



**DIETARY DATA IN THE NORWEGIAN
WOMEN AND CANCER STUDY**

Validation and analyses of health related aspects

Anette Hjartåker

Oslo 2000



Institute of Community Medicine
University of Tromsø



The Norwegian Cancer Society



Section of Medical Statistics
University of Oslo

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LIST OF PAPERS

- I. Hjartåker A, Lund E, Bjerve KS. Serum phospholipid fatty acid composition and habitual intake of marine foods registered by a semi-quantitative food frequency questionnaire. *Eur J Clin Nutr* 1997;51:736-42.
- II: Hjartåker A, Lund E. Relationship between dietary habits, age, lifestyle, and socio-economic status among adult Norwegian women. The Norwegian Women and Cancer Study. *Eur J Clin Nutr* 1998;52:565-72.
- III: Hjartåker A, Laake P, Lund E. Body mass index and weight change attempts among adult women. The Norwegian Women and Cancer Study. *Eur J Public Health* 2001;11:141-6.
- IV: Hjartåker A, Laake P, Lund E. Childhood and adult milk consumption and risk of breast cancer in a cohort of 52 592 women. The Norwegian Women and Cancer Study. *Int J Cancer* 2001;0000 (in press in revised version).

ABSTRACT

The objectives of the present thesis were to design a semi-quantitative food frequency questionnaire for use in epidemiological research among Norwegian women, to validate certain components of the dietary data, to collect dietary data from a large nation-wide sample of women, and to analyse selected nutritional aspects related to health, both cross-sectionally and prospectively.

The data are collected as part of the Norwegian Women and Cancer Study (NOWAC), a large population-based cohort study established in 1991. The dietary data are collected by means of self-administered food frequency questionnaires asking about usual diet during the last year. In this thesis, three different questionnaires and three different study samples are included. First, in 1991-92, 52 592 women aged 34-49 years (mean 41.1 yrs) completed a limited food frequency questionnaire (Appendix A). Second, in 1995, 234 women aged 40-42 years participated in a validation study and completed an extended semi-quantitative food frequency questionnaire (Appendix B). Third, in 1996, 10 249 women aged 45-69 years (mean 54.8 yrs) completed a revised version of the extended semi-quantitative food frequency questionnaire (Appendix C).

The main body of the extended semi-quantitative food frequency questionnaire was developed during 1995. The primary purpose of the questionnaire was to collect data on consumption of marine foods, but also to record 'usual' diet. A pilot study was conducted to obtain suitable frequency and amount categories. After having taken the results from the pilot study into account, a new version of the semi-quantitative questionnaire was designed and applied in a validation study.

In the validation study, reported intake of marine food items and calculated intake of n-3 fatty acids were compared to the fatty acid composition of serum phospholipids (Paper I). Spearman's correlation coefficient between dietary intake of eicosapentaenoic acid (EPA) and serum phospholipid EPA was 0.58, and the correlation coefficient between intake of docosahexaenoic acid (DHA) and serum phospholipid DHA was 0.53. It was concluded that the extended semi-quantitative questionnaire could be used for reporting intake of marine foods, but that fish items of different fat content need to be reported separately. Information on fish species seemed to be more important than information on portion size, and cod liver oil was the single most significant item in explaining variation in the fatty acid composition of the serum phospholipids.

The data collected in 1996 were used in analyses focusing on dietary intake and on body weight concerns in relation to subjects' characteristics like age, lifestyle and socio-economic status (Papers II and III). For calculations of nutrient intake, a computer program was developed. Older women tended to have a diet more in line

with dietary recommendations than younger women. Still, the intake of fat was higher than recommended and the intake of fruits, vegetables, and potatoes lower than recommended. Women reporting a healthy lifestyle and a higher socio-economic status were more likely to report a healthy diet than women reporting a less healthy lifestyle and lower socio-economic status.

More than 50% of the women stated that they were trying to lose weight. Weight loss attempt was strongly associated with body mass index, but also associated with age, lifestyle factors and socio-economic status. Women trying to lose weight reported a different diet than those not trying to lose weight, irrespective of body mass index.

The data collected in 1991-92 with the limited food frequency questionnaire were applied to study a possible relationship between childhood and adult milk consumption and breast cancer risk (Paper IV). The women were followed until December 1997. Linkage to the Cancer Registry of Norway allowed identification of breast cancer cases. The mean follow-up time was 6.2 years, and 371 incident cases of breast cancer were diagnosed. No association was seen for childhood milk consumption and subsequent breast cancer. As for adult milk consumption, the incidence rate ratio of breast cancer was 0.64 (95% confidence interval 0.38–1.08) for women drinking more than three glasses of milk per day compared to women not drinking milk, suggesting a negative association.

The results of the present thesis indicate that efforts to improve dietary habits are still warranted, in particularly efforts to control body weight. Moreover, that breast cancer risk may be related to certain dietary items. The validity of the extended semi-quantitative food frequency questionnaire should be evaluated further to ensure a correct interpretation of the data.

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PAPERS I-IV

1. INTRODUCTION

The present thesis

Nutritional epidemiology joins the scientific fields of human nutrition and epidemiology and aims to further our knowledge about the relationship between diet and health. It aims to improve our knowledge on how we might utilise the great potential of diet on health and how to avoid hazardous dietary effects. In order to do so, efficient tools for data collection are needed. The present thesis comprises development of a semi-quantitative food frequency questionnaire for epidemiological use, collection and evaluation of dietary data, and analyses of three important topics connected to the diet and health relationship in women: nutritional quality, body weight and weight loss attempts, and breast cancer risk.

The material is largely part of the Norwegian Women and Cancer Study (NOWAC). A self-instructive semi-quantitative food frequency questionnaire for recording of 'usual diet', and with special emphasis on consumption of marine foods, has been developed, and applied for collection of dietary data among Norwegian women.

Dietary data are prone to errors and information on the validity of the data is essential. Parts of the dietary data have been validated against a biochemical marker; namely the intake of marine foods and n-3 fatty acids against the fatty acid composition in serum phospholipids (Paper I).

Nutritional quality can be assessed by comparing dietary intake with dietary recommendations. In Norway, both recommendations for intake of specific nutrients (National Nutrition Council 1997) and guidelines for composition of the diet (National Council for Nutrition and Physical Activity 1999) are given. We have examined the dietary habits of adult women according to these recommendations and how the quality of diet varies with age, lifestyle, and socio-economic status (Paper II).

The prevalence of overweight and obesity is increasing world-wide (WHO 1998), and also in Norway (National Council for Nutrition and Physical Activity 2000). At the same time there is a strong demand for leanness and fitness (Fallon 1990), making a considerable gap between actual and desired body weight. In order to minimise the gap, it is important to quantify the extent of discrepancy and to gain knowledge about the subjects experiencing it. In Paper III we investigate the distribution of body mass index among Norwegian women and their attempts to change body weight.

Breast cancer is the most common female cancer in the world (Coleman et al. 1993) and in Norway (Cancer Registry of Norway 2000). The risk of breast cancer has been linked to dietary factors, but the evidences are generally not conclusive (WCRF & AICR 1997). Among the inconsistent findings are the results of studies of milk consumption and breast cancer risk. The consumption of milk is traditionally high in

Norway. Paper IV is a contribution to the further exploration of the relationship between milk consumption and breast cancer.

Study designs in nutritional epidemiology

Most research in nutritional epidemiology has been done by means of ecological or case-control studies. Ecological studies have contributed to formulation of several fruitful diet–disease hypotheses (Keys 1970, Armstrong & Doll 1975), but this type of study design has a number of methodological problems, the most important ones being ecological bias and inappropriate control of confounding factors (Morgenstern 1998). This makes causal inferences problematic in ecological studies. Carefully conducted case-control studies offer the possibility to test diet–disease hypotheses in a non-confounded and sound manner, but this study design also has methodological limitations (Trichopoulos et al. 1991, Rothman & Greenland 1998). One particularly important pitfall in case-control studies regarding diet retrospectively is recall bias (Giovannucci et al. 1993, Holmberg et al. 1996). Another challenge is the selection of an appropriate control group.

Prospective cohort studies largely overcome the methodological weaknesses of ecological and case-control studies (Kromhout et al. 1991, Rothman & Greenland 1998). As dietary information is recorded before onset of disease, there is no risk of recall bias. The problem of confounding can be solved by controlling for potential confounding factors in the analyses, given that such information has been sufficiently collected. Furthermore, one can repeat the collection of dietary data during follow-up, and thereby having the opportunity to examine various intervals between dietary exposure and disease outcome (Willett 1998). The disadvantage of the prospective cohort design is that it makes demands on both time and resources, particularly for research on rare diseases, due to the enrolment of participants being based on exposure rather than outcome (as in case-control studies).

A new generation of large, prospective cohort studies for investigation on diet and diseases are now emerging. In 1998, Willett listed 33 cohort studies using comprehensive food frequency questionnaires (Willett 1998), and more have been initiated later (e.g., UK Women's Cohort (Greenwood et al. 2000)). Nearly all the cohort studies on diet and diseases are established in the West, with an excess of studies in the US. Among these are the Adventist Health Study (n = 34 000) (Beeson et al. 1989), the Nurses Health Study (n = 89 500) (Willett et al. 1992), the Health Professionals Follow-up Study (n = 51 500) (Rimm et al. 1991), the Iowa Women's Health Study (n = 42 000) (Kushi et al. 1992), and the Multi-Ethnic Cohort (n = 215 000) (Kolonel et al. 2000). The European cohorts include a Norwegian cohort established already in 1967 (n = 17 000) (Bjelke 1974), and the Netherlands Cohort Study (n = 121 000) (van den Brandt et al. 1990). The European Prospective Investigation into Cancer and Nutrition (EPIC) was started in 1993 (Riboli & Kaaks

1997), and today comprises more than 520 000 participants from 10 countries. This includes 35 000 women from NOWAC.

Food frequency questionnaires

The number of participants necessary for cohort studies is high even when examining common diseases. Consequently, simple data collection methods are required. For the building of large cohorts with dietary data, the development of self-instructive food frequency questionnaires was therefore essential. In contrast to dietary assessment methods such as 24-hour dietary recalls (interviewed information on previous day's food intake) and diet records (detailed listing of all foods consumed on one or more days), food frequency questionnaires do not attempt to record precisely the subject's diet on one or a restricted number of days, but rather to record their *usual* or *habitual* diet (Nelson & Bingham 1997).

A food frequency questionnaire typically consists of repetitive questions of the form '*How often on average during the last year have you been eating food item x?*', with corresponding predefined answer categories. The reason for using the last year as the reference frame is that the most relevant time-window for exposure is often unknown, that it is difficult to obtain valid data on remote diet, and that current diet has been shown to be an acceptable measure for earlier diet (Wu et al. 1988, Jain et al. 1989, Friedenreich et al. 1992, Nelson & Bingham 1997). The number of answer categories usually varies from 5 to 10, ranging from *never* to *several times per day*. The number and kinds of foods listed in the questionnaire will depend on the aims of the study. In studies of specific nutrients or foods the number of food items may be less than 20 (Coates et al. 1995, Ling et al. 1998, Neuhouser et al. 1999), whilst more than 150 items have been included in studies which seek to cover dietary intake more broadly (Pietinen et al. 1988, Nes et al. 1992, Elmståhl et al. 1996, Ocké et al. 1997).

Food frequency questionnaires may or may not include questions on amounts consumed. Except for food items that come in natural units (e.g., apples, eggs), correct estimation of portion size is usually difficult to obtain (Smith et al. 1991, Faggiano et al. 1992), and it has been claimed that the significance of additional data on individual portion size is limited (Tjønneland et al. 1992, Willett 1998). Still, most food frequency questionnaires ask for some information on portion size.

Evaluation of data from food frequency questionnaires

Data collected by means of food frequency questionnaires are, like all dietary data, prone to errors. The errors may be random or systematic, and may arise due to an insufficient food list, inappropriate response categories, or improper reporting of frequency and/or amount consumed. Careful designing, pre-testing and piloting of the questionnaire reduces the risk of applying a questionnaire with major weaknesses (Nelson & Margetts 1997). However, no matter how thoroughly designed, errors can

not fully be eliminated from questionnaire dietary data. Validity is therefore an essential aspect. In broad terms, a valid finding can be defined as being a reasonable representation of the true situation (Margetts & Nelson 1997). In the field of nutrition the validity term usually refers to the validity of the dietary assessment method (Willett & Lenart 1998).

In order to estimate the magnitude of the errors, the questionnaire data need to be compared with corresponding data of superior quality. As no dietary assessment method provides truly valid data, such comparison will only tell about the validity of the questionnaire data relatively to other dietary data, hence the term relative validity. Some researchers are even more careful in their terminology, naming the comparison of dietary data collected with different methods an evaluation study (Andersen 1998).

In lack of a perfect reference method, the choice of reference method will rather depend on the purpose of the food frequency questionnaire (Nelson 1997). To avoid spurious high estimates of validity, it is important that the errors of the reference method are independent of the errors of the questionnaire (Willett & Lenart 1998). Prospective methods, like diet recording, are less likely to be burdened with the same errors as food frequency questionnaires (memory, ability to estimate portion sizes, restricted number of eligible food items) than retrospective methods like 24-hour dietary recall. Another option, which has only started to evolve, is the use of biochemical markers.

Biochemical markers

By using biochemical measures from blood, urine, hair, nails or other tissues one can obtain an objective marker of dietary exposure (Hunter 1998). Although biochemical markers are also prone to errors (e.g., collection, storage, and analytical problems), these do not correlate with the errors of food frequency questionnaires (or other dietary assessment methods) (Kaaks et al. 1997). However, the use of biochemical markers is limited as only a small number are presently applicable. In order to be a useful biochemical marker of dietary intake, the marker must have a certain degree of sensitivity, its homeostatic mechanisms in the body must not be too strong, its turnover should not be too rapid, and it should not be too sensitive to short time fluctuations in dietary intake (Hunter 1998). Furthermore, the use of a potential marker may be distorted by the influence of genetics, gender, age, lifestyle and environmental factors, disease status, drugs use, interactions between nutrients and between nutrients and other substances in the body, and *de novo* synthesis (Bates et al. 1997).

Currently recognised biochemical markers are 24-hour urine nitrogen excretion to validate protein intake, and blood and tissue fatty acid composition to validate the pattern of fatty acid intake (especially those that cannot be synthesised endogenously)

(Bates et al. 1997). Additionally, the double-labelled water technique may be used as a marker of energy expenditure, which in turn can be used as a comparison measure of energy intake. These markers have all been utilised for validation of food frequency questionnaires applied in epidemiological studies (Bingham 1997, Andersen et al. 1999, Kroke et al. 1999, Pijls et al. 1999).

In contrast to validation studies where dietary data from food frequency questionnaires are compared to dietary data from another dietary assessment method (e.g., food records), validation against a biochemical marker only provides information about a restricted part of the diet. This requires a strict priority as regards which parts of the diet are most essential in a particular study, as the availability to apply several biochemical markers may be limited due to practical, economical and ethical reasons.

Motivated by the interest in the association between fish consumption and breast cancer (Lund & Bønaa 1993, Lund 1994), the present work focuses on validation of reported intake of marine foods and of calculated intake of fatty acids, particularly essential fatty acids. Fish and fish products are unique as contributors of long chain n-3 fatty acids in the diet, and previous studies have reported significant associations between intake of fish and long chain n-3 fatty acids and level of long chain n-3 fatty acids in fat tissue and blood fractions (Bønaa et al. 1992, Andersen et al. 1996a, Andersen et al. 1999). The turnover of fatty acids in fat tissue and different blood fractions varies, and the measures will therefore reflect dietary intake at different points of time. For instance, the fatty acid composition in fat tissue may reflect intake over years, whereas free fatty acids in serum (plasma) may reflect short-term intake (hours) (Riboli et al. 1987, Bates et al. 1997). The fatty acid composition in serum (plasma) phospholipids may reflect intake during the last weeks or months (Hunter 1998), and has been shown to reflect intake of fish and long chain n-3 fatty acids (Andersen et al. 1996a, Grimsgaard et al. 1997, Yaqoob et al. 2000). Use of serum phospholipids was thought to be appropriate for the purposes of our validation study (Paper I).

Aspects of dietary data in relation to age, lifestyle and socio-economic status

In Norway, the National Council for Nutrition and Physical Activity is responsible for monitoring the nutritional situation in the country and for giving recommendations of daily intake of nutrients. Dietary recommendations have been given since 1954 (Øgrim 1958), and both the intake of specific nutrients (National Nutrition Council 1997) and the composition of the diet are emphasised today (National Council for Nutrition and Physical Activity 1999). To obtain knowledge of how the recommendations are followed in the population, dietary surveys at the individual level are needed. It was not until 1993 that the National Council for Nutrition and

Physical Activity started to collect such data. At that time, 3 100 out of a random sample of 5 000 subjects, aged 16-79 years, participated in a study called Norkost (Johansson 1999). The National Health Screening Service collected valuable dietary data during three successive cardiovascular screenings from 1975 to 1983. However, these screenings were done in three out of nineteen Norwegian counties only, and the food frequency questionnaire mainly focused on risk factors for coronary heart diseases known at that time (Solvoll 2000).

In order to successfully promote a healthy diet, more information about current dietary habits of the Norwegian population is warranted. Dietary intake may vary with sex (Andersen et al. 1996b, Johansson et al. 1997a, Roos et al. 1998), age (Whichelow & Prevost 1996, Johansson et al. 1997a), lifestyle (Margetts et al. 1998, Johansson et al. 1999), and socio-economic status (Roos et al. 1996, Uitenbroek et al. 1996, Johansson et al. 1999). Data on how dietary intake varies between different segments of the population are essential to identify groups with unhealthy dietary habits or with marginal intake of certain nutrients. Such data will help pointing out areas where special efforts are required, and give us the opportunity to tailor messages and campaigns on healthy dietary habits. In the present study, we elucidate dietary habits of adult Norwegian women, and how nutritional quality may vary with age, lifestyle and socio-economic status (Paper II).

One of the most profiled dietary recommendations in Norway has been the one concerning fat reduction. The main message has been to reduce the percentage of energy derived from fat, while increasing the percentage of energy from carbohydrates. This recommendation still applies, but today there is also a growing concern about energy quantity per se. As the energy requirements for labour and transportation decreases in the Western world at a time when there is abundance of food, we face the challenge of obtaining a healthy balance between energy intake and energy expenditure. The increasing prevalence of overweight and obesity world-wide (WHO 1998, Lissner et al. 2000, Seidell 2000, National Council for Nutrition and Physical Activity 2000) implies that such a balance is not achieved in many populations. Obesity is defined by the World Health Organisation (WHO) as body mass index (kg/m^2) ≥ 30 (WHO 1998). It is suggested that the prevalence of obesity in European countries has increased with 10-40% during the last 10 years, and is now in the range of 10-20% in men and 10-25% in women (WHO 1998). In Norway, mean body weight for men aged 40-42 years has increased on average with 9.1kg from the beginning of the 1960's and to 1999 (from 76.9 to 86.0kg). For women there has been an average increase of 3.7kg in the same period (from 65.8 to 69.5kg). Surveys in 1994-99 indicated that 12% of Norwegian men and 11% of Norwegian women aged 40-42 were obese according to WHO's definition (National Council for Nutrition and Physical Activity 2000). Alongside the progress of overweight and obesity, there is

tremendous attention on leanness and fitness (Fallon 1990), but obviously, this attention does not prevent the widespread increase in body weight.

The strong interest in health and body look should be utilised in a positive manner. Efficient strategies for preventing unnecessary weight gain and for achieving permanent weight loss are welcomed. Like messages on healthy dietary habits, it is plausible that strategies concerning body weight will be more effective if tailor-made for subjects with certain mutual characteristics, rather than aiming to cover a broad and heterogeneous group of subjects. In addition to the extent of the weight problem, characteristics like sex, age, socio-economic status, and lifestyle may be relevant when modelling weight concern strategies. More knowledge about the subjects experiencing a discrepancy between their present body weight and the body weight they desire will hopefully improve the chances of obtaining healthy body weights in populations. In the present work, we estimate weight loss attempts among Norwegian women, and examine predictors for weight loss attempts (Paper III).

Aspects of dietary data in relation to breast cancer

The association between diet and different types of cancers has been summarised in several reports and papers (HSPH 1996, WCRF & AICR 1997, Winther et al. 1997, Cummings & Bingham 1998), and it has been proposed that 20-50% of all fatal cancers can be ascribed to diet (Doll 1998). The most convincing evidence is the protective effect of fruits and vegetables, especially on cancer of the mouth, pharynx, oesophagus, lung, and stomach, but also on a wide range of other cancer diagnoses (WCRF & AICR 1997, Cummings & Bingham 1998).

For breast cancer, the most common female cancer in the world, the associations with diet are generally not conclusive (Clavel-Chapelon et al. 1997). In Norway, breast cancer comprised 22% of all cancers diagnosed in women in 1997 (n = 2 386), with an incidence rate of 71.4 per 100 000 person-years (Cancer Registry of Norway 2000). From 1988-92 to 1993-97, the age-adjusted incidence rate of breast cancer has on average increased with 16% per year, and one may ask to what extent this increase is related to lifestyle changes.

Intake of alcohol (Smith-Warner et al. 1998, Ginsburg 1999), rapid growth and greater adult height (Tretli 1989, Li et al. 2000, van den Brandt et al. 2000) seem to increase the risk of breast cancer, whereas consumption of vegetables and fruits may decrease the risk (Favero et al. 1998, McKeown 1999, Tavani et al. 1999, Gandini et al. 2000). Much effort has been expended to reveal the association between fat intake and breast cancer risk, but still no final conclusions are reached (Feldman 1999, Holmes et al. 1999, Wu et al. 1999). The association with milk and other dairy products, food items which significantly contribute to fat intake in many Western populations, is also inconclusive (Trichopoulou et al. 1995, Männistö et al. 1999,

Slimani et al. in press). In addition to being a source of fat, milk and dairy products are good sources of calcium and conjugated linoleic acid, which have been hypothesised to restrain the development of breast cancer (Visonneau et al. 1997, Lipkin & Newmark 1999).

