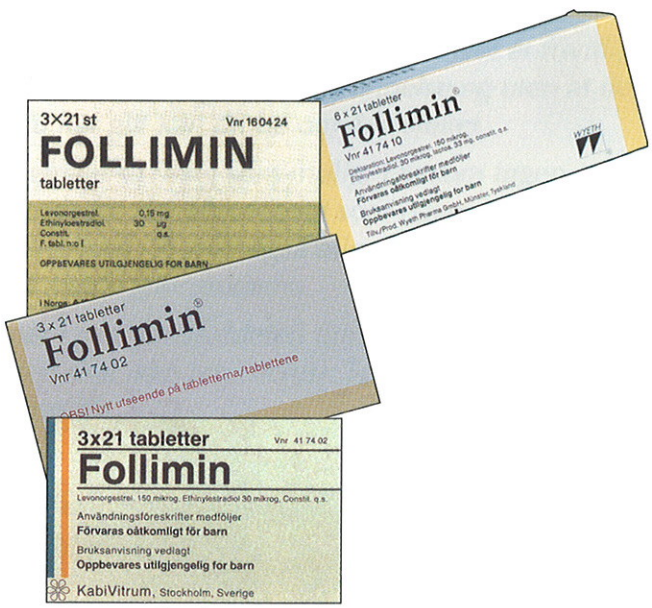
Nr. 11. Solgt fra 1969



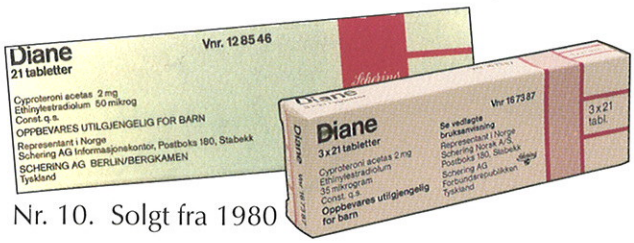
Nr. 12. Solgt fra 1973



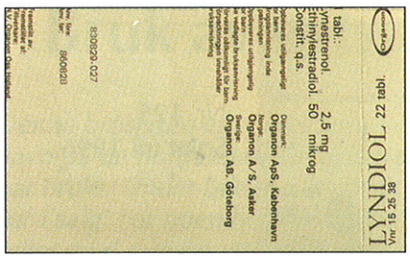
Nr. 7. Solgt fra 1971



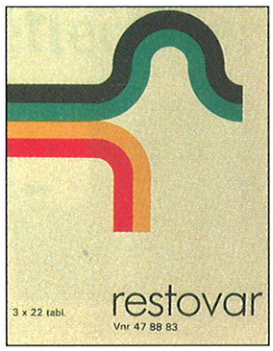
Nr. 13. Solgt fra 1978



Nr. 10. Solgt fra 1980

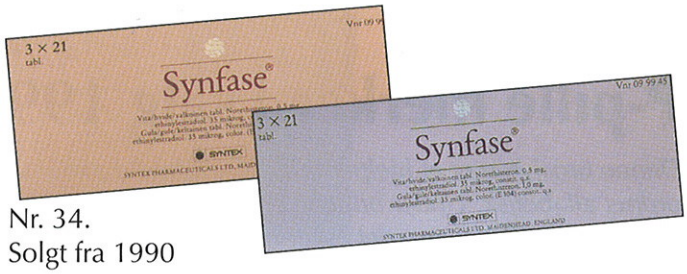


Nr. 16.
Solgt fra 1965



Nr. 31. Solgt fra 1977

Nr. 17. Solgt fra 1985



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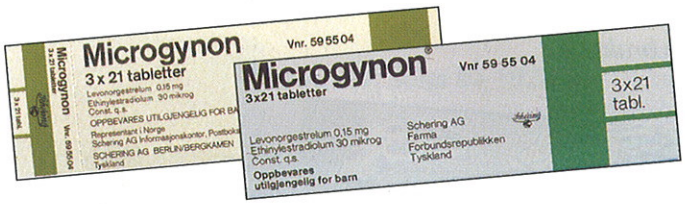