The long latency period between exposure and the manifestation of cancer makes it difficult both to determine the time period at which dietary exposure is most relevant, and to assess diet at this particular point in time. Several studies have indicated that nutritional exposure early in life may be of significant importance for subsequent cancer risk (Frankel et al. 1998, Blot et al. 1999, Robsahm & Tretli 1999), including breast cancer risk (Micozzi 1987, Tretli 1989, Vatten et al. 1992). As for the impact of milk consumption during childhood and adolescence on subsequent breast cancer risk, information is scarce, but an inverse association has been suggested (Hislop et al. 1986, Pryor et al. 1989). The present study gave us an opportunity to examine milk consumption both as a child and as an adult in relation to breast cancer risk (Paper IV).

2. AIMS OF THE THESIS

The general aims of this work were to design a semi-quantitative food frequency questionnaire for use in epidemiological research among Norwegian women, to validate certain components of the dietary data, to collect dietary data from a large nation-wide sample of women, and to analyse selected nutritional aspects related to health, both cross-sectionally and prospectively.

The specific aims of the four papers were:

- to validate semi-quantitative food frequency questions on consumption of fish and fish products by means of fatty acid composition in serum phospholipids (Paper I).
- to study how dietary intake varies with age, and examine the impact of lifestyle and socio-economic status on important dietary aspects (Paper II).
- to estimate body mass index and prevalence of weight change attempts, and to examine how weight loss attempts are related to body mass index, age, socio-economic status, reproductive factors, lifestyle, and diet (Paper III).
- to investigate the relationship between childhood and adult milk consumption and breast cancer risk (Paper IV).

3. MATERIALS AND METHODS

The Norwegian Women and Cancer Study (NOWAC)

NOWAC (in Norwegian: 'Kvinner, livsstil og helse'/'Kvinner og kreft') is a large population-based cohort study designed to examine factors related to cancer, other illnesses, and mortality in a prospective manner. In particular, it is designed for investigation of risk factors for breast cancer. NOWAC was initiated by Eiliv Lund at the Institute of Community Medicine, University of Tromsø, in 1991, and from 1991 to 1997 more than 100 000 Norwegian women born 1927-65 have been included in the cohort. The participants are randomly sampled from the Central Person Register, and the overall response rate is about 60% (Lund & Gram 1998). The participants have received a mailed letter of invitation requesting informed consent and a self-instructive questionnaire to be returned in a prepaid envelope. One written reminder was sent to non-responders. Several different questionnaires (examples given in Appendices A and C), of varying length and with varying content, have been developed, but with a number of common core questions. Women answering the same version of the questionnaire may be viewed as a sub-sample of NOWAC. Since 1998, NOWAC has been part of EPIC, the large European study on diet and cancer. NOWAC is approved by the Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate. A more detailed description of the study is given elsewhere (Hjartåker et al. 2000).

Study populations and designs

The present work includes women from two sub-samples of NOWAC: 52 592 women who joined NOWAC in 1991-92, and 10 249 women who joined NOWAC in 1996. The 1991-92 sub-sample form basis for the follow-up analyses (Paper IV) and the sub-sample from 1996 for the cross-sectional analyses (Papers II and III). Additionally, the present work includes 234 women who participated in a validation study in 1995 (Paper I). The study populations will be described in chronological order. Further information about the study populations and the design of the studies is given in Papers I-IV. A summary is provided in Table 1.

Table 1. Study participants and designs

Year of data collection	Subjects	Response rate	No. eligible for analysis	FFQ ¹	Type of study
1991-92	Women 34-49 yrs in NOWAC	58.4%	52 592	Limited (Appendix A)	Follow-up (Paper IV)
1995	Women 40-42 yrs at cardiovascular screening, Trondheim	91.4%	234	Extended (Appendix B)	Validation (Paper I)
1996	Women 45-69 yrs in NOWAC	51.4%	9 885/ 10 249 ²	Extended (Appendix C)	Cross-sectional (Papers II & III)

¹Food frequency questionnaire

²The number of subjects varies between the analyses in Papers II and III due to different exclusion criteria.

The follow-up study (Paper IV)

The women included in the follow-up analyses were enrolled in NOWAC in 1991-92. At that time, 100 000 women were invited to participate in the study, and the response rate after correction for non-completion was 58.4%. Six thousand of the invited women were given a questionnaire without dietary questions, and the responders of this questionnaire were not included in the present analyses. Excluded from this study were also any women who died before the beginning of the follow-up (defined as three months after mailing of the letter of invitation), had a prior cancer diagnosis, or developed cancer during the first year of follow-up, as were those lost to follow-up due to change of identification number and any who had emigrated at an unknown date. Finally, we excluded women who did not answer any of the major questions, that is, the questions on milk consumption. The number of women eligible for analyses were 52 592. These women completed a limited food frequency questionnaire and answered a wide range of question related to breast cancer risk.

The validation study (Paper I)

The women included in the validation study are not a sub-sample of NOWAC. They were women who met to a cardiovascular screening in Trondheim, Mid-Norway, arranged by the National Health Screening Service in 1995. During eight successive days in November, all women meeting to the screening (apart from those with insufficient knowledge of the Norwegian language or who arrived after closing time, n = 9) were invited to participate in the validation study (n = 256), and 242 agreed to do so. The participants were asked to fill in a semi-quantitative food frequency questionnaire and give a blood sample. Later, eight subjects were excluded from the

analyses due to incomplete dietary data or blood sample. Thus, the sample consisted of 234 subjects. The sample was thought to be comparable to NOWAC participants, and was primarily chosen for practical reasons.

The cross-sectional studies (Papers II and III)

The cross-sectional studies include women who joined NOWAC in 1996. They completed a semi-quantitative food frequency questionnaire, and also answered a number of non-dietary questions, including questions on anthropometry, lifestyle, and socio-economic status. Altogether 10 249 out of 20 000 women returned the questionnaire. After correction for non-completion the response rate was 51.4. A total of 364 questionnaires were excluded from nutrient analyses due to a high number of items non-response and/or a calculated daily energy intake below 2 500 kJ or above 15 000 kJ. The number of participants in the nutrient analyses were thus 9 885, whereas in all other analyses 10 249 subjects were included.

Assessment of diet

Three different food frequency questionnaires are applied in the present work. They will be presented in chronological order.

The limited food frequency questionnaire (Paper IV) (Appendix A)

The questionnaire that was applied in 1991-92 contained 28 dietary questions, including 3 questions on alcohol consumption. The participants were asked to indicate how often on average during the last year that they had consumed the various food items. The primary purpose of the questions was to allow adjustment for dietary intake in prospective studies of breast cancer. The questions are suitable for frequency analyses of food item consumption, but hardly for nutrient calculations.

The questionnaire included three separate questions on milk consumption: one for whole milk (3.9% fat), one for low fat milk (1.5% fat) and one for skimmed milk (0.1% fat). Nine different answer categories were given, ranging from 'almost never' to '6-10 glasses per day'. The questionnaire also included one question on daily milk consumption as a child. The answer categories to this question were 'none', '1-3 glasses', '4-6 glasses' and '7 glasses or more'.

The extended semi-quantitative food frequency questionnaire, validation version (Paper I) (Appendix B)

Given the growing interest in the effect of diet on health in general, and the possible effect of fish consumption on breast cancer risk in particular (Lund & Bønaa 1993, Lund 1994), it was decided to expand the number of dietary questions asked in the NOWAC study.

The new questionnaire was designed as a self-instructive semi-quantitative food frequency questionnaire, asking about habitual food consumption during the last year. It covered a wide range of food items traditionally consumed in Norway, but with a particular focus on consumption of marine foods. For most food items, separate questions were given for recording the frequency of consumption and the usual amount consumed. A pilot study was conducted in autumn 1995 to see how the questionnaire performed and to get more information about adequate food choices and suitable consumption categories. Twenty-two subjects, predominantly women, from the municipalities Alta (Finnmark) and Fusa (Hordaland) participated in the pilot study. In addition to answering the dietary questionnaire, the participants were asked to estimate the time needed to complete the questionnaire and to answer a couple of open-ended questions on how they found the questionnaire. Based on the findings of the pilot study, we designed a questionnaire containing 25 questions on marine food items, including 3 questions on cod liver oil and fish oil capsules, and 70 questions on other foods and beverages expected to be frequently consumed among Norwegian women. Thus the questionnaire in the validation study contained 95 questions. Non-dietary questions were not included in this questionnaire.

The extended semi-quantitative food frequency questionnaire, revised version (Papers II and III) (Appendix C)

In addition to the dietary questions, a wide range of non-dietary questions were to be included in the NOWAC questionnaire. To investigate how the length of the questionnaire affected the response rate we conducted a trial autumn 1996. Six samples, each of 1000 women, aged 50-69 years (none of which are part of the material in the present study) were invited, and six different questionnaire versions were tested. These were: 2 pages, 4 pages, 4 pages compressed to US page standard, 6 pages, 6 pages asking permission to send a new questionnaire later, and 8 pages. The response rate was 52.1%, 57.9%, 53.6%, 54.4%, 52.4%, and 51.1%, respectively (unpublished data). It was decided that doubling the amount of information by using an 8-paged questionnaire instead of a 4-paged questionnaire was worth the cost of a reduced response rate. Expanding the questionnaire beyond 8 pages was not considered.

The findings from the validation study motivated some changes in the dietary part of the questionnaire. The number of questions on marine foods were reduced from 25 to 19, and the number of questions on other foods were reduced from 70 to 55, giving a total of 74 dietary questions. Generally, we omitted food items that were infrequently used and/or were not of particular interest for us at the time. Some food items were added in broader question categories. In addition to the frequency and amount questions, the revised questionnaire included a number of qualitative food questions and a few questions about food habits as a child. Nearly 100 non-dietary questions were included.

The relationship between the various dietary questionnaires applied in this thesis is shown in Figure 1. More information about the questionnaires is given in the papers.

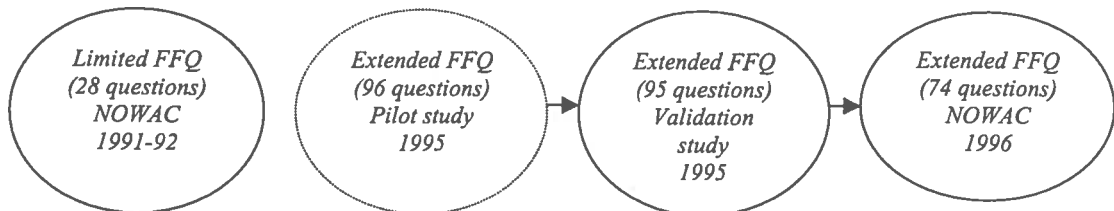


Figure 1. The relationship between the food frequency questionnaires (FFQ) applied in the present work.

Nutrient calculations

We wanted to perform analyses both on food and nutrient level. As no appropriate software was available, we developed a new computation program. The program was made using SAS software (SAS Institute 1996). Energy and nutrient values were obtained from the Norwegian Food Composition Table 1995 (National Nutrition Council & Norwegian Food Control Authority 1995) and portion weights were largely derived from a Norwegian table of household measures and weights for foods (National Association for Nutrition and Health 1989). The program calculates daily intake of foods and nutrients by multiplying the recorded frequencies and amounts of consumption (in grams). In cases where a frequency was given without indicating the amount consumed, the smallest amount option was assumed. Likewise, if an amount of consumption was given without a frequency mark the lowest frequency option (never/seldom) in the questionnaire was chosen. If both frequency and amount indication were missing, the food item was considered as not consumed.

Assessment of non-dietary variables

Both the questionnaire used in 1991-92 and the one used in 1996 contained a wide range of non-dietary questions (Appendices A and C). For the present thesis, questions concerning the following topics were relevant: anthropometry, socio-economic status (income and years of education), level of physical activity, smoking history, weight change attempts, hormonal and reproductive factors, rating of own current state of health, and maternal history of breast cancer.

Body mass index was calculated from self-reported weight (kg) and height (m) as kg/m^2 . Underweight was defined as body mass index < 18.5 , normal weight as body mass index 18.5-24.9, overweight as body mass index 25.0-29.9, and obese as body mass index ≥ 30 (WHO 1998).

Blood sample analyses

The participants in the validation study gave a 10ml non-fasting venous blood sample while at the screening centre. The blood samples were drawn by the Health Screening Service and analysed by the Regional Hospital, University of Trondheim. Serum phospholipids fatty acids were analysed essentially as described by Bønaa et al. (1990). Briefly, serum lipids were extracted with n-butanol (Bjerve et al. 1974) and phospholipids isolated from the lipid extracts using Sep-Pack C18 columns. Diheptadecanoyl-glycerophosphocholine and butylated hydroxytoluene were added as internal standard and antioxidant, respectively. Phospholipids were transmethylated and fatty acid methyl esters quantified as mg fatty acid/l serum by gas liquid chromatography on a SP2330 column (Supelco Inc., Bellefont, PA) (Bjerve et al. 1987).

Identification of cancer, death and emigration

For the follow-up study, data collected in 1991-92 were matched with records at the Cancer Registry of Norway to identify incident breast cancer cases. Accuracy of the linkage was ensured by the unique 11-digit identification number that all Norwegians have. The data were likewise linked to records at Statistics Norway for information on death and emigration. End of follow-up was 31.12.1997, and mean follow-up time was 6.2 years.

Statistical methods

All analyses were performed with the SAS statistical package, version 6.12 (SAS Institute 1996).

The validation study (Paper I)

The relationship between serum phospholipid fatty acid content and dietary data was assessed by Pearson's correlation coefficients when the variables could be assumed to be normally distributed, otherwise Spearman's correlation coefficients were used. Analysis of variance, performed by general-linear-models procedures, was used to study how the phospholipid fatty acid composition varied between quartiles of fish intake. Multiple linear regression analysis was applied to examine simultaneously the effect of all fish items on the phospholipid fatty acid composition. Residual plots were made to examine the assumptions of the multiple regression model. All tests of significance were two-sided, and a significance level of 1% was chosen due to a large number of tests performed.

The cross-sectional studies (Papers II and III)

The nutrient variables were generally non-normally distributed (skewed to the right), and non-parametric methods were therefore applied. Statistical comparisons between groups were made by Wilcoxon rank sum test, Kruskal-Wallis test or chi-square test when appropriate. The relationship between a binary outcome variable (e.g., presence vs. absence of a feature) and selected independent variables was analysed by estimating odds ratios and corresponding 95% confidence intervals using simple and multiple logistic regression models. A number of models were examined and possible interaction terms were tested. Statistical significance was calculated by using the likelihood ratio test. To test whether there was a significant trend in the odds ratios for ordered levels of exposure, the exposure variable was included in the model as a continuous variable. Model fit was assessed by the Hosmer and Lemeshow goodness of fit statistic. All tests of significance were two-sided, and a significance level of 5% was used.

The follow-up study (Paper IV)

The reproducibility of the dietary variables was evaluated by calculating weighted kappa estimates. Cox proportional hazards regression analyses were carried out to investigate the simultaneous effect of selected dietary variables and covariates on breast cancer incidence rate. Incidence rate ratios and 95% confidence intervals were estimated. Person years at risk were calculated as the time elapsed from date of entry into the cohort, to the time of cancer (any type), to time of death or emigration, or to the end of follow-up (31.12.1997), whichever came first. To test whether there was a significant trend in the incidence rate ratio for ordered levels of exposure, the exposure variable was included in the model as a continuous variable. The assumptions of proportional hazards for the exposures of interest were examined by cumulative hazard plots and log-log plots. All tests of significance were two-sided, and a significance level of 5% was used.

4. SUMMARY OF PAPERS

Paper I

Serum phospholipid fatty acid composition and habitual intake of marine foods registered by a semi-quantitative food frequency questionnaire.

Hjartåker A, Lund E, Bjerve KS.

Background

Before collecting data on fish consumption in a large sample of Norwegian women, it was wise to examine how the dietary questionnaire performed in a smaller sample of women.

Objective

The objective was to examine the relationship between consumption of fish and fish products registered by a semi-quantitative food frequency questionnaire and the composition of fatty acids in serum phospholipids.

Methods

The study design was a cross-sectional analysis of diet and blood values among women attending a cardiovascular screening in Mid-Norway in autumn 1995. Altogether 234 middle-aged women (participation rate 91.4%) completed the questionnaire and gave a valid blood sample.

Results

Total frequency consumption of fish showed only weak associations with serum phospholipid fatty acid composition. In separate analyses of lean and fatty fish, consumption of fatty fish was negatively associated with n-6 and positively associated with n-3 fatty acids in serum phospholipids, while no significant associations were found for lean fish consumption. Cod liver oil consumption was strongly related to the phospholipid fatty acid composition. The associations improved moderately when portion size information was added. Spearman's correlation coefficient between dietary intake of eicosapentaenoic acid (EPA) and serum phospholipid EPA was 0.58, and the correlation coefficient between intake of docosahexaenoic acid (DHA) and serum phospholipid DHA was 0.53.

Conclusion

The study suggests that habitual intake of fish and cod liver oil registered by our semi-quantitative food frequency questionnaire can be reflected in serum phospholipid fatty acid composition. However, as the fat content of fish is highly variable, separate registration of lean and fatty fish consumption is necessary.

Paper II

Relationship between dietary habits, age, lifestyle, and socio-economic status among adult Norwegian women. The Norwegian Women and Cancer Study. Hjartåker A, Lund E.

Background

Dietary data on individual level from population-based samples has been scarce in Norway.

Objective

The objective was to examine how dietary intake varies with age in a nation-wide sample of Norwegian women, and to evaluate the impact of lifestyle and socio-economic status on important aspects of diet.

Methods

The study was designed as a cross-sectional analysis of dietary habits in a random nation-wide sample of women aged 45-69 years. In summer 1996, 20 000 women were invited, and 10 249 agreed to participate. In total, 9 885 semi-quantitative food questionnaires were acceptable for nutritional analyses.

Results

Dietary habits differed moderately with age. The oldest women reported a higher consumption of potatoes and fish, whereas the youngest reported more coffee, meat, and alcohol. The reported intake of fruit, vegetables, and potatoes was lower than recommended in all age groups. Older women had a slightly better distribution of energy yielding nutrients than younger women, although the median percentage of energy from fat was too high in all age groups. The median dietary fibre density of the diet was close to the recommended level in all age groups, yet lowest among the youngest women. Practising a healthy lifestyle and higher socio-economic status were associated with reporting a healthier diet. However, adjusting for lifestyle and socio-economic factors did not substantially alter the associations between diet and age.

Conclusion

Older women tend to have a healthier diet than younger women. The relationship does not seem to be strongly confounded by lifestyle and socio-economic status, though these factors are also related to dietary habits.

Paper III

Body mass index and weight change attempt among adult women. The Norwegian Women and Cancer Study.

Hjartåker A, Laake P, Lund E.

Background

The increasing prevalence of overweight and obesity, together with a substantial demand for leanness, is a matter of concern, both nationally and globally.

Objective

The objective was to estimate body mass index and prevalence of weight change attempts in a population-based sample of Norwegian women, and to examine how weight loss attempts are related to body mass index, age, socio-economic status, reproductive factors, lifestyle, and diet.

Methods

The study was designed as a cross-sectional analysis among a random, nation-wide sample of women aged 45-69 years. In 1996, a total of 20 000 women were mailed a questionnaire and 10 249 women agreed to participate.

Results

Based on self-reported data, mean body mass index was 24.6 kg/m², 40% of the women had a body mass index ≥ 25 , and 8% had a body mass index ≥ 30 . More than 50% of the women were trying to lose weight, and weight loss attempt was strongly associated with body mass index. Age, education, income, smoking status, and perception of diet's importance to health were also significant predictors of weight loss attempt. The effect of age, education, and income on weight loss attempt was modified by the level of body mass index. Women trying to lose weight reported a different diet than those not trying to lose weight, irrespective of body mass index.

Conclusion

A large proportion of middle aged women are trying to lose weight. Body mass index is predominant in explaining weight loss attempts, but age, lifestyle, and socio-economic status also predict weight loss attempts to some extent.

Paper IV

Childhood and adult milk consumption and risk of breast cancer in a cohort of 52 592 women. The Norwegian Women and Cancer Study.

Hjartåker A, Laake P, Lund E.

Background

Breast cancer is the most common female cancer in the world. Analyses of consumption of dairy products and breast cancer incidence have yielded conflicting results.

Objective

The objective was to examine the relationship between childhood and adult milk consumption and breast cancer incidence.

Methods

The study design was a prospective analysis of 52 592 Norwegian women aged 34-49 years at entry. Information on childhood and adult milk consumption was obtained from frequency questions mailed to the participants in 1991-92. Linkage to records at the Cancer Registry of Norway and Statistics Norway gave information on cancer incidence, and on death and emigration, respectively. End of follow-up was 31.12.1997.

Results

A total of 371 incident cases of breast cancer were diagnosed during follow-up. No association was found between milk consumption as a child and subsequent breast cancer. Adult milk consumption was negatively related to breast cancer incidence after adjustment for known and potential risk factors (P-value for trend 0.04). The incidence rate ratio of breast cancer was 0.64 (95% confidence interval 0.38–1.08) for women drinking more than three glasses of milk per day compared to women not drinking milk. The estimate was about the same when looking at premenopausal women only. Analyses according to type of milk consumed and milk fat consumption did not reveal any clear associations. Combining childhood and adult milk consumption gave similar incidence rate ratios as when analysing adult milk consumption alone.

Conclusion

No association was observed between childhood milk consumption and subsequent breast cancer. Adult milk consumption tended to be negatively associated with breast cancer.

5. GENERAL DISCUSSION

NOWAC is the largest ongoing cancer epidemiological study linked to diet in Norway. From the modest collection of dietary data at the onset of the study in 1991 and to today's extended semi-quantitative food frequency questionnaire, a large amount of data on Norwegian women's diet have been collected. The NOWAC cohort provides valuable opportunities to improve our knowledge of the relationship between diet and health. This thesis comprises work from the development of the extended semi-quantitative food frequency questionnaire, through validation of dietary data, to application of dietary data in cross-sectional and follow-up analyses related to health.