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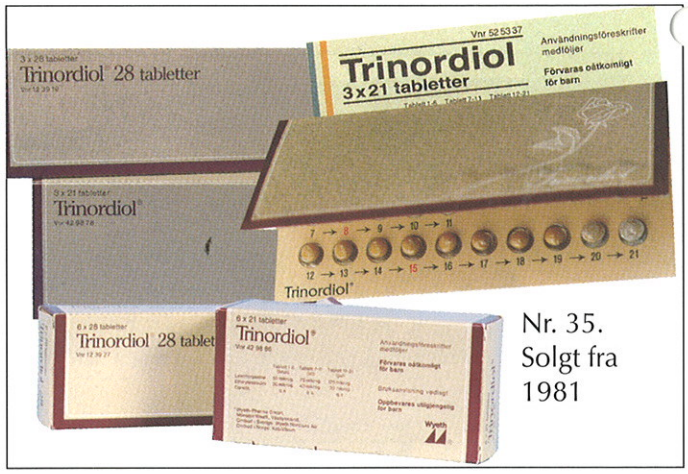
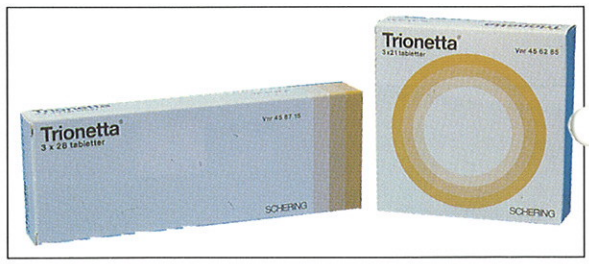


Nr. 35.
Solgt fra
1981

Nr. 19. Solgt fra 1973

Nr. 28. Solgt fra 1970



Nr. 36.
Solgt
fra
1981

TAKK FOR INNSATSEN!

LUNDBLAD GRAFISK AS TROMSØ - TLF 77 67 51 01

KVINNER OG KREFT

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.

wts. 26

Hvis du vil være med, så ber vi deg fylle ut spørreskjemaet så nøye som mulig, se orienteringen på brosjyren for nærmere opplysninger.

Med vennlig hilsen

Eiliv Lund
Professor dr. med

Jeg samtykker i å delta i spørreskjema-undersøkelsen JA ☐ NEI ☐

Forhold i oppveksten

I hvilken kommune har du bodd lengre enn ett år?

Kommune: **Alder**

1. Fødested: ..... Fra 0 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

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

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. legemiddelbruk, p-piller, sykdom, trening, annet)
☐ 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

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
1		
2		
3		
4		
5		
6		
7		

Hormonbruk i overgangsalderen

Har du noen gang brukt hormontabletter/plaster? ☐ Ja ☐ Nei

Hvis Ja; hvor lenge har du brukt hormontabletter/plaster i alt? ..... år

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

Hvorfor begynte du å bruke hormontabletter/plaster?

Lindre plager i overgangsalderen (hetetokter, uopplagthet, underlivsplager mm) ☐
Forebygge benskjørhet ☐
Forebygge hjerte/kar sykdom ☐
Annet ..... ☐

Bruker du tabletter/plaster nå? ☐ Ja ☐ Nei

HORMONPREPARAT TIL LOKAL BRUK I SKJEDEN

Har du noen gang brukt hormonkrem/stikkpille? ☐ Ja ☐ Nei

Hvis Ja; hvor lenge har du brukt krem/stikkpille i alt? ..... år

Hvor gammel var du første gang du brukte hormonkrem/stikkpille? ..... år

Bruker du krem/stikkpille nå? ☐ Ja ☐ Nei

Hvis du har svart «nei» på begge spørsmålene om hormonbruk (tabletter, plaster, krem eller stikkpiller) 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/kremen/stikkpillen som står i brosjyren.