Data evaluation

The validation study (Paper I)

The most important reason for expanding the dietary questionnaire in NOWAC was to collect proper information on fish consumption. This focus guided the choice of validation study; namely, to validate the reported intake of fish and fish products against the content of fatty acids in serum phospholipids. By using a biochemical marker we avoided correlated errors of the test and the reference method (Kaaks et al. 1997). Based on the results of the validation study we concluded that our questions on fish and fish product consumption had adequate validity. The reason for this conclusion was a close association between the calculated intake of long chain n-3 fatty acids and the composition of the same fatty acids in serum phospholipids, compared to findings in similar studies and our a priori expectations (Ma et al. 1995, Andersen et al. 1996a). As typically in validation papers, we did not include any judgement of how the agreement between the test method and the reference method will affect the results of studies applying the test method.

Generalisability of the results from the validation study

Ideally, the validity of a method should be examined in a representative sub-sample of the study participants in order to minimise the concern regarding the generalisability of the results (Willett 1998). This is often not the case. The participants in our validation study were women voluntarily attending a cardiovascular screening. Theoretically, these women were eligible (to be sampled) for the NOWAC cohort. Also, one may speculate that women participating in a health screening or postal health survey are generally health-conscious. Still, we do not know whether the participants in the validation study differed systematically from the NOWAC participants in any way. The participation rate in the validation study was high (91%), making the risk for self-selection bias small at this stage of the inclusion. However, the attendance rate for the health screening was 65% (National Health Screening Service 1996), and the sample from which the validation study participants were recruited may thereby have been biased. The response rate in the NOWAC sample which received the revised version of the extended semi-quantitative food frequency questionnaire (Papers II and III) was 51%, and the women were somewhat older than

the women in the validation study (mean 54.8yrs vs. 40-42yrs). Therefore, even though the response rate in the validation study itself was high, generalisation of the results of the validation study to the NOWAC cohort is open to objections.

Considerations concerning energy intake (Papers II and III)

A recurring problem in dietary assessment is the reporting of total energy intake. Methods like diet records (Martin et al. 1996, Sawaya et al. 1996) and 24-hour dietary recalls (Buzzard 1998, Kroke et al. 1999) are known to generally underestimate the energy intake. For food frequency questionnaires, which vary considerably in extension, the results are more diverse. Both underestimation (Kroke et al. 1999) and overestimation (Nes et al. 1992, Kaskoun et al. 1994, Klipstein-Grobusch et al. 1998) of food intake have been reported. To consider whether the reported energy intake is likely to be a measure of usual energy intake over time, one may use cut-off limits for *habitual* energy intake. These cut-off limits are calculated based on fundamental principles of energy physiology and defines levels of energy intake below which a person of given sex, age and body weight cannot live a normal sedentary life (Goldberg et al. 1991). The cut-off limits are expressed as a multiple of the basal metabolic rate (BMR), and the 'survival' limit is set to $1.27 * BMR$ (FAO/WHO/UNU 1985). For all 'normal' circumstances the limit is set to $1.35 * BMR$, and it is concluded that it is highly unlikely that any normal, healthy, free-living person could habitually exist on energy intake below this value. Other cut-off limits are given for judgement of *actual* energy intake during the measurement period (Goldberg et al. 1991).

Our extended semi-quantitative food frequency questionnaire aimed to cover *usual* diet during the past year. Still, it did not aim to cover the whole diet, and the calculated energy intake cannot be taken as a measure of total energy intake. Therefore, we have not applied BMR-factors to appraise the degree of misreporting of energy intake in our sample. In epidemiology, information of absolute exposure dose is often not essential, but rather to get a correct ranking of subjects according to exposure. When we analysed energy intake by level of physical activity we found a consistent positive association, although less so with increasing body mass index (data not shown). A negative association was found between energy intake and age (Paper II). These findings are as could be expected.

Considerations concerning the milk questions in the limited food frequency questionnaire (Paper IV)

No validation has been done of the questions in the limited food frequency questionnaire, apart from two questions on fish which were included in the extended questionnaire version. In particular, one may be concerned about the validity of the information on childhood milk consumption. The subject's ability to recall childhood

food consumption is uncertain. Also, only one question was asked about this topic, and it may be too insensitive to detect real differences in early eating habits.

The reproducibility, that is, the degree of consistency with which a measure of exposure measures the exposure (Margetts & Nelson 1997), of the milk questions has been examined in a sub-sample of the participants. A total of 555 women who had answered the limited questionnaire in 1991 were asked to fill in the same questionnaire again four months later, and 341 agreed to do so. The agreement between the answers on the three questions on adult milk consumption in the first and the second questionnaire was moderate (weighted kappa 0.43-0.55) (Altman 1991). A number of women (14-24%) indicated milk consumption on one of the two recording occasions only. On examining the data, we observed a clear tendency for missing values on either the first or the second recording corresponding to the answer category 'almost never' on the other occasion. Accordingly, excluding women with missing values improved the agreement between the two recordings considerably (weighted kappa 0.73-0.80). As for childhood milk consumption, the number of missing values on one of the occasions was lower (3%), and the agreement between the first and the second recording was about the same whether women with missing values were included or not (weighted kappa 0.54 and 0.60, respectively).

Considerations concerning non-dietary variables (Papers II, III and IV)

None of the non-dietary questions applied in this thesis have been validated. Age was one of the inclusion criteria for the study. The age variable was therefore taken from Statistics Norway's sampling file, and should be accurate. All other variables are self-reported and may be burdened with errors. Special attention should be paid to the body mass index variable, as self-reported weight and height are prone to reporting errors. Studies in the US and the UK have found women to underestimate their body weight by an average of about 1kg and overestimate their height by 0.7cm (Rowland 1990, Roberts 1995), but substantial discrepancies may occur in subgroups (among older women and among overweight subjects).

Considerations concerning breast cancer cases (Paper IV)

The outcome variable in Paper IV is breast cancer. The information on breast cancer cases was provided by the Cancer Registry of Norway, which has an almost complete record of all cancer cases (Lund 1981, Harvei et al. 1996). It is mandatory by law for physicians, hospital departments, and pathological laboratories to report all incident cancer cases to the Registry. Moreover, information at the Registry is matched with information mentioning cancer in the Register of Deaths at Statistics Norway to achieve a high degree of completeness and high data quality (Cancer Registry of Norway 2000). Consequently, the reporting system is based on pathology reports, clinical records, and death certificates. For the sample in Paper IV, 97.8% of the cancer cases were histologically verified. Similarly, it is mandatory by law to report

all deaths to Statistics Norway (Statistics Norway 1998), which also keeps information on emigration. The 11-digit personal identification number of all Norwegian citizens allowed linkage of data from the Cancer Registry of Norway, Statistics Norway, and NOWAC. We consider the endpoint and the censoring times in Paper IV to be of high validity.

Aspects of dietary data in relation to age, lifestyle and socio-economic status. The cross-sectional studies

Cross-sectional data can provide information about frequency distribution of exposures and diseases at a specified time, that is, giving prevalence figures. They can also be used for examining associations between exposure and outcome, but as exposure and outcome variables are recorded at the same time, no inference about causality can be made (Hennekens & Buring 1987). In our cross-sectional analyses we were both interested in obtaining prevalence data and examining exposure-outcome relationships. Prevalence data were obtained by counting, whereas associations were examined by calculating odds ratios. The odds ratio gives the odds of having a given outcome if being exposed compared to the odds of having the outcome if not being exposed.

The validity of the prevalence data will depend on whether the study participants are representative of the study population and instrument validity. The validity of the estimated associations between exposure and outcome will also depend on whether potential confounding factors have been properly controlled for.

Response rate and selection bias

In 1996, 20 000 women were sampled and invited to participate in NOWAC. Corrected for non-completion the response rate was 51.4% (10 249 out of 20 000). By mistake, 2 072 women previously asked to participate in NOWAC were not excluded from the sampling file at Statistics Norway. Excluding these women, the response rate for the 1996 sample was 52.5% (9 407 out of 17 928). Our response rate is as can be expected in population-based studies using postal questionnaires without offering any reward to the participants (Brussaard et al. 1997, Johansson et al. 1997b, Kolonel et al. 2000, Turnbull et al. 2000). Nevertheless, the response rate makes the study vulnerable to self-selection bias and demands careful interpretation of the results, particularly when trying to estimate prevalence data.

We have only limited information about the non-responders. We know that the response rate declined with age, ranging from 55.5% in the youngest age group (45-49 yrs) to 41.6% in the oldest age group (65-69 yrs). Moreover, we know that women living in Northern Norway were more likely to respond than women living in Southern Norway (55.3% and 50.8%, respectively). An inverse association between age and response rate was also observed in another Norwegian nation-wide study on

diet (Johansson et al. 1997b), but generally the literature does not provide consistent findings on the relationship between age and response rate (Andersen et al. 1996b, Brussaard et al. 1997, Etter & Perneger 1997, Cotterchio et al. 2000). The reason for the lower response rate among the older women is unknown. It could be related to interest in the research questions or to difficulties in filling in the questionnaire. The higher response rate in Northern Norway could be related to the location of the responsible research unit, that is, the University of Tromsø (Lund & Gram 1998), or to the distribution of rural, urban, and city areas. The population density is lower in Northern Norway, and other Nordic studies have experienced a higher response rate in rural than in urban areas (Andersen et al. 1996b, Johansson 1999).

Unfortunately, we did not have the opportunity to link data from this sub-sample of NOWAC to the Education Register at Statistics Norway or to the Central Person Register to get figures on parity. Linkages of another sub-sample of NOWAC to the records at Statistics Norway revealed no major differences in the distribution of parity and length of education among the NOWAC responders and the general female population in the same age groups (see page 29). Also, two trials concerning the response rate have been conducted in sub-samples of NOWAC. The first trial was conducted in 1992, and examined the effect of length and title of the questionnaire on response rate. Altogether, 5 000 women aged 34-49 years were invited (of whom 3 000 are part of the sampling population in Paper IV). The response rate ranged from 57.1% to 70.2%. The distribution of factors such as smoking, years of education, use of oral contraceptives, and parity were the same irrespective of response rate and questionnaire design (Lund & Gram 1998). The second trial was conducted in 1996, and examined the impact of questionnaire length on response rate among 6 000 women 50-69 years (see page 14). The preliminary results from this trial seem to be in accordance with findings from the first trial, that is, the distribution of socio-economic and lifestyle factors do not seem to vary according response rate (unpublished data).

Can our findings on age and diet and on body mass index and weight change attempts be generalised to populations outside NOWAC (Rothman & Greenland 1998)? Although we have no strong indications that the women participating in the study differs systematically from those who are not, caution is needed, particularly when interpreting the prevalence data. Body mass index usually increases with increasing age, and we can assume that the overall distribution of body mass index found in our study being more or less erroneously skewed towards lower values. As for the associations between exposure variables and various outcomes, these will only be biased if the non-responders differ from the responders not only on the exposure variable (e.g., age) but also on outcome status (e.g., having a healthy diet). That is, older women respond less to the study than younger women, and those of the older women who do respond have a different diet than non-responders of the same age. If

so, the associations between age and diet may be biased (Hennekens & Buring 1987). We believe this to be unlikely in our study.

Information bias

The observed associations may also be biased due to errors in the assessment of exposure or of outcome. For continuous variables, we talk about measurement errors, whilst for categorical variables, we talk about misclassification. If the measurement error/misclassification is not dependent on the values of other variables, the error is referred to as non-differential. If the error is dependent on the values of other variables, it is referred to as differential (Margetts & Nelson 1997). Differential errors may arise from differential recall of exposure by those having a given outcome and those who do not (recall bias), and from differences in obtaining, recording, processing, and interpreting of data by the interviewer/researcher according to characteristics of the study participants (interviewer bias). One should note that it may also be induced when continuous or categorical data with non-differential errors are collapsed into fewer categories (Flegal et al. 1991, Wacholder et al. 1991, Rothman & Greenland 1998). Categorisation of continuous variables is common in epidemiological analyses of nutrient intake, for instance, percentage of energy from fat and dietary fibre density in the present work.

In the case of non-differential errors, the observed association is usually underestimated (i.e. towards the null value). Still, overestimation of the association (i.e. away from the null value) may occur in situations where the exposure variable has more than two categories (Birkett 1992, Rothman & Greenland 1998). If the errors are differential, the observed association may be either over- or underestimated, depending on the particular situation, distorting the possibilities of correct interpretation of the results (Rothman & Greenland 1998).

In our study, exposure information is collected before disease outcomes have appeared, and there is no personal contact between researcher and study participants. An observed association between exposure and subsequent disease is therefore unlikely to be due to recall or interviewer bias. The outcome measures in Papers II and III are, however, not diseases but rather characteristics of the participants recorded at the same time as the exposure. Nonetheless, recall and interviewer bias is unlikely. Still, both the exposure variables (body mass index, level of physical activity, smoking status, years of education, income and importance of diet) and the outcome variables (healthy diet and weight loss attempts) may be subject to differential errors due to categorisation (Flegal et al. 1991). Differential errors may also arise if women who report a healthy diet and women who are trying to lose weight have different errors in their exposure measurement than those who do not report a healthy diet and those who do not try to lose weight. Though, in our view, differential errors in the outcome variables are more likely. The complexity behind the

construction of the three dichotomised variables used to assess 'healthy diet' in Paper II is important. All of the variables - percentages of energy from fat, dietary fibre density, and 'five a day' (number of servings of fruit, vegetables, and potatoes per day) - are based on information from several questionnaire items. A correct division of the study participants into the outcome categories, 'healthy diet' versus 'not healthy diet,' and 'trying to lose weight' versus 'not trying to lose weight' may be impeded by so-called social desirability bias, that is, subjects' wishing to convey a desirable image (Hebert et al. 1997, Margetts & Nelson 1997). For instance, some of the women stating that they believe their diet is very important to their health may, consciously or unconsciously, overestimate their consumption of healthy food items. Correspondingly, overweight women may feel more obliged than normal weight women to report an 'acceptable' diet and to say they are trying to lose weight. If this is the case, the observed associations for these aspects may overestimate the true underlying association.

In Paper II, we state that older women tend to have a healthier diet than younger women do. Bearing in mind the possibilities of errors introduced by self-selection bias and confounding, the most serious weakness is the lack of information about the validity of the dietary questionnaire. The paper presents daily intake of energy and several nutrients. These figures should not be taken as absolute intakes. If we assume that the errors are independent of age, the figures can rather be applied for comparison between age groups. If the errors depend on age, correct evaluation of the data is difficult. Also, the errors may differ between food items, contributing to a complex error structure for the calculated nutrients. As suggested in the paper, the omission of questions on orange juice consumption in the questionnaire could give rise to differential errors if the consumption of orange juice varies with age. This would have implications both for the calculations of vitamin C intake and the 'five a day' index.

Confounding

In addition to selection bias and information bias, the observed associations in Papers II and III may be biased by confounding factors. A confounding factor can be defined as an extraneous factor that is associated with both the exposure variable in question and the outcome, and may thereby distort the observed relation between exposure and outcome. The confounding factor should not be an intermediate factor in the causal chain between exposure and outcome (Rothman & Greenland 1998). If information about confounding factors is available, it can be included in the statistical analyses, and controlled for. Without control for confounding factors, the observed association between exposure and outcome can be overestimated, underestimated, or even show the opposite direction of the true association (Rothman & Greenland 1998). In order to achieve appropriate control of confounding factors, they need to be recorded in a valid manner. If the information on confounding factors is poor, there may still be

some residual confounding of the results even after information about the confounding factors have been taken into account (Clayton & Gill 1997).

Our multivariate models include a number of variables that act simultaneously as exposure variables and potential confounding variables. As we do not know the validity of the self-reported variables, any residual confounding by these variables cannot be ruled out. Also, the impact of any residual confounding may vary between sub-groups of participants. For instance, in Paper III, the association between body mass index and weight change attempt could be burdened with residual confounding by physical activity, and one might speculate that the validity of the physical activity variable varies with body mass index. Furthermore, the observed results may be confounded by unknown and unmeasured factors. The analyses on body mass index and weight change attempts lack information on numbers of weight change attempts and on actual weight changes, and these factors could influence the observed results.

Aspects of dietary data in relation to breast cancer. The follow-up study

In cohort studies, where exposure data are collected prior to the onset of the outcome, analyses can only be performed after sufficient follow-up time. What qualifies as 'sufficient time' depends on sample size, incidence of the given outcome and the required power of the study. For the NOWAC subjects answering the extended semi-quantitative food frequency questionnaire in 1996, follow-up analyses of breast cancer and diet can first be performed after about five years of follow-up. Before that time there will not be enough breast cancer cases to carry out meaningful analyses. For the subjects enrolled in NOWAC in 1991-92, follow-up analyses on breast cancer could be done during the work on this thesis.

The limited questionnaire used in 1991-92 contained only two simple questions on fish consumption, and we decided to delay the exploration of our hypothesis on fish consumption and breast cancer until sufficient follow-up time has passed from 1996.

Milk is another food item that traditionally has been, and still is, important in the Norwegian diet, and for which the association with breast cancer is uncertain. Information on milk consumption was collected in 1991-92 and gave us an opportunity to examine the relationship with breast cancer in follow-up analyses. The analyses showed no association between childhood milk consumption and subsequent breast cancer, whereas adult milk consumption tended to be negatively associated with breast cancer.

Response rate and selection bias

Could these findings be due to bias, confounding or chance? The response rate for the subjects enrolled in NOWAC in 1991-92 was 58.4%. Typically, this level of response could raise the concern about self-selection bias. To obtain more information about

whether the responders were representative of the total sample of eligible women, the distribution of age, length of education, and parity were examined among 15 000 women that were invited to participate in NOWAC in 1992. Compared to the total sample of eligible women, the responders were slightly younger. The distribution of women in age groups 35-39 years, 40-44 years and 45-49 years were 35.9%, 32.2% and 31.9%, respectively for responders, and 34.3%, 32.8% and 32.9%, respectively for the total eligible sample. Among the responders, 25.9% of the women had 13 years or more of education; the corresponding figure for the total eligible sample was 21.9%. As for parity, 32.4% of the responders had three or more children, whereas for the eligible sample the figure was 32.0%. The percentage of nulliparous women was 8.6 among responders and 10.4 and among the eligible sample. Acknowledging these differences, for bias to occur, the relationship between exposure and outcome needs to be different for those responding to the study and those who are not (Rothman & Greenland 1998).

More likely in prospective studies is selection bias due to loss of study subjects during the follow-up period (Kirkwood 1988). Loss of study subjects may be due to withdrawal of willingness to participate, migration out of the study area, or censoring by competing risk. The follow-up period in our study was relatively short (mean 6.2 years) and the number of subjects censored due to reasons other than breast cancer was low. None of the participants demanded to be removed from the cohort, 308 women were censored due to death, and 191 women emigrated from Norway. As regards cancer (any cancer), women diagnosed during the first year were never included in the analyses (n = 104). For the remaining of the follow-up period, 897 women were diagnosed with cancer other than of the breast, and censored. We have no reason to believe that women lost to follow-up had both a different milk consumption pattern and a different risk of breast cancer than those being observed for the whole follow-up period.

Information bias

We do not know the validity of the milk questions. However, as the information on milk consumption was given before occurrence of breast cancer, it is unlikely that errors are differential. To reduce the risk that any preclinical cancer could effect the consumption of milk, and thereby introducing differential errors, women developing cancer during the first year of follow-up were excluded from the analyses. Analyses including cancer cases diagnosed the first year of follow-up showed essentially the same incidence rate ratios as analyses excluding these cases (data not shown). Still, as discussed previously, differential misclassification might have arisen when collapsing the information on adult milk consumption into categories (Rothman & Greenland 1998).

Confounding

All known reproductive and hormonal risk factors for breast cancer were controlled for in the analyses, together with a number of potential risk factors (body weight, height, years of education, level of physical activity, and alcohol intake). Residual confounding by these variables cannot be ruled out, although sub-group analysis showed no indication of this.

Confounding by other factors is possible. For instance, dietary variables, such as energy or fat intake, could be of relevance. Unfortunately, the food frequency questionnaire distributed in 1991-92 provided only limited information on these items, thus impeding opportunities for appropriate adjustment. Information on energy and fat intake was therefore not included in the multivariate analyses. However, the association between breast cancer and fat intake is still under debate (Feldman 1999, Holmes et al. 1999, Wu et al. 1999), and we find it unlikely that our results are strongly confounded by fat intake. As for total energy intake, this is been reported to be positively associated with breast cancer risk, although not very strongly (Favero et al. 1999, Fioretti et al. 1999, Jasienska & Thune in press), and it may also be related to milk consumption. We cannot dismiss any confounding by energy intake in our analyses. Still, adjustment for energy intake did not alter the association between milk consumption and breast cancer in a Finnish cohort study (Knekt et al. 1996). Adjustment for fat intake and other dietary variables in the Finnish study had no major impact on the results either.

Chance

The role of chance can be assessed by hypothesis testing or calculation of confidence intervals (Margetts & Nelson 1997). In Paper IV, we applied 95% confidence intervals to represent the range within which the estimated incidence rate ratios were likely to lie, and hypothesis testing to test whether there were any significant linear trends in the incidence rate ratios with increasing exposure. The width of the confidence interval depends on sample size and estimated standard deviation of the incidence rate ratio. A wide confidence interval indicates that the estimated incidence rate ratio is not very precise. The confidence intervals presented in Paper IV include the value 1. By strict statistical evaluation we would conclude that there is no association between milk consumption and risk of breast cancer. Examining the data according to linear trends in the estimates showed a number of borderline significant trends. When evaluating the results, it should be recalled that the 5% significance level was chosen by the researchers and is not an unalterable value for determining significant and non-significant results. Overall, we judge our results as an indication of a negative association between breast cancer and adult milk consumption, although the statistical tests are barely significant.

Causality

If the observed findings of a study cannot be explained by biases, confounding or chance, we can conclude that a valid statistical association exists between exposure and outcome (Hennekens & Buring 1987). This does not imply that the exposure causes the outcome. Still, a primary object in epidemiology is to judge whether there is a causal association between exposure and outcome. Such a judgement goes beyond the validity of any single result, and should include consistency with previous results from both epidemiological and biological studies. There is no absolute means of distinguishing between causal and non-causal relationships, but criteria for assisting our judgement has been proposed. A well-known set of criteria is that proposed by Hill (1965). His criteria are strength, consistency, specificity, temporality, biologic gradient, plausibility, coherence, experimental evidence, and analogy. Hill states that none of these criteria give indisputable evidence for or against a cause-effect hypothesis and that none of them are absolutely necessary. Rothman and Greenland (1998) have evaluated Hill's criteria and generally found them to be useful when judging cause-effect associations, but they also have some objections. For one thing, Rothman and Greenland claim that the criterion of temporality is an absolute condition for causality; that is, the cause needs to precede the effect in time. Another objection concerns the criterion of specificity (a cause leads to one single effect), which they find useless and misleading. Hennekens and Buring (1987) focus on the strength of the association, biologic credibility and consistency with other investigations, but also mention time sequence and dose-response relationship as criteria for assessing causality. Notwithstanding the various criteria suggested, there will always be an element of belief when judging whether an association is causal or not.

Our observed negative association between adult milk consumption and breast cancer risk is not strong. This does not rule out that the association is causal, but it does increase the chance that the association may be explained by undetected biases. Now, diet and cancer risk associations are not expected to be very strong (WCRF & AICR 1997), and our results did show a consistent dose-response relationship. Our finding is consistent with the findings of thorough analyses of breast cancer and consumption of dairy products done in a Finnish cohort study (Knekt et al. 1996). In the Finnish study, the relative risk for breast cancer was 0.42 (95% confidence interval 0.24-0.74) for women with the highest milk consumption (tertile) as compared to women with the lowest consumption. Previous prospective work on Norwegian women (n = 25 892) by Gaard et al. (1995) did, however, indicate that there might be a positive association between consumption of whole milk and risk of breast cancer. No association was found for total milk consumption. Another prospective analysis on Norwegian women (n = 2 679) by Ursin et al. (1990) did not find any association with total milk consumption either. The same goes for the results from other prospective studies (Mills et al. 1988, 1989, Toniolo et al. 1994). Also the results from case-

control studies have been inconsistent (e.g., Trichopoulou et al. 1995, Favero et al. 1998, Männistö et al. 1999). The lack of consistency may weaken the probability that a causal relation exist. However, it may be due to different study methods, different study populations, and different errors in the exposure variables (Rothman & Greenland 1998).

The critical time period in which milk may influence the development of breast cancer is unknown. Even if the participants in our study were asked to report their diet during the last year, the critical time period may well have preceded this time. As discussed in Paper IV, it may be that diet during childhood or adolescent is of greater importance for breast cancer development than adult diet (Micozzi 1987, Tretli 1989, Ziegler et al. 1993). However, valid information on early food consumption is hard to obtain, and only a few published papers have shown data on milk consumption in childhood or adolescence and subsequent breast cancer. A negative association between childhood milk consumption and breast cancer has been indicated (Hislop et al. 1986), but this was not supported by our analyses. The results from studies on adolescence milk consumption and breast cancer are also inconclusive (Pryor et al. 1989, Potischman et al. 1998).

Is it biological plausible that milk may reduce the risk of breast cancer? No biological mechanism is currently accepted, but several suggestions have been made. These include the protective effect of calcium on the mammary gland (Lipkin & Newmark 1999) and the blocking effect of conjugated linoleic acid on local growth and systematic spread of human breast cancer (Visonneau et al. 1997). The substance of these suggestions may be revealed in the future, and other biological explanations may arise. The presence of a biological mechanism strengthens the hypothesis of a causal relationship, whereas the lack of a biological mechanism can be put down to current limitations in knowledge. A causal association between milk consumption and breast cancer risk does not conflict with what is known about the natural history and biology of breast cancer. However, it has been postulated that dairy products may increase breast cancer risk through their content of oestrogen and growth factors (Outwater et al. 1997).

6. CONCLUDING REMARKS AND FURTHER RESEARCH

Main conclusions

During work on the present thesis, a semi-quantitative food frequency questionnaire has been developed, partly validated by means of a biochemical marker, and applied in epidemiological studies. The main conclusions of the four papers are:

- The extended semi-quantitative food frequency questionnaire seems to perform adequately in registration of habitual intake of fish and fish products.
- Older women report a more healthy diet than younger women, but the differences are not substantial. Healthy dietary habits are strongly associated with one another, as well as being associated with other healthy lifestyle habits, such as smoking and level of physical activity. Healthy dietary habits are also related to socio-economic status, but not as strongly.
- Based on self-reported data, about 40% of the women have a body mass index of 25 or above. More than 50% of the women are trying to lose weight. Body mass index is the major predictor of weight loss attempt, but weight loss attempts are also predicted by age, lifestyle, and socio-economic factors. Women trying to lose weight report a different diet than those not trying to lose weight, irrespectively of body mass index.
- Milk consumption in childhood is not related to breast cancer risk. Adult milk consumption tends to be negatively related to breast cancer risk.

The findings indicate that there is still room for improvement in Norwegian women's diet. The tendency of a healthier diet among older women may be due to an ageing effect, but may also be explained by a cohort effect. The high number of middle-aged women trying to lose weight should be recognised by public health society. On the one hand, overweight and obese subject should be supported in their efforts to lose weight, while on the other hand unnecessary emphasis on leanness should be avoided. The number of various predictors of weight loss attempts in addition to body mass index underlines the complexity of the field.

The indication of lower breast cancer risk among women drinking milk compared to non-milk-drinkers needs to be explored in future studies. For now, we can at least say that our study does not support a hypothesis that consumption of milk in adult life increases the risk of breast cancer.

Further research

As of today, the NOWAC cohort includes more than 100 000 women. Most of them have provided detailed information about their diet, whereas others have provided more limited dietary data (Hjartåker et al. 2000). The women answering the limited food frequency questionnaire in 1991-92 were in 1998-99 asked to give more and updated information about their diet using a revised version of the extended semi-quantitative food frequency questionnaire. Altogether 35 000 women answered this questionnaire and are now included in the EPIC study. The revisions of the questionnaire were made from experiences with the extended semi-quantitative food frequency questionnaire as used in 1996. The 1998-99 version of the questionnaire includes 85 frequency questions. Among the added items are orange juice, soft drinks, salty snacks, desserts, cakes, cookies, pancakes, and waffles.

The validity of more food items in the questionnaire needs to be examined. This will be done in future studies. We are planning to validate the questionnaire in a random sample of women already included in NOWAC. The reference method will be 24-hour recall. As part of our collaboration with EPIC, we have collected 1 800 single 24-hour recalls (Hjartåker et al. 2000). Repeated 24-hour recalls will be collected from a sub-sample of the women that have already given one 24-hour recall. We will investigate how one single 24-hour recall from many subjects performs compared to repeated 24-hour recalls from fewer subjects. We also wish to investigate ways of utilising the data from the validation study in combination with the 24-hour recalls.

The collaboration in EPIC assures further utilisation of our data and contributes to a thorough investigation of the impact of diet on health. EPIC emphasises the importance of biological material. In Norway, we are planning to collect 10 000 blood samples from women included in NOWAC. Application of the doubly-labelled water technique in validation of reported energy intake is under discussion.

Knowing more about the validity of the extended semi-quantitative food frequency questionnaire, the next step is to examine how the validity affects the results of different follow-up studies applying the instrument. This will also be looked into in our further research.

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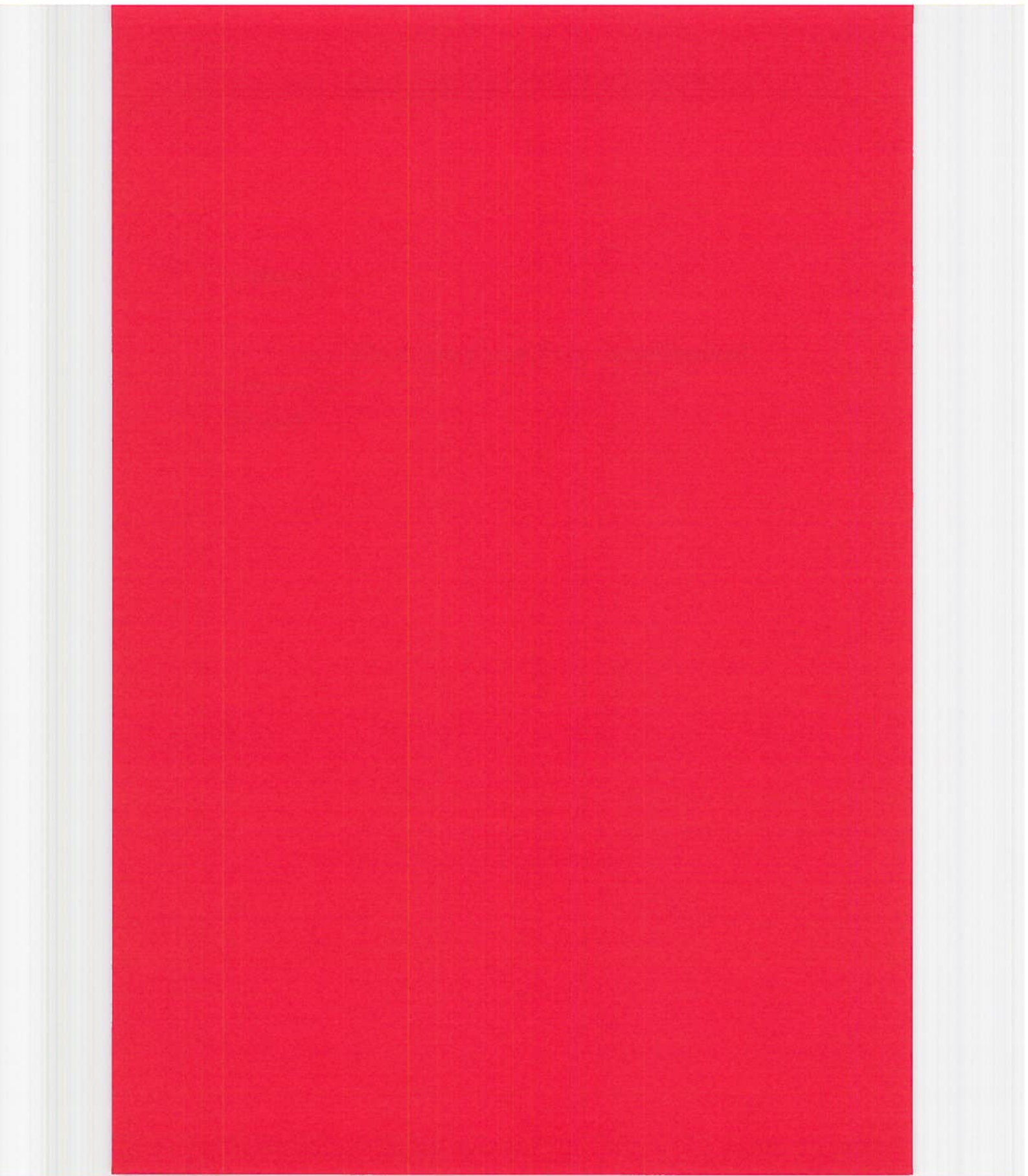
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Appendix A

Invitation letter and questionnaire applied in NOWAC in 1991-92

(in Norwegian)

(Paper IV)





KVINNER, LIVSSTIL OG HELSE

Orientering om undersøkelsen

Institutt for samfunnsmedisin ved Universitetet i Tromsø gjennomfører en spørreundersøkelse om livsstil og helse blant norske kvinner. En slik undersøkelse gir et verdifullt grunnlag for å studere mulige sammenhenger mellom livsstil og helse, f.eks. hvordan forhold under oppveksten, barnefødsler, kosthold eller røyking kan påvirke helsetilstanden. På lengre sikt er vi interessert i å sammenligne resultatene av undersøkelsen med utviklingen av kreftsykdommer som særlig rammer kvinner. Ansvarlig for undersøkelsen er professor Eiliv Lund.

Du inviteres hermed til å delta i undersøkelsen sammen med 60.000 andre kvinner i alderen 33—48 år. Vi har fått tillatelse til å trekke et tilfeldig utvalg fra Det sentrale personregister som inneholder navn og adresseopplysninger for alle norske statsborgere.

Vi vil be deg om å besvare det vedlagte spørreskjemaet så riktig som mulig. Gi et anslag hvis du ikke vet det nøyaktige svaret. Dersom ingen av oppgitte svaralternativer dekker din situasjon, sett kryss for det alternativet som ligger nærmest. Gi eventuelle merknader eller tilleggsopplysninger i skjemaet.

Med noen års mellomrom framover vil vi sammenholde opplysningene som er 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 opplysninger i undersøkelsen og fra registrene vil bli behandlet konfidensielt og etter de regler som Datatilsynet har gitt i sin tillatelse for denne undersøkelsen.

*Det er frivillig om du vil være med i undersøkelsen.
Det er også adgang til å trekke seg senere, hvis du skulle ønske det.*

Vi håper du vil være med. Din del av undersøkelsen vil være å svare på spørsmålene i det spørreskjemaet som følger med. For spørsmål om føflekker og p-pille bruk finner du i denne brosjyren bilder 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.

P-PILLE MERKER

Denne brosjyren er et hjelpemiddel for å huske riktig navn på de p-piller du har brukt. Bildene er ordnet alfabetisk. Under bildene er det oppgitt hvilke år p-pillen 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.

Av tre p-pillemerker har vi ikke bilder, det gjelder:

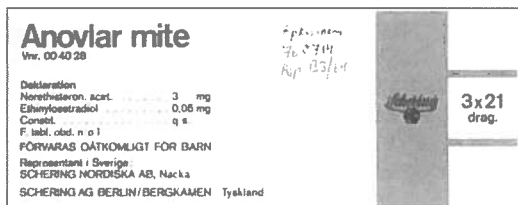
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Nr. 2. Menokvens, solgt 1971–72

Nr. 3. Novokvens, solgt 1969–70



Nr. 4. Solgt fra 1965–68



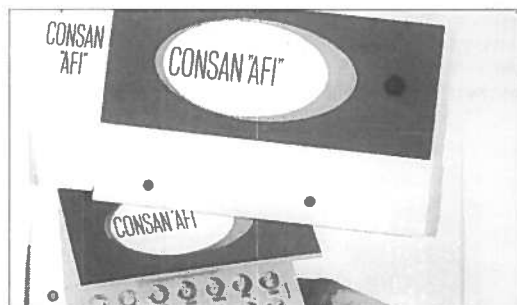
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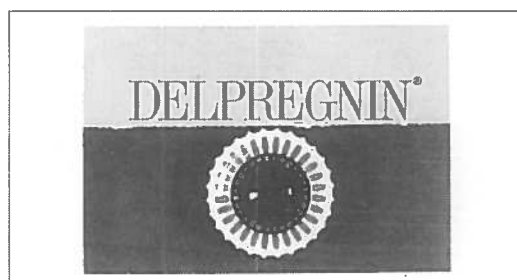
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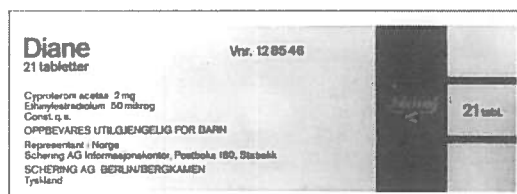
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Nr. 8. Solgt fra 1968–70



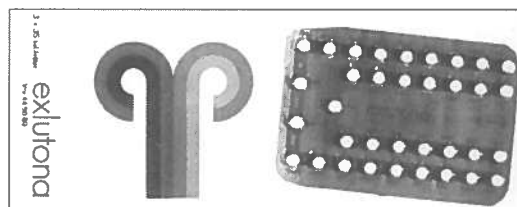
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Nr. 10. Solgt fra 1980



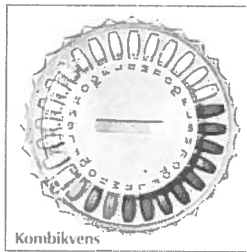
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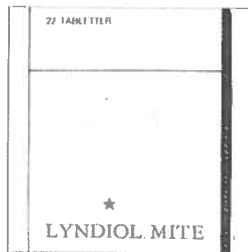
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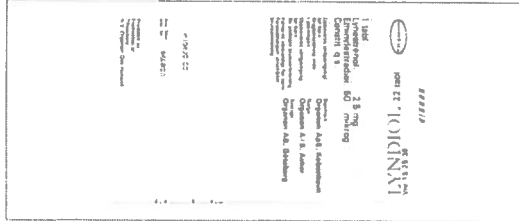
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Nr. 14. Solgt fra 1971-75



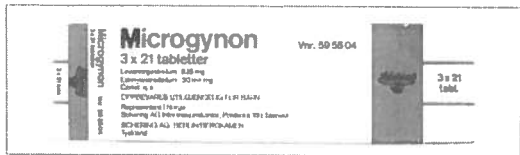
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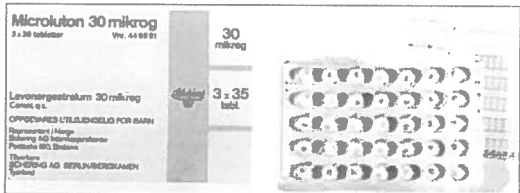
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Nr. 17. Solgt fra 1985



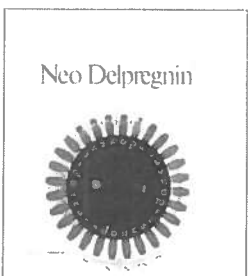
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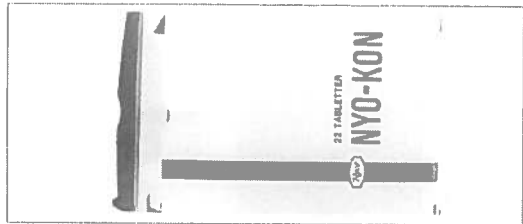
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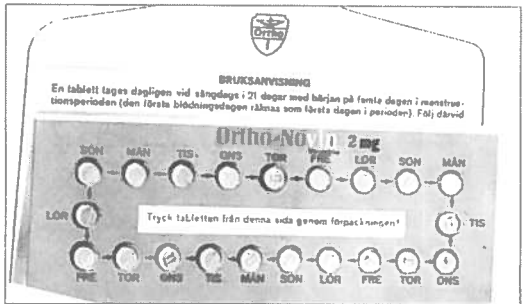
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Nr. 23. Solgt fra 1968-70



Nr. 24. Solgt fra 1971-81



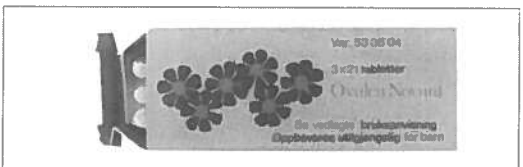
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Nr. 26. Solgt fra 1968-72



Nr. 27. Solgt fra 1965-71



Nr. 28. Solgt fra 1970



Nr. 29. Solgt fra 1973–82



Nr. 34. Solgt fra 1990



Nr. 30.
Solgt fra 1968–84



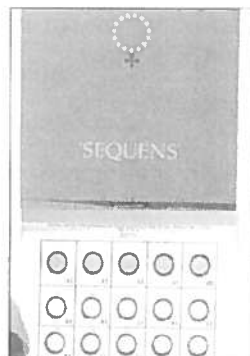
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Nr. 35. Solgt fra 1981



Nr. 32. Solgt fra 1969–70



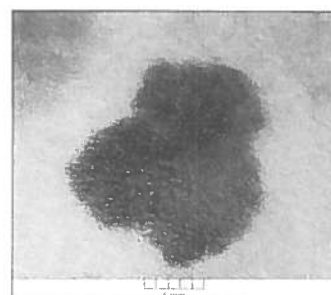
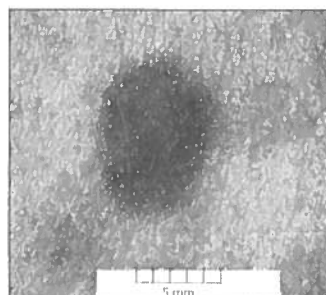
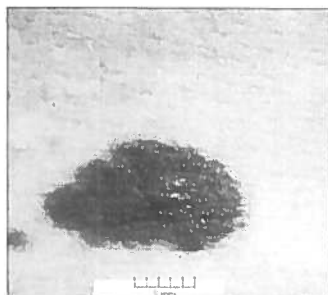
Nr. 33. Solgt fra 1967–69



Nr. 36. Solgt fra 1981

UREGELMESSIGE, STORE FØFLEKKER

(Hjelpemiddel for å svare riktig på spørsmål om solvaner)



Tre eksempler på føflekker større enn 5 mm med uregelmessig form.

KVINNER, LIVSSTIL OG HELSE

KONFIDENSIELT

Vi ber deg fylle ut spørreskjemaet så nøye som mulig, se orienteringen på brosjyren for nærmere opplysninger.

Sett kryss for JA i ruten ved siden av hvis du samtykker i å være med. Dersom du ikke ønsker å delta, sett kryss for NEI og returner skjemaet i vedlagte frankerte svarkonvolutt, så slipper du å bli purret på.

Med vennlig hilsen
Eiliv Lund
Professor dr. med.

Jeg samtykker i å delta i undersøkelsen JA
NEI

Forhold i oppveksten

I hvilke(n) kommune vokste du opp (0-7 år)?

Hvem var forsørger i familien? (Sett ett kryss)

far mor begge andre

Hvordan var de økonomiske forhold i oppveksten?

Meget gode
Gode
Dårlige
Meget dårlige

Kroppstype i 1. klasse. (Sett ett kryss)

veldig tynn tynn normal tykk veldig tykk

Hvor mange års skolegang har du i alt, ta med folkeskole og ungdomsskole?

..... år

Hvilken yrkesutdannelse har du?

Er din arbeidssituasjon: (Sett ett kryss)

hjemmeværende deltids arbeid
 heltids arbeid utenfor hjemmet
 uførepensjon skolegang

Er du;

gift samboer annet

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

Hvor lang tid gikk det mellom 1. dag i en menstruasjonsblødning til 1. dag i neste menstruasjonsblødning da du var 18 år?