Periode	Alder ved start	Brukt samme hormontablett/plaster/krem/stikkpille Sammenhengende år	måned	Hormontablett/plaster/krem stikkpille (se brosjyre) Nr.	Navn
Første					
Andre					
Tredje					
Fjerde					
Femte					

Har hormonpreparatene gitt deg bivirkninger? ☐ Ja ☐ Nei

Hvis ja; kryss av for hvilke bivirkninger:

- Uregelmessige blødninger ☐
- Brystspenning ☐
- Kvalme/magesmerter ☐
- Hodepine ☐
- Hudreaksjoner ☐
- Vektøkning ☐
- Annet ..... ☐

Førte de overnevnte bivirkninger til at du forandret hormonbehandlingen din? ☐ Ja ☐ Nei

Hvis ja;

- Skiftet fra ett hormonpreparat til et annet ☐
- Sluttet på egen hånd? ☐
- Sluttet i samråd med lege ☐
- Annet ..... ☐

Har vekten din økt etterat du begynte å bruke hormoner ☐ Ja ☐ Nei

Hvis ja; Hvor mange kg? .....kg

Hvis du har brukt hormonpreparater i 1 år eller mindre; hvorfor har du brukt midlene så kort tid?

- Har nettopp startet behandlingen ☐
- Er kvitt plagene ☐
- Manglende effekt av legemidlene ☐
- Redd for skadevirkninger ☐
- Fikk plagsomme bivirkninger ☐
- Annet ..... ☐

Hvor har du skaffet deg informasjon/kunnskap om hormonbehandling?

	Lite viktig	viktig	meget viktig
Allmenpraktiserende lege	☐	☐	☐
Gynekolog	☐	☐	☐
Apotek	☐	☐	☐
Radio/TV	☐	☐	☐
Ukeblader/aviser	☐	☐	☐

P-Piller

Har du noen gang brukt p-piller, minipiller inkludert? ☐ Ja ☐ Nei

Hvis Ja;

Hvor lenge har du brukt p-piller i alt? .....år

Hvor gammel var du første gang du brukte p-piller? .....år

Hvis du har født barn, brukte du p-piller før første fødsel? ☐ Ja ☐ Nei

Bruker du p-piller nå? ☐ Ja ☐ Nei

Vi vil be deg om å besvare spørsmålene om p-pille bruk mer nøye. For hver periode med sammenhengende bruk av samme p-pille merke håper vi du kan si oss hvor gammel du var da du startet, hvor lenge du brukte det samme p-pille merket og navnet på p-pillene.
Dersom du har tatt opphold eller skiftet merke, skal du besvare spørsmålene for en ny periode. Dersom du ikke husker navnet på p-pille merket, sett usikker. For å hjelpe deg til å huske navnet på p-pille merkene ber vi deg bruke den vedlagte brosjyren som viser bilder av p-pille-merker som har vært solgt i Norge. Vennligst oppgi også nummeret på p-pillen som står i brosjyren.

Periode	Alder ved start	Brukt samme p-pille sammenhengende år	måneder	Nr.	P-pillene (se brosjyren) Navn
Første					
Andre					
Tredje					
Fjerde					
Femte					

Abort og infertilitet

Har du hatt noe svangerskap som varte mindre enn seks måneder dvs. spontanabort eller selvbestemt abort? Ja ☐ Nei ☐

Hvis Ja, hvor gammel var du ved første abort? .....år

Hvor mange aborter har du hatt i alt? .....

Har du noen gang prøvd i mer enn 1 år å bli gravid? Ja ☐ Nei ☐

Hvis Ja, hvor gammel var du? ..... år

Hvor lenge prøvde du? ..... år

Sykdom

Har du eller har du hatt noen av følgende sykdommer?

	Ja	Nei	Hvis Ja: Alder ved start
Høyt blodtrykk	☐	☐	☐
Hjertesvikt/hjertekrampe	☐	☐	☐
Årebetennelse	☐	☐	☐
Blodpropp i legg eller lår	☐	☐	☐
Hjerteinfarkt	☐	☐	☐
Slag	☐	☐	☐
Migrene	☐	☐	☐
Epilepsi	☐	☐	☐
Sukkersyke (diabetes)	☐	☐	☐
Osteoporose	☐	☐	☐
Depresjon (besøkt lege)	☐	☐	☐