..... dager

Hvor lang tid gikk det mellom 1. dag i en menstruasjonsblødning til 1. dag i neste menstruasjonsblødning da du var 30 år?

..... dager

Har menstruasjonen noen gang vært borte mer enn en måned? (Se bort fra svangerskap)

Ja Nei

Hvis Ja;

	Hvis Ja; Hvor lenge	
	Ja	Nei
Spisevevning	<input type="checkbox"/>	<input type="checkbox"/>
Etter slanking	<input type="checkbox"/>	<input type="checkbox"/>
Etter p-pille bruk	<input type="checkbox"/>	<input type="checkbox"/>
Ved stress i arbeidet (skift)	<input type="checkbox"/>	<input type="checkbox"/>
Ved trening	<input type="checkbox"/>	<input type="checkbox"/>
Andre årsaker	<input type="checkbox"/>	<input type="checkbox"/>

Har du vanligvis før-menstruelle plager?

ingen brystsprenge depresjon annet

Har du hete- eller svettetokter som du mener skyldes overgangsalderen (klimakteriet)? (Sett ett kryss)

Ingen Lette Plagsomme

Har du regelmessig menstruasjon fremdeles? Ja Nei

Hvis Nei;

har den stoppet av seg selv?	<input type="checkbox"/>
operert vekk eggstokkene?	<input type="checkbox"/>
operert vekk livmoren?	<input type="checkbox"/>
annet?	<input type="checkbox"/>

Hvor gammel var du da menstruasjonen opphørte?

..... år

Hormonbehandling

Har du brukt hormontabletter i overgangsalderen?

Ja Nei

Hvis Ja, hvor gammel var du første gang du fikk det?

..... år

Hvor lenge har du i alt brukt hormontabletter?

..... mnd..... år

Graviditeter, fødsler og amming

Fyll ut for hvert barn opplysninger om fødselsår og antall måneder du ammet hvert barn (fylles ut også for dødfødte eller for barn som er døde senere i livet). I tillegg ber vi deg oppgi hvor mange kilo du la på deg i løpet av svangerskapet. Dersom du ikke har født barn fortsetter du ved neste spørsmål.

Barn	Fødselsår	Antall måneder med amming	Vektøkning i svangerskapet
1			
2			
3			
4			
5			
6			
7			

Har du hatt noe svangerskap som varte mindre enn seks måneder dvs. spontan abort 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 hatt svangerskap utenfor livmoren?

Ja Nei

Hvis Ja;

Hvor gammel var du første gang?

.....år

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

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?

Har du fått p-piller av andre årsaker enn prevensjon?

Har du blitt anbefalt å slutte med p-piller av medisinske årsaker?

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 brosjyre 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		P-pillene (se brosjyren)	
		år	måneder	Nr.	Navn
Første					
Andre					
Tredje					
Fjerde					
Femte					
Sjette					
Syvende					
Åttende					

Annen prevensjon

Hvor ofte har du eller partner benyttet en av følgende prevensjonsmetoder, og hvor mange år?

	Aldri	Av og til	Ofte	Alltid	Antall år
Kondom					
Pessar					

Har du hatt spiral?

Ja Nei

Hvis Ja;

Hvor gammel var du første gang den ble satt inn?

.....år

Hvor mange år har du hatt spiral i alt?

.....år

Er du sterilisert?

Ja Nei

Hvis Ja;

Hvor gammel var du da du ble sterilisert?

.....år

Sykdom

Har du hatt noen av følgende sykdommer? Hvis Ja; Alder ved start

	Ja	Nei	start
Høyt blodtrykk			
Sukkersyke (diabetes)			
Årebetennelse			
Blodpropp i legg eller lår			
Hjerneslag, uansett type			
Hjerteinfarkt			
Reumatoid artritt (leddgikt)			
Crohns sykdom, ulcerøs colitt			
Psoriasis			
Fibromyalgi/Fibromyositt			
Deprimert mer enn 14 dager			

Allergi

Har du følgende allergiske sykdommer? Hvis Ja; Alder ved start

	Ja	Nei	start
Eksem			
Høysnue			
Astma			

Er du allergisk overfor

	Ja	Nei
Bestemte typer mat		
Pollen		
Husdyr		
Annet		

Egen opplevelse av helse

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

meget god god dårlig meget dårlig

Brystkreft i nærmeste familie

Har noen nære slektninger hatt brystkreft; Vet

	Ja	Nei	ikke
mor			
søster			
mormor			
farmor			

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	
Hver 3. år eller oftere	

Høyde og vekt

Hvor høy er du?

Hvor mye veier du i dag?

Hvor mye veide du da du var 18 år?

Røykevaner

Har du noen gang røkt? Ja Nei

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

Alder	Antall sigaretter hver dag						
	0	1-4	5-9	10-14	15-19	20-24	25+
10-14							
15-19							
20-24							
25-29							
30-34							
35-39							
40-44							
45-49							

Bor du sammen med noen som røker? Ja Nei

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

Røkte noen av de voksne hjemme mens du var barn? Ja Nei

Hvis ja, røkte

bare far bare mor far og mor andre

Fysisk aktivitet

Vi ber deg angi din fysiske aktivitet etter en skala fra svært liten til svært mye ved 14 års alder, ved 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 ol.

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

Har du drevet konkurransedrett? Ja Nei

Hvis Ja, hvor mange år i alt?

Kosthold

For hver matsort nedenfor ber vi deg krysse av i den ruten som passer hvor ofte du i gjennomsnitt i løpet av siste år har spist slik mat.

	6-10 pr dag	4-5 pr dag	2-3 pr dag	1 pr dag	5-6 pr uke	2-4 pr uke	1 pr uke	1-3 pr måned	Nesten pr aldri
Heimelk (glass)									
Skummet melk (glass)									
Lettmelk (glass)									
Kokekaffe (kopper)									
Traktekaffe (kopper)									
Pulverkaffe (kopper)									
Grov brød (skiver)									
Fint brød (skiver)									
Ost (skiver)									
Poteter									
Epler/pærer									
Appelsiner o.l.									

Middag

	6-7 pr uke	4-5 pr uke	3 pr uke	2 pr uke	1 pr uke	2-3 pr måned	1 pr måned	Nesten pr aldri
Rent kjøtt								
Oppmalt kjøtt								
Fet fisk (makrell, laks o.l.)								
Mager fisk (torsk o.l.)								
Ris, spaghetti								
Gulerøtter								
Kål								
Kålrot								
Salat								
Broccoli/Blomkål								

Hva slags fett blir vanligvis brukt i din husholdning?

	På brød	Til matlagning
Smør eller hard margarin		
Myk (soft) margarin eller olje		
Smør/margarin blanding		

Hvor mye melk drakk du som barn hver dag?

drakk ikke melk 1-3 glass 4-6 glass 7 glass eller mer

Hvor ofte spiste du grønnsaker til middag som barn?

aldri 1 gang i uken eller mer sjelden
 2-3 ganger i uken 4 eller flere ganger

Alkohol

Er du total avholdskvinne?

Ja Nei

Hvis Nei, hvor ofte og hvor mye drakk du i gjennomsnitt siste året?

	6-10 pr dag	4-5 pr dag	2-3 pr dag	1 pr dag	5-6 pr uke	2-4 pr uke	1 pr uke	1-3 pr måned	Nesten pr aldri
Øl (1/2 liter)									
Vin (glass)									
Brennevin (drinker)									

Solvaner

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

brun uten å først være rød rød
 rød med svie rød med svie og blommer

Etter gjentatt og lenge soiling, 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)?

(På siste side av brosjyren er det bilder som viser hva vi mener med uregelmessige føflekker.)

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

Hvilken øyefarve har du? (Sett ett kryss)

brun grå, grønn eller blanding blå

Hvilken hårfarve har du? (Sett ett kryss)

mørkbrun, svart brun blond, gul rød

Hvor mange ganger pr. år er du blitt forbrent av solen slik at du har fått svie eller blommer 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					
30-39 år					
40-49 år					

Hvor mange uker i gjennomsnitt pr. år har du vært på badeferie i syden eller i Norge?

Alder	Aldri	1 uke	2-3 uker	4-6 uker	7 uker eller mer
Før 10 år					
10-19 år					
20-29 år					
30-39 år					
40-49 år					

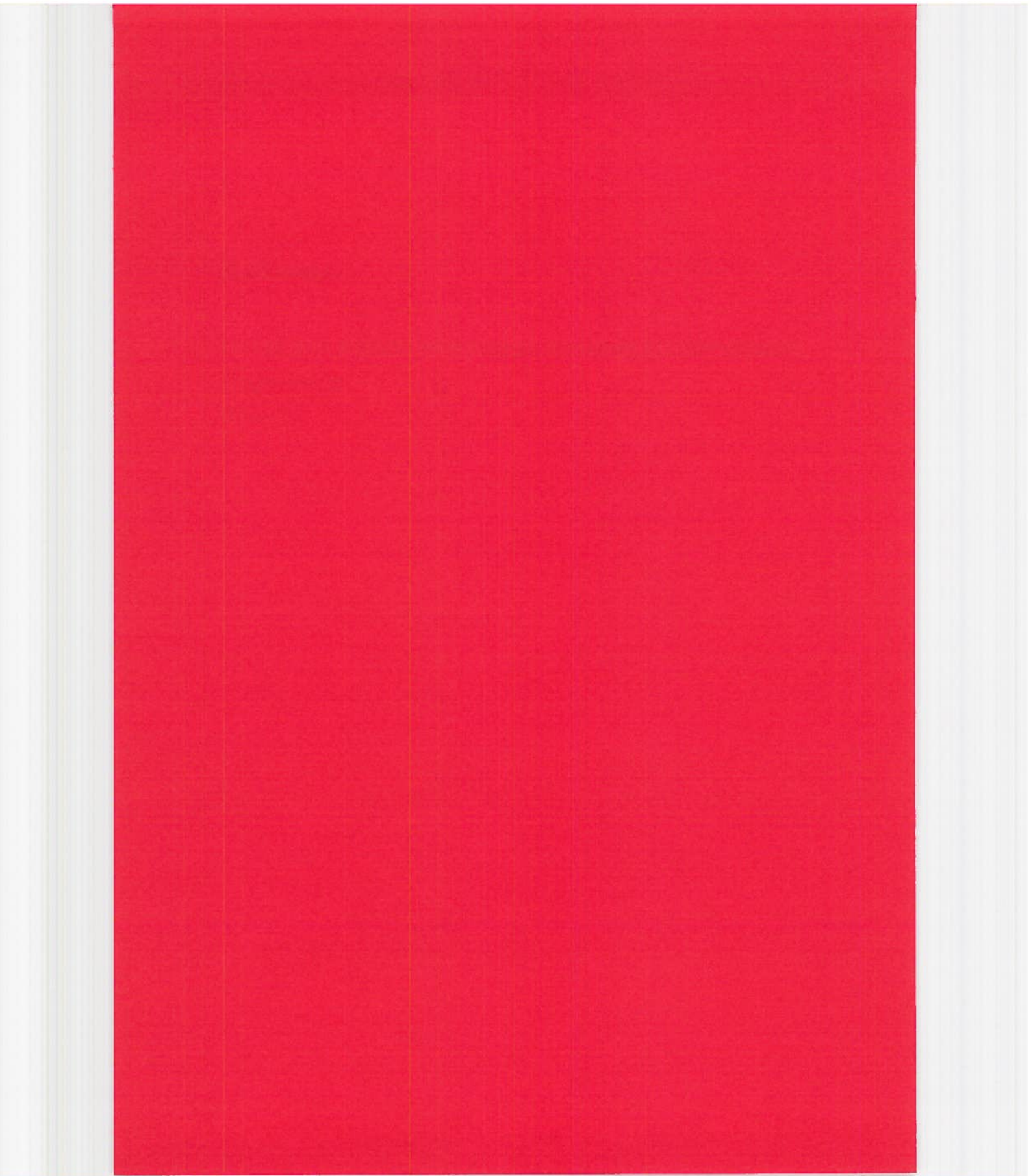
Hvor ofte har du solt deg i solarium?

Alder	Aldri	Sjelden	1 gang pr. mnd.	2 gang pr. mnd.	3-4 gang pr. mnd.	oftere enn 1 gang pr. uke
Før 10 år						
10-19 år						
20-29 år						
30-39 år						
40-49 år						

Takk for at du ville delta i undersøkelsen!

Appendix B

Invitation letter and questionnaire applied in the validation study in 1995
(in Norwegian)
(Paper I)





KVINNERS KOSTHOLD

Orientering

Institutt for samfunnsmedisin ved Universitetet i Tromsø skal gjennomføre en større spørreundersøkelse om livsstil og kreft blant kvinner. Som et første trinn i prosjektet vil vi kartlegge i hvor stor grad opplysningene fra et spørreskjema om kostvaner gjenspeiler de fettsyreverdier man finner i blodet.

I den forbindelse vil vi spørre deg om å delta i denne første delen av prosjektet. Undersøkelsen gjennomføres i samråd med Fylkeslegen i Sor-Trøndelag, kommuneoverlegen i Trondheim og Statens helseundersøkelser. Vi vil be deg fylle ut et spørreskjema om kostvaner så korrekt som mulig. Samtidig vil vi be om å få tappe et ekstra glass blod. Det gjøres spesielt oppmerksom på at dette gjøres fortlopende slik at det ikke blir noe ekstra sprøytstikk.

Vi ber deg om å fylle ut skjemaet mens du er her; det tar ca 15 - 25 minutter. Dersom dette ikke passer, kan du få med en frankert svarkonvolutt hjem og returnere skjemaet til oss.

Undersøkelsen er anonym. Spørreskjemaet og blodproveglasset vil kun bli merket med nummer for at vi skal kunne sammenlikne spørreskjemasvar og blodverdier. Du vil ikke bli kontaktet senere.

Det er frivillig om du vil være med.

Din avgjørelse om du vil delta eller ikke har ingen betydning for hjerte-karundersøkelsen.

Eiliv Lund
Professor dr. med.

Anette Hjartåker
Stipendiat

INSTITUTT FOR SAMFUNNSMEDISIN

SEKSJON FOR EPIDEMIOLOGI OG MEDISINSK STATISTIKK

Universitetet i Tromsø, N-9037 Tromsø, Telefon 77 64 48 16, Telefax 77 64 48 31

Hvor ofte bruker du majones? (Sett ett kryss for hver type)

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2 pr. uke	3+ pr. uke
Lettmajones	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Ekte majones	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Dersom du bruker majones, hvor mye bruker du vanligvis hver gang? (Sett ett kryss)

1 ts 1/2 ss 1+ ss

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
- lettmargin (f. eks. Soft light, Letta)
- annet fett

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)

Hva slags fett blir vanligvis brukt til matlagning 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
- annet fett

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	3+ 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	<input type="checkbox"/> 1/2 stk.	<input type="checkbox"/> 1 stk.	<input type="checkbox"/> 1 1/2 stk.	<input type="checkbox"/> 2+ stk.
- kål	<input type="checkbox"/> 1/2 dl	<input type="checkbox"/> 1 dl	<input type="checkbox"/> 1 1/2 dl	<input type="checkbox"/> 2+ dl
- kålrot	<input type="checkbox"/> 1/2 dl	<input type="checkbox"/> 1 dl	<input type="checkbox"/> 1 1/2 dl	<input type="checkbox"/> 2+ dl
- broccoli/blomkål	<input type="checkbox"/> 1-2 buketter	<input type="checkbox"/> 3-4 buketter		
	<input type="checkbox"/> 5-6 buketter	<input type="checkbox"/> 7+ buketter		
- blandet salat	<input type="checkbox"/> 1 dl	<input type="checkbox"/> 2 dl	<input type="checkbox"/> 3 dl	<input type="checkbox"/> 4+ dl
- grønnsakblanding	<input type="checkbox"/> 1/2 dl	<input type="checkbox"/> 1 dl	<input type="checkbox"/> 2 dl	<input type="checkbox"/> 3+ dl

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

spiser ikke/spiser sjelden poteter

<input type="checkbox"/> 1-4 pr. uke	<input type="checkbox"/> 5-6 pr. uke
<input type="checkbox"/> 1 pr. dag	<input type="checkbox"/> 2 pr. dag
<input type="checkbox"/> 3 pr. dag	<input type="checkbox"/> 4-5 pr. dag
<input type="checkbox"/> 6+ 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 o.l					

Hvor ofte spiser du risengrynsgrøt? (Sett ett kryss)

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

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, sel, hyse, lyr						
Steinbit, flyndre, uer						
Laks, ørret						
Makrell						
Slid						

Med tanke på de periodene av året der du spiser fisk, hvor ofte pleier du 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	4+ pr. uke
Kokt torsk, sel, hyse, lyr							
Stekt torsk, sel, hyse, lyr							
Steinbit, flyndre, uer							
Laks, ørret							
Makrell							
Slid							

Dersom du spiser fisk, hvor mye spiser du vanligvis pr. gang? (1 skive/stykke = 50 gram)

(Sett ett kryss for hver linje)

- kokt fisk (skive) 1 2 3 4+
- stekt fisk (stykke) 1 2 3 4+

Hvor mange ganger pr. år spiser du fiskeinnmat?

(Sett ett kryss pr. linje)

- 0 1-3 4-5 6-8 9-12 13+
- Rogn
- Fiskelever

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

- 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
-

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	3+ pr. uke
Fiskekaker, fiskepudding						
Fiskeboller						
Plukkfisk, fiskegrateng						
Frityrfisk, fiskepinner						
Fiskesuppe						
Andre fiskeretter						

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

- fiskekaker, fiskepudding (stk.) 1 2 3 4+
- fiskeboller (stk.) 1-2 3-4 5-6 7+
- plukkfisk, fiskegrateng (dl) 1-2 3-4 5-6
- frityrfisk, fiskepinner (stk.) 1-2 3-4 5-6 7+
- fiskesuppe (dl) 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. Vi ber deg derfor krysse av for hvor ofte du pleier bruke ulike typer tilbehør til fisk.

Hvor ofte spiser du følgende til fisk? (Sett ett kryss pr. linje)

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

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

- smelte/fast fett (ss) 1/2 1 2-3 4+
- baconfett (ss) 1/2 1 2-3 4+
- remulade (ss) 1/2 1 2 3+
- 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 pleier du bruke 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	3+ pr. uke
Steik (okse, svin, får)						
Koteletter						
Biff						
Kjøttkaker, karbonader						
Kjøttpølser						
Wienerpølser						
Gryterett, lapskaus						
Pizza m/kjøtt						
Kylling						
Andre kjøtetter						

Dersom du spiser steik eller koteletter, hvor mye pleier du å spise? (Sett ett kryss for hver linje)

- Steik (skiver) 1-2 3-4 5-6 7+
- Koteletter (stk.) 1/2 1 1 1/2 2+

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

- kjøttkaker, karbonader (stk.) 1 2 3 4+
- kjøttpølser (stk.) 1 2 3+
- wienerpølser (stk.) 1 2 3 4+
- gryterett, lapskaus (dl) 1-2 3-4 5-6 7+
- 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 disse bakervarene?

(Sett ett kryss for hvert slag)

	aldri/sjelden	1 pr. mnd	2-3 pr. mnd	1 pr. uke	2-3 pr. uke	4-5 pr. uke	6+ pr. uke
Søt gjærbakst (boller, kringle)							
Wlenerbrød							
Kake							
Vafler, pannekaker							
Småkaker, kjeks							

Dersom du spiser søt gjærbakst, hvor mye pleier du vanligvis å spise hver gang? (Sett ett kryss)

1 stk. 2 stk. 3+ stk.

Hvor mange vaffelplater/pannekaker pleier du spise hver gang? (1 vaffelplate = en stor pannekake).

(Sett ett kryss)

mindre enn 1 stk. 1 stk. 2 stk. 3+ stk.

Hvor ofte spiser du is krem (til dessert, krone-is osv.)?

(Sett ett kryss for hvor ofte du spiser is krem om sommeren, og ett kryss for resten av året)

	aldri/sjelden	1-3 pr. mnd	1 pr. uke	2-3 pr. uke	4-5 pr. uke	6+ pr. uke
- om sommeren	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- resten av året	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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

1 dl 2 dl 3 dl 4+ dl

Hvor ofte spiser du dessert laget med krem,

(f. eks. rismkrem, fromasj, multekrem)? (Sett ett kryss)

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

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.

(Sett ett kryss)

1/4 1/2 3/4 1 1,5 2+

Hvor ofte pleier du spise salt snacks? (Sett ett kryss pr. linje)

pr. linje)

	aldri/sjelden	1-3 pr. mnd	1 pr. uke	2-3 pr. uke	4+ pr. uke
Potetchips o.l.					
Peanotter o.l.					

Hvor ofte tar du følgende kosttilskudd? For tran og tranpiller vær vennlig å sette ett kryss for vinteren og ett kryss for resten av året; også om du bruker det like ofte gjennom hele året.

	aldri/sjelden	1-3 pr. mnd	1 pr. uke	2-3 pr. uke	4-6 pr. uke	daglig
Tran,						
- om vinteren	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- resten av året	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Tranpiller,						
- om vinteren	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
- resten av året	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Fiskeolje-kapsler	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Andre kosttilskudd	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Dersom du tar tran, hvor mye pleier du ta hver gang?

1 ts 1/2 ss 1+ ss

Dersom du tar tranpiller/kapsler, hva heter de og hvor mange tar du hver gang?

navn: stk. pr. gang:.....

Dersom du tar fiskeoljekapsler, hva heter de og hvor mange tar du hver gang?

navn: stk. pr. gang:.....

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

	6-7 pr. uke	4-5 pr. uke	3 pr. uke	2 pr. uke	1 pr. uke	2-3 pr. mnd	1 pr. mnd	nesten aldri
Rent kjøtt	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Oppmalt kjøtt	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Fet fisk (makrell, laks o.l.)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Mager fisk (torsk o.l.)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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 (1/2 L)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Vin (glass)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Brennevln (driker)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

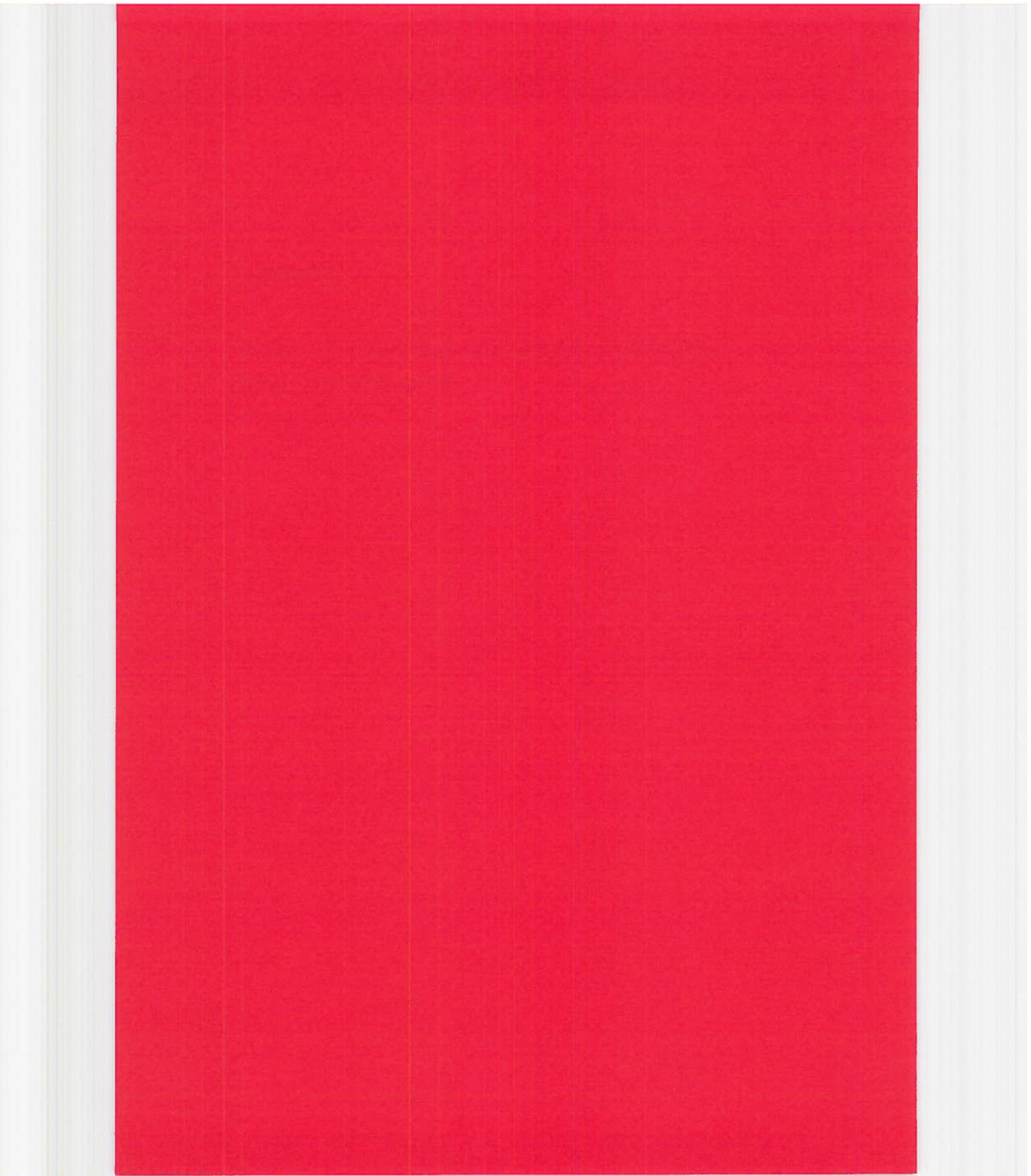
I hvilken grad mener du kostholdet ditt har betydning for helsa?

ingen/svært liten noen stor svært stor

Takk for hjelpen!

Appendix C

Invitation letter and questionnaire applied in NOWAC in 1996
(in Norwegian and English)
(Papers II and III)





KVINNER OG KREFT

Orientering om undersøkelsen

Institutt for samfunnsmedisin ved Universitetet i Tromsø gjennomfører en spørreundersøkelse om leveste og kreft blant norske kvinner. En slik undersøkelse gir et verdifullt grunnlag for å studere mulige sammenhenger mellom leveste og helse, f. eks. hvordan barnefødsler, bruk av hormoner i overgangsalderen eller fiskekonsum kan påvirke kreftutvikling. På lengre sikt er vi interessert i å sammenligne resultatene av undersøkelsen med utviklingen av kreftsykdommer som særlig rammer kvinner. 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 2016 vil vi sammenholde opplysningene som er 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 opplysninger fra undersøkelsen og fra registrene vil bli behandlet konfidensielt og etter de regler Datatilsynet har gitt i sin tillatelse for denne undersøkelsen. 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 den regionale etiske komite for Nord-Norge.

Vi vil be deg om å besvare det vedlagte spørreskjemaet så riktig som mulig. Gi et anslag hvis du ikke vet det nøyaktige svaret. Dersom ingen av oppgitte svaralternativ dekker din situasjon, sett kryss for det alternativet som ligger nærmest. Gi eventuelt merknader eller tilleggsopplysninger i skjemaet.

Det er frivillig om du vil være med i undersøkelsen.

Det er også adgang til å trekke seg senere, hvis du skulle ønske det.

Ditt bidrag til undersøkelsen vil være å svare på spørsmålene i det spørreskjemaet som følger med. 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.

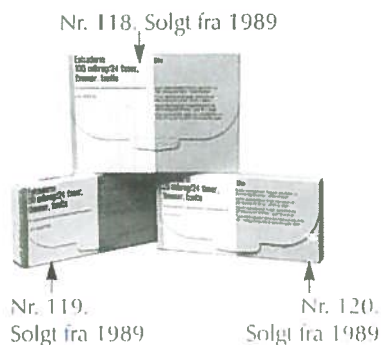
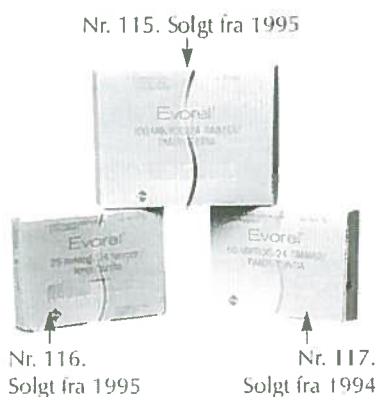
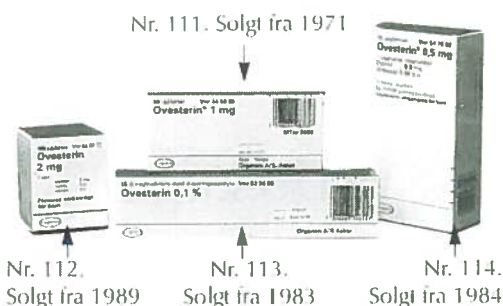
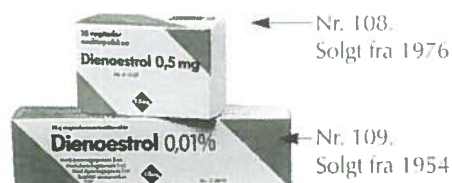
Med hilsen

*Eiliv Lund
Professor dr. med.*

Bruk av hormoner 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 **Dietylstillbøstrol** 1 mg stikkpiller til skjeden (1976-92)
- Nr. 202 **Dietylstillbøstrol** 0,1 mg tabletter (1980-85)
- Nr. 203 **Dietylstillbøstrol** 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)



P-Pille Merker

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, 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. Av noen p-pillemerker 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. 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. 10. Solgt fra 1980



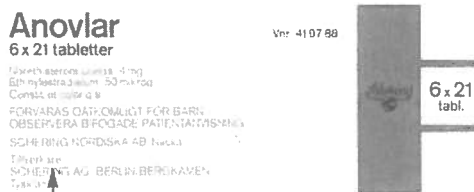
Nr. 11. Solgt fra 1969



Nr. 12. Solgt fra 1973



Nr. 13. Solgt fra 1978



Nr. 4. Solgt fra 1965-68



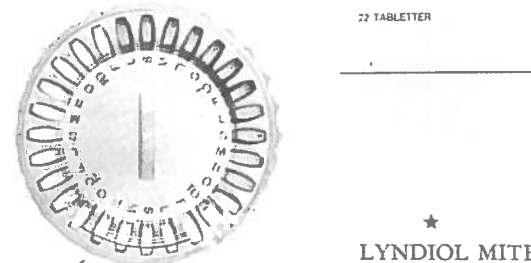
Nr. 6. Solgt fra 1980



Nr. 7. Solgt fra 1971



Nr. 9. Solgt fra 1968-71

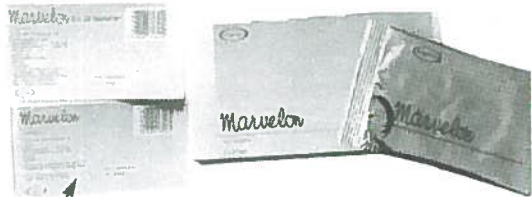


Nr. 14. Solgt fra 1971-75

Nr. 15. Solgt fra 1966-72



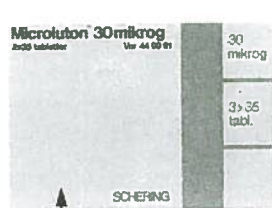
Nr. 16. Solgt fra 1965



Nr. 17. Solgt fra 1985



Nr. 18. Solgt fra 1975



Nr. 19. Solgt fra 1973

Neo Delpregnin



Nr. 21. Solgt fra 1971-79



Nr. 25. Solgt fra 1966-69



Nr. 24. Solgt fra 1971-81

Nu OVULEN ny forpakning 21 tabl.



Nr. 27. Solgt fra 1965-71



Nr. 28. Solgt fra 1970



Nr. 29. Solgt fra 1973-82



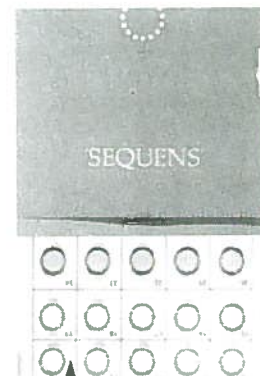
Nr. 30. Solgt fra 1968-84



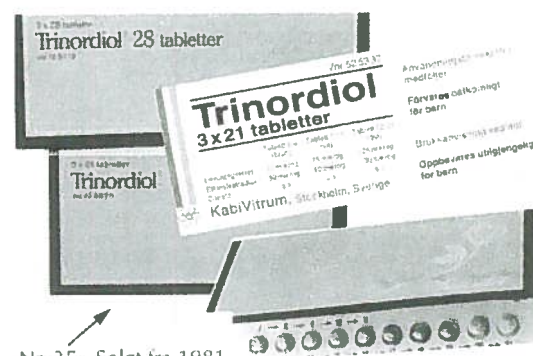
restovar
Nr. 31. Solgt fra 1977-86



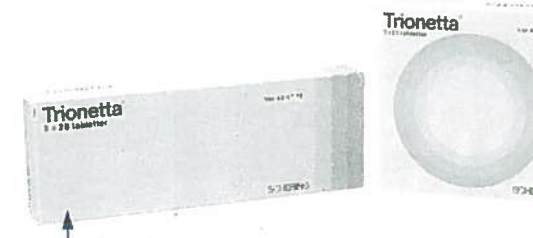
Nr. 32. Solgt fra 1969-70



Nr. 33. Solgt fra 1967-69



Nr. 35. Solgt fra 1981



Nr. 36. Solgt fra 1981

KVINNER OG KREFT

KONFIDENSIELT

Vi ber deg fylle ut spørreskjemaet så nøyte som mulig, se orienteringen på brosjyren for nærmere opplysninger.

Sett kryss for JA i ruten ved siden av hvis du samtykker i å være med. Dersom du ikke ønsker å delta, sett kryss for NEI og returner skjemaet i vedlagte svarbrevkuff, så slipper du å bli påført på.

Med vennlig hilsen

Elliv Bjnd
Professor i med

Jeg samtykker i å delta i JA
spørreskjema-undersøkelsen NEI

Forhold i oppveksten

I hvilke(n) kommune vokste du opp (0-7 år)?

Hvordan var de økonomiske forhold i oppveksten?

- Meget gode
Gode
Dårlige
Meget dårlige
Usikker

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 Nei
 Har uregelmessig menstruasjon

Hvis Nei;

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

Hvor gammel var du da menstruasjonen opphørte? år

Graviditeter, fødsler og amming

Fyll ut for hvert barn opplysninger om fødselsår og antall måneder du ammet hvert barn (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

HORMONTABLETTER/PLASTER/KREM/STIKKPILLER
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

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

Vi vil be deg om å besvare spørsmålene om bruk av hormontablett/ plaster/krem/stikkpille (hormonpreparater) mer nøye. 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 hormonpreparat 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 hormontabletter/plasteret/-kremen/stikkpillen som står i brosjyren.

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

P-Piller

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

Ja Nei

Hvis Ja;

Hvor lenge har du brukt p-piller i alt?

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

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 brosjyre 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 brosjyre) 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?

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?

Hvor lenge prøvde du?

Sykdom

Har du hatt noen av følgende sykdommer?

	Ja	Nei	Hvis Ja: Alder ved start
Høyt blodtrykk	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Hjertesvikt	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Årebetennelse	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Blodpropp i legg eller lår	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Hjerteinfarkt	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Slag	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Migrene	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Epilepsi	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Kreft	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>
Sukkersyke (diabetes)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="text"/>

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

meget god god dårlig meget dårlig

Allergi

Er du allergisk overfor Ja Nei

bestemte typer mat

Hvis Ja, angi:

Melk o.l.

Sitrus (appelsin o.l.)

Skalldyr

Annet

Hjerte- karepreparater

BRUKER DU LEGEMIDLER FAST

- mot høyt blodtrykk? Ja Nei
mot hjertekrampe (angina)? Ja Nei
mot hjertesvikt og/eller uregelmessig hjerterytme? Ja Nei

Hvis ja ved ett eller flere av spørsmålene, vennligst angi hvilke hjerte-karepreparater du bruker, og når behandlingen ble påbegynt.

Preparat	Behandlingsstart	
	år	måned
.....
.....
.....

Bruk av smertestillende midler

Har du det siste året periodevis brukt smertestillende midler daglig eller nesten daglig? Angi hvor mange måneder du brukte dem og sett 0 hvis du ikke har brukt smertestillende midler.måneder

Bruker du acetylsalicyltabletter fast? Ja Nei

Hvis Ja, angi navn:
hvor mange pr. dag?tabletter
hvor lenge har du brukt i alt?mndår

Har du brukt smertestillende midler siste 14 dager?

Ja Nei

Hvis Ja;

Var dette reseptbelagte smertestillende midler? Ja Nei

- Brukte du Paralgin forte? Ja Nei
Codalgin forte? Ja Nei
Codacetyl? Ja Nei

Andre reseptbelagte smertestillende:

Var dette reseptfrie smertestillende midler? Ja Nei

- Hvis Ja, var det Albyl-E? Ja Nei
Dispril? Ja Nei
Globentyl? Ja Nei
Globoid? Ja Nei
Novid? Ja Nei

- Fenozonpreparater (f.eks. Fanalgin, Fenazon, Fenazon-koffein, Antineuralgica)? Ja Nei

- Paracetamolpreparater (f.eks. Panodil, Paracet, Paracetamol, Pinex)? Ja Nei

- Ibuprofenpreparater (f.eks. Brufen, Ibux, Ibumetin)? 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 ilvmorhaisen 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
mor	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
mormor	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
farmor	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
søster	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

Høyde og vekt

Hvor høy er du? cm

Hvor mye veler du i dag? kg

Hvor mye veide du da du var 18 år? kg

Har du i løpet av kort tid (noen måneder) uten å være gravid, endret din vanlige vekt med mer enn fem kilo?

Ja Nei

Hvis Ja, angi din laveste vekt kg

angi din høyeste vekt kg

Gjør du noe forsøk på å endre kroppsvekten din?

- Nei
 Ja, jeg ønsker å legge på meg
 Ja, jeg ønsker å gå ned i vekt

Røykevaner

Har du noen gang røkt? Ja Nei

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							

Røker du daglig nå? Ja Nei

Bor du sammen med noen som røker? Ja Nei

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

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

Har du drevet konkurransedrett? Ja Nei

Hvis Ja, hvor mange år i alt? år

Sosiale forhold

Er du: (Sett ett kryss)

gift samboer skilt/separert ugift enke

Hvor mange personer er det i ditt hushold? Antall:

Hvor mange inntekter er det i husholdet?

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

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 spise/drikke hver gang. Dersom du aldri/sjelden bruker matvaren, trenger du ikke krysse av for mengde.

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)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Lettmelk (søt, sur)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Skummet (søt, sur)	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Traktekaffe	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>
Pulverkaffe	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>	<input type="checkbox"/>

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

aldri/sjelden 1 pr. uke 2-3 pr. uke
 4-6 pr. uke daglig

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

Dersom du spiser kornblanding e. i., hvor stor porsjon pleier du vanligvis å spise hver gang? (Sett ett kryss)

mindre enn 1 dl 1 dl 1,5 dl 2+ dl

Hvor mange skiver brød/rundstykker og knekkebrød/skonrokker spiser du vanligvis? (1/2 rundstykke = 1 brodskive) (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 brødskeer 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 hensyn til dette når du besvarer spørsmålene.

På hvor mange brødskeer 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						
Salater med majones						

Videre kommer spørsmål om fiskepålegg.

På hvor mange brødskeer 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, rokt 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
- lettmargin (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 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 risengrynsgrot? (Sett ett kryss)

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

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

Hva slags fett blir vanligvis brukt til matlagning 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 ofte bruker du fersk eller frossen fisk?
(Sett ett kryss for hver linje)

	aldri/sjelden	1 pr. mnd	2-3 pr. mnd	1 pr. uke	2+ pr. uke
Fersk fisk					
Frossen filet					

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.) 1 2 3 4+
(2 fiskeboller=1 fiskekake)
- 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.
(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					
Seterømme (35%)					
Lettrømme (20%)					
Saus med fett (hvilt/brun)					
Saus uten fett (hvilt/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+
- seterømme (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+

Spiser du etter egen oppfatning nok fisk?

- Ja Nei

Hvis nei,

hvorfor spiser du ikke mer fisk

Lite viktig Viktig Meget viktig

- for høy pris
- for lite utvalg
- for liten tilgang på fersk fisk
- kvaliteteten varierer
- liten tilgang på ferdigretter
- lukt ved tilberedning
- vanskelig å tilberede
- smaken
- familien liker ikke fisk
- annet, angi

Mikrobølgeovn

Har du mikrobølgeovn? Ja Nei

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

annet?

Hvor mange ganger pr. måned spiser du på:
kafeteria/kantine

pizza/hamburger restaurant

hvitduks-restaurant

Kosthold som barn

Hvor mye melk drakk du som barn hver dag?

drakk ikke 1-3 glass 4-6 glass
 7 glass eller mer

Hvor ofte spiste du grønnsaker til middag som barn?

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 som barn?

(Sett ett kryss)
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

Solvaner

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

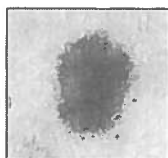
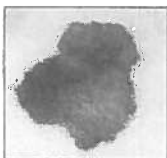
brun uten først å være rød rød
 rød med svie rød med svie og blemmer

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 nedenfor.

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



5 mm

Hvilken øyefarge har du? (sett ett kryss)

brun grå, grønn eller blanding blå

Hvilken hårfarge har du? (sett ett kryss)

mørkbrunt, svart brun blond, gul rød

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	Hoyst 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 i gjennomsnitt pr. år har du vært på badeferie i syden eller i Norge?

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 ofte har du soilt deg i solarium?

Alder	Aldri	Sjelden	1 gang pr. mnd.	2 ganger pr. mnd.	3-4 ganger pr. mnd.	oftere enn 1 gang pr. uke
Før 10 år						
10-19 år						
20-44 år						
45+ år						

Hvilken solfaktor bruker du?

Påske Sommer

I dag

For 10 år siden

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							

Takk for at du ville delta i undersøkelsen

Department of Community Medicine
University of Tromsø
9037 Tromsø
Tel. 77 64 48 16

Women and Cancer

An outline of the survey

The Department of Community Medicine at the University of Tromsø is conducting a questionnaire survey on lifestyle and cancer among Norwegian women. A survey of this kind provides a valuable means of studying possible connections between lifestyle and health; for example, how childbirth, use of hormones in menopause, or fish consumption might affect the development of cancer. In the longer term, we are interested in comparing the results of the survey with the development of cancers affecting women in particular. The study is being conducted under the direction of Professor Eiliv Lund.

We would like to invite you to take part in this survey. All those invited have been randomly selected. Those receiving the questionnaires have been selected by Statistics Norway. Every couple of years until 2016, we will check the information collected for this survey against information held in the Cancer Registry of Norway and the Registry of Cause of Death. By studying the same material every couple of years, we hope to find out why some women get cancer. All information from the survey and the registers will be treated confidentially in accordance with the rules laid down by Norwegian Data Inspectorate in licensing this survey. On the questionnaire, your name and social security number are replaced by a serial number so that no-one who receives or processes the forms will know your identity. The study has been approved by the Regional Board of Research Ethics for North Norway.

We would like to ask you to fill out the enclosed questionnaire as accurately as possible. Give an estimate if you cannot give an exact answer. If none of the suggested answers covers your circumstances, tick the alternative that fits best. If you have any comments or would like to provide any additional information, you may do so on the form.

Your participation in the study is voluntary.
You may also withdraw at a later stage if you wish.

Your contribution to the study will be to provide answers to the questions on the enclosed questionnaire. You will find illustrations in this booklet that may help you to answer the questions about hormones and birth control pills (you need not return the brochure). Return the filled-in questionnaire in the enclosed stamped addressed envelope.

Yours sincerely,
Eiliv Lund Professor dr. med.