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

☐ meget god ☐ god ☐ dårlig ☐ meget dårlig

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

☐ meget god ☐ god ☐ dårlig ☐ meget dårlig

Hjerte- karpreparater

BRUKER DU LEGEMIDLER FAST

mot høyt blodtrykk? ☐ Ja ☐ Nei

mot hjertekrampe (angina)? ☐ Ja ☐ Nei

mot hjertesvikt og/eller uregelmessig hjerterytme? ☐ Ja ☐ Nei

Undersøkelser for kreft

Hvor ofte undersøker du brystene dine selv?
(Sett ett kryss)

Aldri..... ☐

Uregelmessig..... ☐

Regelmessig (omtrent hver måned)..... ☐

Går du til regelmessig undersøkelse av brystene dine med mammografi? (Sett ett kryss)

Nei..... ☐

Ja, med 2 års mellomrom eller mindre..... ☐

Ja, med mer enn 2 års mellomrom..... ☐

Har du tatt kreftprøve fra livmorhalsen regelmessig?

Aldri..... ☐

Sjeldnere enn hvert 3. år..... ☐

Hvert 3. år eller oftere..... ☐

Brystkreft i nærmeste familie

Har noen nære slektninger hatt brystkreft;

	Ja	Nei'	Vet ikke	Alder ved start
datter	☐	☐	☐	☐
mor	☐	☐	☐	☐
mormor	☐	☐	☐	☐
farmor	☐	☐	☐	☐
søster	☐	☐	☐	☐

Høyde og vekt

Hvor høy er du? ..... cm

Hvor mye veier du i dag? ..... kg

Hvor mye veide du da du var 18 år? ..... kg

Har du lagt på deg etter at du ble 50 år? ☐ Ja ☐ Nei

I tilfelle Ja; hvor mange kg? ..... kg

Røykevaner

	Ja	Nei
Har du noen gang røkt?	☐	☐

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

	Antall sigaretter hver dag						
Alder	0	1-4	5-9	10-14	15-19	20-24	25+
15-19							
20-29							
30-39							
40-49							
50-59							
60-69							

	Ja	Nei
Røker du daglig nå?	☐	☐
Bor du sammen med noen som røker?	☐	☐

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

Sosiale forhold

Er du: (Sett ett kryss)

☐ gift ☐ samboer ☐ skilt/separert ☐ ugift ☐ enke

Hvor mange personer er det i ditt hushold?

Antall: .....

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
☐ over 600 000 kr

Yrke: .....

Arbeider du utendørs i yrkessammenheng? Ja ☐ Nei ☐

Hvis ja:
hvor mange timer pr. uke? .....Sommer .....vinter

Fysisk aktivitet

Vi ber deg angi din fysiske aktivitet etter en skala fra svært lite til svært mye ved 14 og 30 års alder og i dag. 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 ring rundt 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

Hvilken fysisk aktivitet har du i fritiden?
(Sett kryss i den ruten hvor «Ja» passer best.)

	Ja
Leser, ser på fjernsyn eller annen stillesittende beskjeftigelse?.....	☐
Spaserer, sykler eller beveger deg på annen måte minst 4 timer i uken?... (Heri medregnes også gang eller sykling til arbeidsstedet, søndagsturer m.m.)	☐
Driver mosjonsidrett,tyngre hagearbeid el.? (Merk at virksomheten skal vare minst 4 timer i uka.)	☐
Trener hardt eller driver konkurranse-idrett, regelmessig og flere ganger i uka.	☐

Hvis du har drevet konkurranseidrett, hvor mange år i alt? ..... år

Hvor mye går du pr. uke? ..... timer
(spasere, skiturer, turer i skog og mark, går til arbeid)

Kosthold

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)	☐	☐	☐	☐	☐	☐
Skummet (søt, sur)	☐	☐	☐	☐	☐	☐

Hvor mange kopper kaffe 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	☐	☐	☐	☐	☐	☐	☐

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

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

Hvor ofte har du i gjennomsnitt siste året spist kornblanding, havregryn eller müsli? (Sett ett kryss)

☐ aldri/nesten aldri ☐ 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						
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 og annet søtt pålegg						
Brun ost, helfet						
Brun ost, halvfet/mager						
Hvit ost, helfet						
Hvit ost, halvfet/mager						
Kjøttpålegg, leverpostei						