Please fill in this questionnaire, giving as much detail as possible.
 Consult the enclosed brochure for further details.
 Tick YES in the box on the right if you agree to take part.
 If you do not wish to take part, tick NO and return the questionnaire
 in the envelope provided. You will not then receive reminders.

I agree to take part in YES
the questionnaire survey NO

Best wishes,
 Eiliv Lund
 Professor dr. med.

Your childhood and youth

In which local district council area did you live between the
 ages of 0-7 years?

How would you describe your family's financial situation in
 your childhood/youth?

- Very good.....
- Good.....
- Poor.....
- Very poor.....
- Don't know.....

Body type on starting school. (Tick one box only)

....Very thinThinNormalFatVery Fat

How many years' schooling/training have you had in total,
 including primary and middle/secondary school?
years

Menstruation

How old were you when you had your first period?
years

How many years did it take before your periods became
 regular?

-One year or less
-More than one year
-Never
-Don't remember

Are your periods still regular?
YesNo
My periods are irregular

If not:
 have they stopped of their own accord?
 have your fallopian tubes been removed?
 have you had your womb removed (hysterectomy)?
 have they stopped for some other reason?

How old were you when you stopped having periods?
years

Pregnancies, births and breast-feeding

For each child, give details of year of birth and number
 of months' breast-feeding (please give information for
 still-births and children who have since died). If you
 have not had any children, go on to the next question.

Child	Year of birth	Months breast-fed
1		
2		
3		
4		
5		
6		
7		

Use of hormones in menopause

**HORMONE PILLS/PLASTERS/CREAMS/
 SUPPOSITORIES**

Have you ever used hormone pills/plasters?
YesNo

If Yes, how long have you used hormone
 pills/plasters in all?years
 How old were you when you first
 used hormone pills/plasters?years
 Are you currently using pills/plasters?
YesNo

**HORMONE PREPARATIONS FOR VAGINAL
 USE**

Have you ever used hormone creams/suppositories?
YesNo

If Yes, how long have you used creams/
 suppositories in all?years
 How old were you when you first used
 hormone creams/suppositories?years

Are you currently using creams/
 suppositories?YesNo

Now we would like you to give more detailed answers to
 the questions on use of hormone pills/plasters/creams/
 suppositories (hormone preparations). For each period of

continuous use of the same hormone preparation, we hope you can tell us how old you were when you started, how long you used the same hormone preparation, and what it was called. If you stopped using it for a while, or switched to other preparations, you should count this as a new period. If you cannot remember the name of the hormone preparation, write 'Unsure'. To help you remember the names of hormone preparations, please use the brochure provided, which contains pictures of hormone preparations that have been sold in Norway. Please also give the number of the hormone pill/plaster/cream/suppository given in the brochure.

Period	Age at beginning	Used same hormone pill/plaster/cream/suppository Continuously year(s)	month(s)	Hormone pill/plaster/cream/suppository (see brochure) No.	Name
First					
Second					
Third					
Fourth					
Fifth					

Contraceptive pill

Have you ever been on the pill or minipill?YesNo
If Yes:

How long have you been on the pill in total?years

How old were you when you first started taking the pill?years

Are you currently on the pill?YesNo

Now we would like you to give more detailed answers to the questions on your use of the pill. For each period of continuous use of the same brand of contraceptive pill, we hope you can tell us how old you were when you started, how long you used the same brand of pill, and the name of the pill you used.

If you stopped using the pill or switched to another brand, you should count this as a new period. If you do not remember the name of the brand of pill, write 'Unsure'. To help you remember the name of brands of contraceptive pill, we would like you to use the enclosed brochure, which shows pictures of brands that have been sold in Norway. Please also tell us the number of the pill as given in the brochure.

Period	Age at beginning	Used same contraceptive pill continuously year(s)	month(s)	Contraceptive pill (see brochure) No.	Name
First					
Second					
Third					
Fourth					
Fifth					

MISCARRIAGE, ABORTION AND INFERTILITY

Have you had a pregnancy that lasted less than six months (i.e., miscarriage or voluntary abortion)?

.....YesNo

If Yes, how old were you at the time of your first miscarriage/abortion?years

How many miscarriages/abortions have you had in total?

Have you ever spent more than one year trying to get pregnant?YesNo

If Yes, how old were you?years

How long did you spend trying?years

Illness

Have you had any of the following illnesses?

Yes No If Yes, age
(when first discovered)

High blood pressure

Heart failure

Phlebitis (inflammation of the veins/arteries)

Thrombosis of the lower or upper leg

Heart attack

Stroke

Migraine

Epilepsy

Cancer

Diabetes

How would you rate your own current state of health (tick one box only):

.....Very goodGoodPoorVery poor

Allergy

Are you allergic to certain kinds of foodYesNo

If Yes, mark which kinds:

Milk, etc.

Citrus fruits (oranges, etc.)

Shellfish

Others

Medicines for heart and circulatory conditions

DO YOU TAKE MEDICINES ON A REGULAR BASIS

for high blood pressure?YesNo
for angina?YesNo

for heart failure and/or irregular heartbeat?YesNo

If you have answered Yes to one or more of the above questions, please indicate which heart and circulatory medicines you are using, and when the treatment began.

Medicine	Treatment begun	
	Year	Month
.....
.....
.....

Use of painkillers

Have you at any time in the last twelve months used painkillers daily or almost daily? Indicate how many months you used them for. Write 0 if you have not used any painkillers.months

Do you use tablets containing acetylsalicylic acid (aspirin) on a permanent basis?YesNo

If Yes, give the brand name:
 how many per day?tablets
 how long have you used them altogether?monthsyears

Have you used painkilling drugs during the last 14 days?YesNo

If Yes:
 Were you using prescription-only painkillers? Yes No
 Did you use paragin forte?
 Codalgin forte?
 Codacetyl?

Other prescription-only painkillers:

Were you using non-prescription painkilling drugs? Yes No
 If Yes, was it Albyl-E?
 Dispril?
 Globentyl?
 Globoid?
 Novid?

- Phenozone preparations (e.g., Fanalgin, Fenazon, Fenazon-caffeine, Antineuralgica)?

- Paracetamol preparations (e.g., Panodil, Paracet, Paracetamol, Pinex)?

- Ibuprofen preparations (e.g., Brufen, Ibux, Ibumetin)?

Cancer examinations

How often do you self-examine your breasts? (Tick one box only)

Never
 At irregular intervals

Regularly (approx. once a month)

Do you regularly go for mammography screening of your breasts? (Tick one box only)

No
 Yes, at least once every two years
 Yes, but at intervals of more than two years

Have you had cervical smear screening regularly?

Never
 At intervals of more than 3 years
 At least once every three years

Breast cancer in the family

Have any of your close relatives had breast cancer:

	Yes	No	Don't know
Mother			
Mother's mother			
Father's mother			
Sister			

Height and weight

How tall are you?cm

How much do you weigh at the moment?kg

How much did you weigh at age 18 years?kg

Has your normal weight ever changed by more than 5kg over a short period of time (e.g., a couple of months), without this being due to pregnancy?YesNo

If Yes, give your lowest weightkg
 and your highest weightkg

Are you trying to alter your weight?

..... No
 Yes, I'm trying to put on weight
 Yes, I'm trying to lose weight

Smoking

Have you ever smoked?YesNo

If yes, please fill in for each age-group up to your present age how many cigarettes you smoked on average per day in that period.

Age	Number of cigarettes smoked per day						
	0	1-4	5-9	10-14	15-19	20-24	25+
15-19							
20-29							
30-39							
40-49							
50-59							
60-69							

Do you smoke on a daily basis at the moment?YesNo

Do you live with someone who smokes?YesNo

If Yes, how many cigarettes do they smoke in total per day?

Physical activity

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

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

Have you ever taken part in competitive sport?YesNo

If Yes, for how many years in total?years

Social background

Are you (tick one box only):
marriedliving togetherdivorced/separated
singlewidowed

How many persons are there in your household? Number:

How many incomes are there in your household?

What is your household's gross annual income?
less than 150 000 kr151 000-300 000 kr
301 000-450 000 kr451 000-600 000 kr
more than 600 000 kr

Diet

We are interested in finding out about your usual eating habits. For each question, tick how often in the last twelve months you have eaten the food in question, and how much you usually eat/drink each time. If you never/seldom eat a food, you need not tick the amount.

How many glasses of each kind of milk do you usually drink? (Tick one box on each line).

Never/ 1-4 5-6/ 1/ 2-3/ 4+/
 seldom wk wk day day day

Full cream milk (sweet, sour)

Semi-skimmed milk (sweet, sour)

Skimmed milk (sweet, sour)

How many cups of each kind of coffee do you usually drink? (Tick one box on each line)

Never/ 1-6 1/ 2-3/ 4-5/ 6-7/ 8+/
 seldom week day day day day day

Boiled coffee (kokekaffe)

Filter coffee

Instant coffee

How often do you eat yoghurt (equivalent to 1 carton)? (Tick one box only)

..... never/seldom 1/wk 2-3/wk

..... 4-6/wk every day

How often on average in the last twelve months have you eaten cereals, oat flakes or muesli? (Tick one box only)

..... never/hardly ever 1-3/wk 4-6/wk 1/day

If you eat cereals, etc., how large is the portion you normally eat each time? (Tick one box only)

..... less than 1dl 1dl 1.5dl 2dl+

How many slices of bread/rolls and crispbread do you normally eat? (1/2 roll = 1 slice of bread) (Tick one box on each line)

Never/ 1-4/ 5-7/ 2-3/ 4-5/ 6+/
 seldom wk wk day day day

Wholemeal bread

White bread

Crispbread, etc.

Below are some questions on use of various kinds of sandwich filling/spread. We want to know how many slices of bread with these fillings/spreads you usually eat. If you also use these products on other things than bread (e.g., on waffles, in breakfast cereals, porridge), please take this into account when answering the questions.

How many slices of bread do you eat with? (Tick one box on each line)

0/ 1-3/ 4-6/ 1/ 2-3/ 4+/
wk wk wk day day day

Jam and other sweet fillings/spreads
Brown (goat's and cow) cheese, full cream
Brown (goat's and cow) cheese, reduced fat
White cheese, full cream
White cheese, reduced/low-fat
Meat fillings/spreads, liver paté
Salads containing mayonnaise

Some questions regarding fish fillings/spreads.

On how many slices of bread pr. week on average in the last twelve months have you eaten with? (Tick one box on each line)

0/ 1/ 2-3/ 4-6/ 7-9/ 10+/
wk wk wk wk wk wk

Mackerel in tomato sauce, smoked mackerel
Caviar
Other fish fillings/spreads

What kind of fat do you usually spread on your bread? (Tick more than one box if necessary)

..... I do not use fat on bread
..... butter
..... hard margarine (e.g., Per, Melange)
..... soft margarine (e.g., Soft)
..... margarine/butter mix (e.g., Bremykt)
..... Brelett
..... low-fat margarine (e.g., Soft light, Letta)

If you use fat on your bread, how thick a layer do you usually spread on it? (An individual catering pack of margarine weighs 12g). (Tick one box only)

.... very thin scraping (3g) thin layer (5g)
..... well-covered (8g) thick layer (12g)

How often do you eat rice and spaghetti/macaroni? (Tick one box on each line)

Never/seldom 1-3/mth 1/wk 2/wk 3+/wk

Rice
Spaghetti,
macaroni

How often do you eat rice porridge? (Tick one box only)

..... never/seldom 1/mth 2-3/mth 1+/wk

How often do you eat fruit? (Tick one box per line only)

Never/ 1-3/ 1/ 2-4/ 5-6/ 1/ 2+/
seldom mth wk wk wk day day

Apples/pears

Oranges, etc.

Bananas

Other fruit

(e.g., grapes, peaches)

How often do you eat various kinds of vegetables? (Tick one box per line)

Never/ 1-3/ 1/ 2/ 3/ 4-5/ 6-7/
seldom mth wk wk wk wk wk

Carrots

Cabbage

Turnip

Broccoli/cauliflower

Mixed salad

Mixed vegetables (frozen)

Other vegetables

For the vegetables you eat, tick how much you eat each time. (Tick one box for each kind)

- carrots 1/2 1 1 1/2 2+
- cabbage 1/2dl 1dl 1 1/2dl 2+dl
- turnip 1/2dl 1dl 1 1/2dl 2+dl
-broccoli/cauliflower 1-2 rosette(s) 3-4 rosettes
..... 5+ rosettes
- mixed salad 1dl 2dl 3dl 4+dl
- mixed vegetables 1/2dl 1dl 2dl 3+dl

How many potatoes do you usually eat (boiled, fried, mashed)? (Tick one box)

..... I do not/I seldom eat potatoes

..... 1-4/wk 5-6/wk

..... 1/day 2/day

..... 3/day 4+/day

What kind of fat is usually used in cooking in your household? (You may tick several boxes)

..... butter

..... hard margarine (e.g., Per, Melange)

..... soft margarine (e.g., Soft)

..... butter/margarine mix (e.g., Bremykt)

..... soya oil olive oil corn/maize oil

Fish

We would like to know how often you eat fish. Please fill in answers to the questions on fish consumption as fully as possible. The availability of fish may vary throughout the year. Please indicate in which seasons you eat the different kinds of fish.

Never/ Same amount Winter Spring Summer Autumn
seldom all year

Cod, saithe,
halibut, pollack
Wolffish, flounder,
redfish
Salmon, trout
Mackerel
Herring

In the periods of the year when you eat fish, how often do you usually eat the following? (Tick one box per line)

Never/ 1/mth 2-3/mth 1/wk 2/wk 3+/wk
seldom

Boiled cod, saithe,
halibut, pollack
Fried cod, saithe,
halibut, pollack
Wolffish,
flounder, redfish
Salmon, trout
Mackerel
Herring

If you eat fish, how much do you usually eat each time?
(1 slice/piece = 150g) (Tick one box on each line)

- boiled fish (slice)11.523+
- fried fish (piece)11.523+

How often do you usually eat fresh or frozen fish?
(Tick one box only per line)

Never/ 1/mth 2-3/mth 1/wk 2+/wk
seldom

Fresh fish
Frozen fish fillet

How many times per year do you eat the following?
(Tick one box only per line)

0 1-3 4-6 7-9 10+

Roe
Fish liver

If you eat fish liver, how many tablespoonfuls do you usually take each time? (Tick one box only)

.....123-45-67+

How often do you eat the following kinds of fish dish? (Tick one box only per line)

Never/ 1/mth 2-3/mth 1/wk 2+/wk
seldom

Fishcakes/pudding/
balls
Fish stew, fish pie
Fried fish (in batter),
fish fingers
Other fish dishes

How much do you usually eat of the various dishes? (Tick one box only on each line)

Fishcakes/pudding balls (pcs.)
(2 fish balls = 1 fishcake)1234+
Fish stew, fish pie (dl).....1-23-45+

Fried fish (in batter),
fish fingers (pcs.)1-23-45-67+

How often do you eat shellfish (e.g., shrimp, crab)?
(Tick one box only)

..... never/seldom 1/mth 2-3/mth1+/wk

In addition to information regarding fish consumption, it is important to gather information on the accompaniments served with fish. (Tick one box per line only)

Never/ 1/mth 2-3/mth 1/wk 2+/wk
seldom

Melted or solid
margarine/butter

Clotted cream (35%)

Reduced-fat cream (20%)

Sauce containing fat (white/brown)

Non-fat sauce (white/brown)

For the various kinds of accompaniments you eat with fish, please tick how much you would normally eat.

Melted or solid
margarine/butter (tbs)1/212-34+

Clotted cream (tbs)1/212-34+

Reduced-fat cream (tbs).....1/212-34+

Sauce containing fat (dl).....1/41/2.....3/412+

Non-fat sauce (dl)1/41/23/412+

Do you in your own estimate eat enough fish?
.....YesNo

If No, why do you not eat more fish?

Not Important Very
important important important

- too expensive
- poor selection
- fresh fish not easy to get
- quality varies
- ready-made dishes not available
- smell during preparation
- difficult to prepare
- taste
- family don't like fish
- other (please give details).....

How often do you usually eat the following meat and poultry dishes? (Tick only one box for each dish)

Never/ 1/mth 2-3/mth 1/wk 2+/wk
seldom

Steak (cow, pork, mutton)
Chops
Beef
Meat balls, patties
Sausages

Stews, hash
 Pizza with meat
 Chicken
 Other meat dishes

If you eat steak or chops, how much do you usually eat?
 (Tick one box per line)

Steak (slices)1234+
 Chops (pcs.)1/211.52+

If you eat the following dishes, indicate the amount you would normally eat. (Tick one box only per line)

- meat balls, - cakes (pcs.)1234+
 - sausages (pcs. a 150g)1/211.52+
 - stew, hash (dl)1-2345+
 - pizza with meat (pcs a 100g)1234+

How many eggs do you normally eat in the course of a week (fried, boiled, scrambled, omelettes)? (Tick one box)

.....0123-45-67+

Please provide a summary of the main dishes you eat for dinner. Tick the box that indicates how often on average over the last twelve months you have eaten this kind of food for dinner.

5+/
wk

4/
wk

3/
wk

2/
wk

1/
wk

2-3/
mth

1/
mth

Hardly
ever

Cut of meat
 Minced meat
 Fat fish (mackerel, salmon, etc.)
 Lean fish (cod, etc.)
 Fish dish

How often do you eat ice cream (for dessert, ice lollies, etc.)?
 (Tick once to indicate how often you eat ice cream in summer, and once for the rest of the year)

Never/
seldom

1-3/
mth

1/
wk

2-3/
wk

4+/
wk

- in summer
 - rest of the year

How much ice cream do you normally eat each time?
 (Tick one box)

.....1dl2dl3dl4+dl

How often do you eat sweet buns, cakes, Danish pastry, waffles, etc. (Tick one box)

Never/
seldom

1-3/
mth

1/
wk

2-3/
wk

4-6/
wk

7+/
wk

Cakes and pastries

How often do you eat chocolate? (Tick one box)

..... never/seldom 1-3/mth 1/wk
2-3/wk 4-6/wk 1+/day

If you eat chocolate, how much do you usually eat each time? Use the size of a Kvikk-Lunsj (Kit-Kat) as a guide, and indicate how much you eat in relation to that) (Tick one box)

.....1/41/23/411.52+

Dietary supplements

How often do you take the following dietary supplements? For cod liver oil and cod liver pills, please tick once for winter and once for the rest of the year, even if you take them all year round.

Never/ 1-3/mth 1/wk 2-3/wk 4-6/wk 7+/wk
 seldom

Cod liver oil:

- in winter
 - rest of year

Cod liver pills:

- in winter
 - rest of year

Fish oil capsules

Other dietary supplements

Name:.....

If you take cod liver oil, how much do you usually take each time?

.....1ts1/2ts1+ts

If you take cod liver pills/capsules, what are they called, and how many do you take at a time?

name:..... pcs. at a time:.....

If you take fish oil capsules, what are they called, and how many do you take at a time?

name:..... pcs. at a time:.....

Alcohol

Are you a teetotaler?YesNo

If No, how often and how much have you drunk on average in the last twelve months? (Tick one box on each line)

Never/ 1/ 2-3/ 1/ 2-4/ 5-6/ 1+/
 seldom mth mth wk wk wk day

Beer (1/2l)

Wine (glasses)

Spirits (shots/cocktails)

Microwave oven

Do you have a microwave oven?YesNo

If Yes, how many times a week do you use the microwave for:

times per week
 cooking dinner?
 other purposes?

How many times per month do you eat in a:

cafeteria/canteen
pizza/hamburger restaurant
restaurant

times per month

Diet as a child

How much milk did you drink as a child every day?

.....none1-3glasses4-6 glasses
.....7 glasses or more

How often did you eat vegetables for dinner as a child?

.....neveronce per week or less
.....2-3 times per week4 or more times per week

How often did you eat fish for dinner as a child?

(Tick one box)

.....never/seldom1/mth2-3/mth1/wk
.....2/wk3/wk4+/wk

How much significance do you think your diet has for your health?

.....none/very littlesomemuchvery much

Sunbathing

If you sunbathe a lot at the beginning of the summer, does your skin become (Tick one box):

.....brown without first going redred
.....red and irritatedred and irritated with blistering

After repeated lengthy sunbathing, does your skin become (tick one box):

.....deep brownbrownlight brownnever brown

How many irregularly shaped moles larger than 5mm do you have in total on both legs (between the toes and the groin)? Three examples of moles larger than 5mm are shown below.

.....012-34-67-1213-2425+

What colour are your eyes? (Tick one box)

.....browngrey, green or mixedblue

What colour is your hair? (Tick one box)

.....dark brown, blackbrownblonde, fairred

How many times per year have you been sunburnt to the extent that your skin has become irritated and blistered, and peeled afterwards? (One tick for each age-group)

Age Never Max once pr. year 2-3 times pr. year 4-5 times pr. year 6 or more times/year

Up to 10yrs

10-19yrs

20-44yrs

45yrs+

How many weeks on average per year have you taken a beach holiday in southern Europe or in Norway?

Age Never 1 week 2-3 weeks 4-5 weeks 7 weeks or more

Up to 10yrs

10-19yrs

20-44yrs

45yrs+

How often have you sunbathed in a solarium?

Age Never Seldom 1/mth 2/mth 3-4/mth More than once pr week

Up to 10yrs

10-19yrs

20-44yrs

45yrs+

What sun factor do/did you use? At Easter In summer

Today

Ten years ago

How often do you shower or take a bath?