Videre kommer spørsmål om fiskepålegg.
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						
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)

☐ smørblandet margarin (f. eks. Bremykt)
☐ Brelett
☐ lettmargarin (f. eks. Soft light, Letta)

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 (f.eks. druer, fersken)							

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							
Broccoli/blomkål							
Blandet salat							
Grønnsakblanding (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
- broccoli/blomkål ☐ 1-2 buketter ☐ 3-4 buketter ☐ 5+ buketter
- blandet salat ☐ 1 dl ☐ 2 dl ☐ 3 dl ☐ 4+ dl
- 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 spaghetti/makaroni ? (Sett ett kryss pr. linje)

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

Hvor ofte spiser du risengrynsgrøt? (Sett ett kryss)

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

Hva slags fett blir vanligvis brukt til matlaging i din husholdning? (Sett gjerne flere kryss)

☐ smør
☐ hard margarin (f. eks. Per, Melange)
☐ myk margarin (f. eks. Soft)
☐ smørblandet margarin (f. eks. Bremykt)
☐ soyaolje ☐ olivenolje ☐ maisolje

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	vinter	vår	sommer	høst
Torsk, sei, hyse, lyr						
Steinbit, flyndre, uer						
Laks, ørret						
Makrell						
Sild						

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	3+ pr. uke
Kokt torsk, sei, hyse, lyr						
Stekt torsk, sei, hyse, lyr						
Steinbit, flyndre, uer						
Laks, ørret						
Makrell						
Sild						

Dersom du spiser fisk, hvor mye spiser du vanligvis pr. gang? (1 skive/stykke = 150 gram)
(Sett ett kryss for hver linje)

- 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+

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

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

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 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/fast fett (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+

Andre matvarer

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 m/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+

Vi ber deg fylle ut hovedrettene til middag en gang til som en oppsummering. Kryss av i den ruten som passer hvor ofte du i gjennomsnitt i løpet av siste år har spist slik mat til middag

	5+ pr. uke	4 pr. uke	3 pr. uke	2 pr. uke	1 pr. uke	2-3 pr. mnd	1 pr. mnd	nesten aldri
Rent kjøtt	☐	☐	☐	☐	☐	☐	☐	☐
Oppmalt kjøtt	☐	☐	☐	☐	☐	☐	☐	☐
Fet fisk (makrell, laks o.l.)	☐	☐	☐	☐	☐	☐	☐	☐
Mager fisk (torsk o.l.)	☐	☐	☐	☐	☐	☐	☐	☐
Fiskemat	☐	☐	☐	☐	☐	☐	☐	☐

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

	aldri/ sjelden	1-3 pr mnd	1 pr. uke	2-3 pr. uke	4+ pr. uke
– om sommeren	☐	☐	☐	☐	☐
– resten av året	☐	☐	☐	☐	☐

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

☐ 1 dl ☐ 2 dl ☐ 3 dl ☐ 4+ dl

Hvor ofte spiser du bakervarer som boller, kaker, wienerbrød, vafler, småkaker? (Sett ett kryss)

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-3 pr. uke	4-6 pr. uke	7+ pr. uke
Bakervarer						

Hvor ofte spiser du sjokolade? (Sett ett kryss)

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

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+

Tilberedningsmåte

Har du mikrobølgeovn? ☐ Ja ☐ Nei

Hvis Ja; hvor mange ganger pr. uke bruker du mikrobølgeovnen til ganger pr. uke

middagslaging? .....

annet? .....

Hvilken farve foretrekker du på stekeskorpen?

☐ Lys brun ☐ Middels ☐ Mørk brun

Hvor ofte spiser du stekt eller grillet mat?

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-3 pr. uke	4-6 pr. uke	7+ pr. uke
Mørkt kjøtt (biff ol.)						
Lyst kjøtt (kylling ol.)						
Oppmalt kjøtt (kjøttkaker ol.)						
Bacon						
Fisk						

Bruker du stekefettet eller sjyen etter steking?

☐ nei, aldri ☐ av og til

☐ som oftest ☐ ja, alltid

Kosthold som barn

Hvor mye melk drakk du <u>som barn</u> hver dag?

☐ drakk ikke ☐ 1-3 glass ☐ 4-6 glass ☐ 7+ glass

Hvor ofte spiste du grønnsaker til middag <u>som barn</u>?

☐ aldri ☐ 1 gang i uken eller mer sjelden

☐ 2-3 ganger i uken ☐ 4 eller flere ganger pr. uke

Hvor ofte spiste du fisk til middag <u>som barn</u>?

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

2 pr. uke ☐ 3 pr. uke ☐ 4+ pr. uke ☐

I hvilken grad mener du kostholdet ditt har betydning for helsa?

☐ ingen/svært liten ☐ noen ☐ stor ☐ svært stor

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 ☐ 1/2ss ☐ 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?

	ja	antall pr. gang
Møllers trankapsler	☐	.....
Møllers omega-3 kapsler	☐	.....
Møllers dobbel	☐	.....
annet, navn	☐	.....

Bruker du fiskeoljekapsler? ☐ 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?

	ja	antall pr. gang
Triomar	☐	.....
Almarin	☐	.....
Nycomed Omega-3	☐	.....
annet, navn	☐	.....

Kosttilskudd

Bruker du annet kosttilskudd (eks. vitaminer, mineraler)? ☐ Ja ☐ Nei

Hvis ja; hvor ofte tar du slike kosttilskudd?

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

Navn .....

Alkohol

Er du total avholdskvinne? ☐ 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. mnd	1 pr. uke	2-4 pr. uke	5-6 pr. uke	1+ pr. dag
Øl (½ L)	☐	☐	☐	☐	☐	☐	☐
Vin (glass)	☐	☐	☐	☐	☐	☐	☐
Brennevin (drinker)	☐	☐	☐	☐	☐	☐	☐

Solvaner

Dersom du i begynnelsen av sommeren soler deg kraftig, blir huden din; (sett ett kryss)

☐ brun uten først å være rød ☐ rød

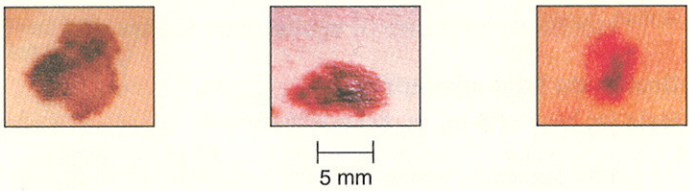
☐ rød med svie ☐ rød med svie og blemmer

Etter gjentatt og lenge soling, blir huden din; (sett ett kryss)

☐ dypt brun ☐ brun ☐ lys brun ☐ aldri brun

Hvor mange uregelmessige føflekker større enn 5 mm har du sammenlagt på begge beina (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 mange små, regelmessige føflekker har du sammenlagt på begge beina (fra tærne til lysken)?

☐ 0 ☐ 1-10 ☐ 11-50 ☐ 51+

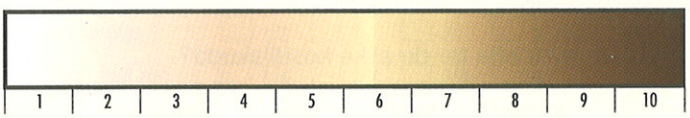
Hvilken øyefarge har du? (sett ett kryss)

☐ 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 den fargen som best passer din hudfarge (uten soling)



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. uke	2-3 g pr. mnd.	Sjelden aldri
Med såpe/shampo							
Uten såpe/shampo							

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					
20-44 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					
20-45 år					
45+ år					

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					
20-45 år					
45+ år					

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

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

Hvilke solfaktorer bruker du i disse periodene?

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

Hvilke solkremmerker bruker du? Angi faktor hvis du husker.

	Ja	faktor
Piz Buin	☐	.....
Ambre Solairé	☐	.....
Delial	☐	.....
Nivea	☐	.....
Natusan	☐	.....
HTH	☐	.....
Cosmica	☐	.....
Andre.....	☐	.....

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						
20-44 år						
45+ år						

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

Takk for at du ville delta i undersøkelsen

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