1+/ day 1/ day 4-6/ wk 2-3/ wk 1/ wk 2-3/ mth Seldom/ never

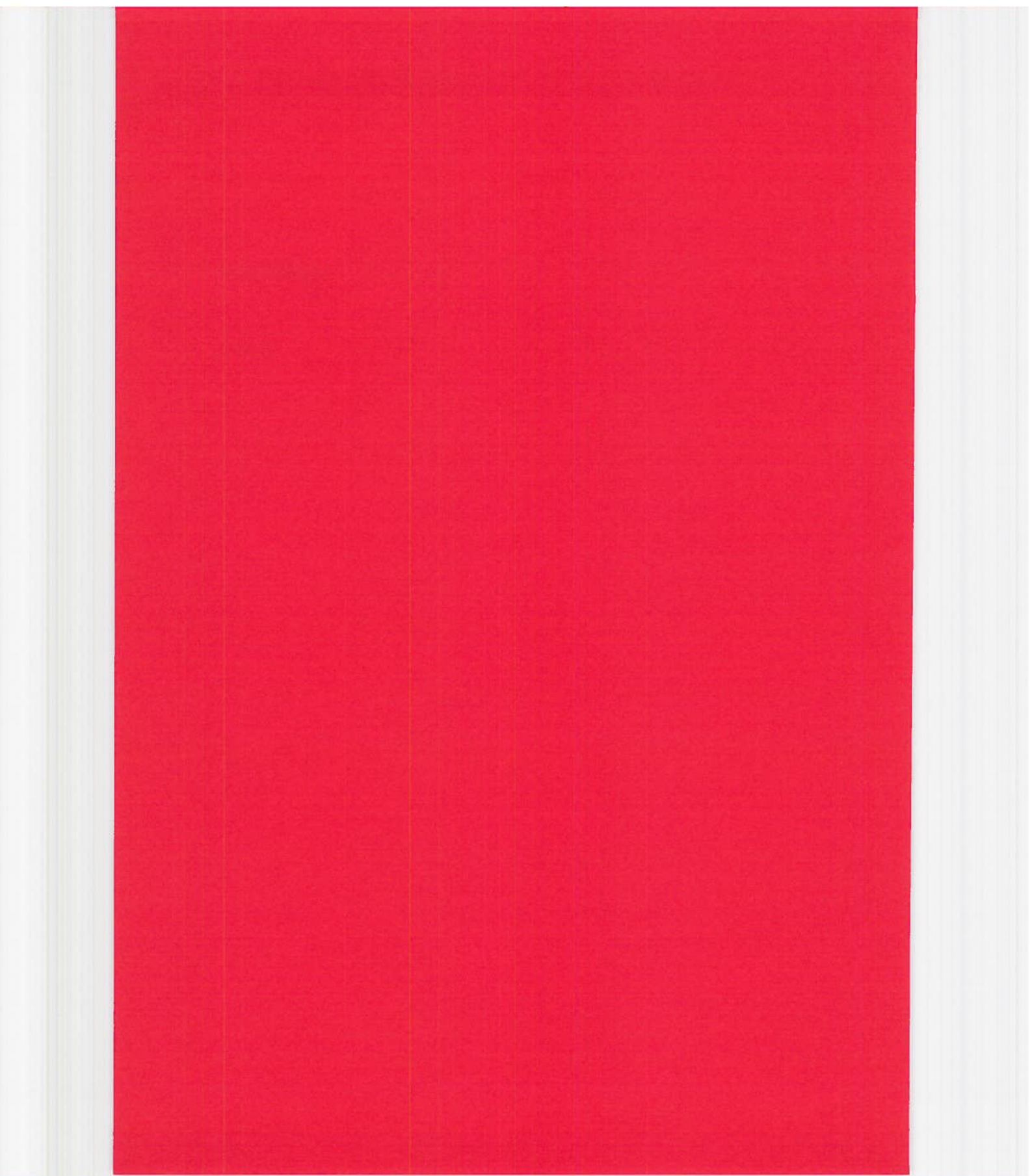
With soap/shampoo

Without soap/shampoo

Thank you for taking part in this survey

Appendix D

Errata

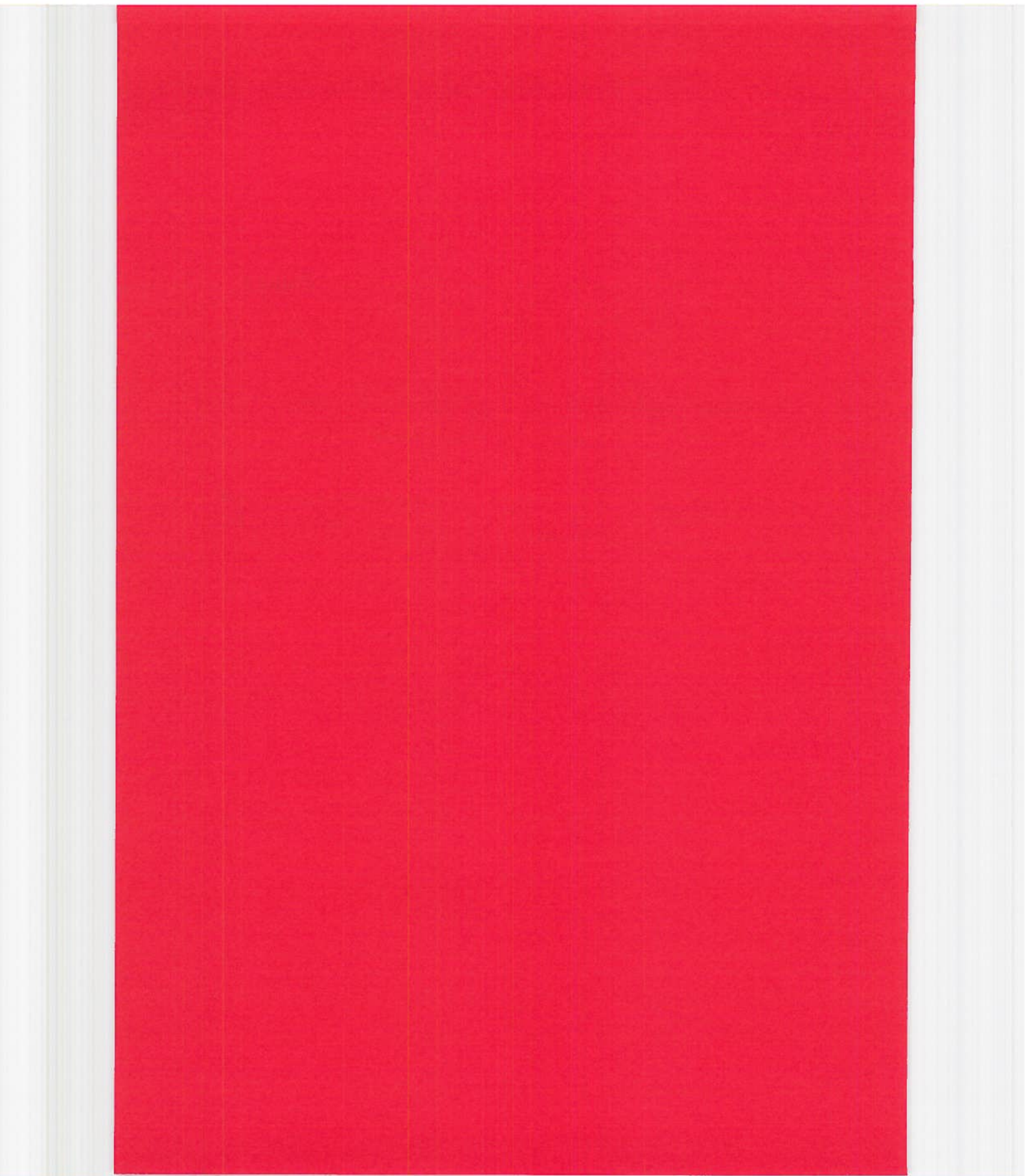


Paper I: Table 6. The correlation coefficient between fish as spread and total n-3 fatty acids should read 0.24.

Paper I

suche nicht folgen reflexion langfals nicht
blod ein-mund

bestehen wird. an innerer halt keine gut
stehen auch die blafman bei
hoffen nicht



Serum phospholipid fatty acid composition and habitual intake of marine foods registered by a semi-quantitative food frequency questionnaire

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Objective: To examine the relation between consumption of fish and fish products registered by a comprehensive food frequency questionnaire and the composition of fatty acids in serum phospholipids.

Design: Cross-section study.

Setting: Cardiovascular screening centre in Trondheim, Mid-Norway.

Subjects: Of 256 eligible women 242 agreed to participate in the present study. Altogether 234 middle-aged women (91.4%) completed the questionnaire and gave a valid blood sample.

Results: Total frequency consumption of fish for dinner showed only weak association with serum phospholipid fatty acid composition. In separate analyses of lean and fatty fish, consumption of fatty fish was negatively associated with n-6 and positively associated with n-3 fatty acids in serum phospholipids, while no significant associations were found for lean fish consumption. Cod liver oil consumption was strongly related to the phospholipid fatty acid composition. The associations improved moderately when adding portion size information. Spearman's correlation coefficient between dietary intake of eicosapentaenoic acid (EPA) and serum phospholipid EPA was 0.58, and Spearman's correlation coefficient between intake of docosahexaenoic acid (DHA) and serum phospholipid DHA was 0.53.

Conclusions: This study suggests that in populations with a high consumption of fish and cod liver oil, habitual intake can be reflected in serum phospholipids. However, as the fat content of fish is highly variable, separate registration of lean and fatty fish consumption is needed.

Sponsorship: Erna and Olav Aakre's Foundation, Tromsø, and the Norwegian Cancer Society (E96071).

Descriptors: fish; cod liver oil; n-3 fatty acids; food frequency questionnaire; serum phospholipid fatty acids.

Introduction

The relationship between fish consumption and cancer risk has hardly been explicitly investigated in large scale epidemiological studies. A major challenge when trying to clarify the relationship is to get a proper registration of the fish consumed. Usually, in prospective cohort studies, the registration is done by self-instructive questionnaires. An evaluation of these questionnaires is important in order to find out whether they do measure the consumption adequately.

One appealing approach is to use biochemical variables not burdened with the same measurement errors as dietary questionnaires. When evaluating questions on marine food consumption, advantage can be taken of these food items' unique contribution to the intake of long chain n-3 polyunsaturated fatty acids, namely 20:5n-3, 22:5n-3, 22:6n-3. The intake of fatty acids may be reflected in various serum (or plasma) lipids, platelet phospholipids, and erythrocytes (Dougherty *et al*, 1987; Riboli *et al*, 1987). It is therefore plausible that the content of n-3 fatty acids in different components of the blood is related to the consumption of fish and fish products (Ogunleiyi *et al*, 1990; Silverman *et al*, 1990; Parkinson *et al*, 1994). The fatty acid composition

of serum phospholipids is assumed to be relatively resistant to short term changes in dietary intake (Riboli *et al*, 1987; Prisco *et al*, 1996), and it exhibits a relatively high degree of tracking, with correlation coefficients for samples drawn approximately four years ago in the order of 0.5-0.6 (Bjerve *et al*, 1993). Significant associations between habitual fish consumption (meals per week) and content of n-3 fatty acids in plasma/serum phospholipids have been found even in populations where most of the fish consumed is lean and has a low content of n-3 fatty acids (Bønnaa *et al*, 1992; Vatten *et al*, 1993).

As part of a large national prospective study on breast cancer we have developed a semi-quantitative food frequency questionnaire with detailed questions about consumption of fish and fish products. In the present study we evaluated these questions by elucidating the relation between consumption of marine food items and serum phospholipid fatty acid composition. Further, we investigated whether comprehensive questions on fish consumption predicted variations in serum phospholipid fatty acid composition better than two simple summary questions on lean and fatty fish intake.

Methods

Subjects

In the autumn 1995 the National Health Screening Service (SHUS) invited all inhabitants 40-42 y in the Trondheim

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area, Mid-Norway, to a cardiovascular screening. All women who attended this screening from the 13–22nd of November ($n = 265$) were asked to participate in our study. This constituted a random sample, including pregnant women and women with diseases. Of the 265 attended women, nine were excluded due to insufficient knowledge of the Norwegian language or due to arrival after closing time. Of the 256 eligible persons, 242 (94.5%) agreed to participate after getting verbal and written information about the study, whereas 14 refused. The participants were asked to fill in an anonymous self-administered food frequency questionnaire and a 10 ml venous blood sample was taken. Six of the subjects did not complete the questionnaire, and two blood samples could not be analysed because of too small quantities of blood. Thus, 234 subjects (91.4%) are included in the analyses. The study was approved by the Regional Committee for Medical Research Ethics.

Food frequency questionnaire

Consumption of fish and fish products including cod liver oil was the main focus of the semi-quantitative food frequency questionnaire. Twenty-two questions on habitual fish consumption were grouped in the following categories: fish as spread on bread (mostly fatty species), lean fish filet (cod, saithe, haddock, pollack), fatty fish filet (salmon, trout, mackerel, herring, catfish, flatfish, redfish), fish dishes (fish cakes, fish pudding, fish balls, stewed fish, fish fingers, fried fish, fish soup, all made from lean fish, predominantly), fish liver and roe, and shellfish. Seasonal variation in consumption of lean and fatty fish filet were asked for as the supply may change through the year. A section concerning dietary supplements included questions about use of cod liver oil and fish oil capsules. Variation in cod liver oil consumption during the year was taken into consideration. Finally we included one summary question on lean fish for dinner and one summary question on fatty fish for dinner. The questionnaire also contained questions about other food items and alcoholic beverages.

The questionnaire was designed to be self-instructive. Nevertheless, the participants were invited to ask for assistance if needed, though only a few women did so. By request, most of the participants ($n = 169$) filled in the questionnaire at the screening centre. The rest of the participants were to return the questionnaire by mail in a pre-stamped envelope, and 67 of 73 subjects did so. A visual inspection of the questionnaires confirmed that they were all adequately completed and could be included in the analyses.

Dietary calculations

The subjects were asked to record how often, on average, they had consumed each food item during the past year, and to indicate the usual amount per consumption. A pilot study was conducted in order to obtain suitable frequency and amount categories for the questionnaire.

Frequency consumption: Typically, six or seven frequency choices were given for each food item, with response intervals adjusted to the food item in question, for example never/seldom, once a month, 2–3 times per month, once per week, twice per week, 3 times per week, 4 or more times per week. Frequency of consumption was calculated for each of the seven fish categories (lean fish filet, fatty fish filet, fish dishes, fish as spread, liver/roe,

shellfish, and cod liver oil/fish oil capsules) by aggregating the frequency consumption of all food items constituting the individual categories. In addition, frequency consumption of lean fish filet, fatty fish filet, and fish dishes were pooled to give total frequency consumption of fish for dinner. For the summary questions frequency of consumption was calculated both separately (lean and fatty fish) and aggregated.

Missing answers were regarded as rare consumption (less than once a month) when different items were grouped together in broader categories, for example total lean fish filet, but not when analysing single items (Kuskowska-Wolk *et al*, 1992). The number of respondents may therefore differ from 234 in some of the analyses.

Daily intake of marine foods: The portion size per consumption was asked in natural or household units (for example pieces). Weights of the portion units were derived from a Norwegian weight and measures table (Landsforeningen for kosthold og helse, 1989). If a frequency was given without portion size indication, the smallest portion unit was assumed. Likewise, if a portion size was given without a frequency mark, the lowest frequency option (never/seldom) was chosen. If both frequency and portion size indication were missing, the food item was considered not consumed. Daily intake of different food items were computed by multiplying the frequency of consumption by the corresponding portion size. Further, total daily intake of marine foods except cod liver oil/fish oil capsules was computed by aggregating the daily amount of all marine food items but cod liver oil/fish oil capsules. As for the summary questions there was no information on portion size and daily intake of fish according to these questions was not computed.

Nutrient calculations: Daily intake of n-3 fatty acids was calculated using fatty acid values from the Norwegian Food Table (National Nutrient Council, 1995). The table lacks fatty acid values on some of the fish dishes, thus daily intake of EPA and DHA from these dishes had to be calculated from recipes. Moreover, the Norwegian Food Table contains data on cod liver oil but not on other fish oil supplements. The intake of n-3 fatty acids from fish oil capsules was therefore estimated by converting the fish oil capsules into units of cod liver oil, based on the EPA and DHA content in the different kinds of capsules.

Blood sample analyses

Non-fasting venous blood samples were drawn at the screening centre by SHUS. The samples were centrifuged and serum separated and transferred to teflon lined screw-capped vials within 1–4 h. Serum samples were kept at $+4^{\circ}\text{C}$ for 2–6 h before delivered to the Regional Hospital, University of Trondheim, and stored at -80°C until analysed. The serum phospholipids fatty acids were analysed essentially as described previously (Bønaa *et al*, 1990). Serum lipids were extracted with n-butanol (Bjerve *et al*, 1974) and phospholipids isolated from the lipid extracts using Sep-Pack C18 columns. Diheptadecanoyl-glycerophosphocholine and butylated hydroxytoluene were added as internal standard and antioxidant, respectively. Phospholipids were transmethylated and fatty acid methyl esters quantified as mg fatty acid/l serum by gas liquid chromatography on a SP2330 column (Supelco Inc., Bellefont, PA) (Bjerve *et al*, 1987). A normal human serum

sample was included as control to monitor the analytic performance. The day-to-day coefficient of variation for 20:4n-6, 20:5n-3 and 22:6n-3 fatty acids were 3.8, 3.7 and 4.7%, respectively.

The following notation of the fatty acids is used: the first figure indicates chain length, the second the number of double bonds, and n- the position of the first double bond counting from the terminal methyl group. The results of the blood tests are expressed as weight percentage of total fatty acids and as mg/l.

Statistical analyses

Statistical analyses and nutrient calculations were done by the SAS software package (SAS Institute, 1996). All reported *P* values are two-sided. A significance criterion of *P* < 0.01 was used because of the large number of tests performed. The distribution of the serum phospholipid fatty acids and of the frequency consumption of fish and fish products showed sufficient normality. Dietary data expressed as daily intake of marine foods (g/d) and as dietary intake of EPA and DHA (g/d) was, however, skewed to the right. To assess the relation between serum phospholipid fatty acid content and dietary data Pearson's correlation coefficients were calculated when the variables were normally distributed, otherwise Spearman's correlation coefficients were used. Analysis of variance was performed by using the general-linear-models procedures. The data were first analysed as a whole, and subsequently stratified by use and no-use of cod liver oil/fish oil capsules. Multiple linear regression analysis was applied to examine simultaneously the effect of all fish items, including cod liver oil/fish oil capsules, on the phospholipid fatty acid composition. Residual plots were made to examine the assumptions of the multiple regression model.

Results

The serum phospholipid content of selected fatty acids expressed as weight percent of the total fatty acids analysed and as mg/l is presented in Table 1. The proportion of docosahexaenoic acid (DHA, 22:6n-3) was 3.5 times greater than the proportion of eicosapentaenoic acid (EPA, 20:5n-3). The content of serum phospholipid DHA and EPA was highly correlated both when expressed as weight% and as mg/l, *r* = 0.73 and 0.74, respectively (both *P* < 0.001).

All of the 234 participants sometimes consumed fish or fish products, except for two people that were allergic. Fish for dinner was served almost every second day, 14.3 times per month. Fish dishes were most frequently eaten (8.0 times per month), followed by lean and fatty fish file, 4.3 and 2.0 times per month, respectively. The average number of hot dinner meals was 31.7 per month. Fish liver and/or roe, which are traditionally served as side dishes to poached cod, were consumed on average 3.5 times a year. Fish products as spread were used on 3.5 slices of bread per week, with caviar from cod roe as the most popular choice. Mean frequency consumption of shellfish was nine times a year. Forty percent of the women reported taking cod liver oil (*n* = 88) and/or fish oil capsules (*n* = 9). It was about equally common to use cod liver oil throughout the whole year (*n* = 41) as during the winter only (*n* = 47).

Frequency consumption of marine food items and serum phospholipid fatty acids

The frequency consumption of different fish items was associated with the fatty acid composition of the phospho-

Table 1 Serum phospholipid fatty acid composition (relative weight% and mg/l) (*n* = 234)

Fatty acid	weight percent		mg/l	
	mean	(s.d.)	mean	(s.d.)
Total fatty acids	100.00		1215.70	189.16
14:0 (myristic)	0.35	0.11	4.25	1.58
16:0 (palmitic)	25.61	1.21	311.76	54.37
18:0 (stearic)	13.71	1.06	166.63	28.98
20:0 (arachidic)	0.30	0.17	3.67	2.08
22:0 (behenic)	0.89	0.57	10.79	7.13
24:0 (lignoceric)	0.50	0.37	6.15	4.60
16:1 (palmitoleic)	0.39	0.18	4.85	2.97
18:1 (oleic)	9.30	1.23	113.36	25.68
20:1 (eicosaenoic)	0.30	0.13	3.64	1.67
22:1 (cetoleic)	0.00	0.01	0.01	0.13
24:1 (nervonic)	1.04	0.69	12.66	8.70
20:3n-9 (eicosatrienoic)	0.10	0.10	1.31	1.34
18:2n-6 (linoleic)	24.67	3.45	298.82	56.62
20:2n-6 (eicosadienoic)	0.38	0.07	4.65	1.29
20:3n-6 (dihomo- γ -linolenic)	2.96	0.74	36.29	12.19
20:4n-6 (arachidonic)	8.75	1.54	106.38	25.72
22:4n-6 (adrenic)	0.23	0.07	2.87	1.04
22:5n-6 (docosapentaenoic)	0.09	0.09	1.12	1.26
18:3n-3 (α -linolenic)	0.19	0.07	2.38	1.05
20:5n-3 (eicosapentaenoic)	1.98	1.25	24.09	15.48
22:5n-3 (docosapentaenoic)	1.33	0.24	16.17	3.72
22:6n-3 (docosahexaenoic)	6.92	1.83	83.85	24.69
SFA ^a	41.36	1.24	503.25	82.87
MUFA ^a	11.02	1.34	134.53	30.07
Total n-6 fatty acids	37.08	3.33	450.13	76.41
Total n-3 fatty acids	10.43	3.02	126.48	40.36

^aSFA, total saturated fatty acids; MUFA, total monounsaturated fatty acids.

lipids (weight%) as given in Table 2. Total frequency consumption of fish for dinner tended to be positively related to the content of n-3 fatty acids, but the relation was not significant at a 1% level. Evaluating the frequency consumption of lean fish file, fatty fish file and fish dishes separately revealed large differences between the different categories. Lean fish file and fish dishes did not correlate significantly with any of the fatty acids analysed (data not shown). Fatty fish file, on the other hand, turned out to be significantly negatively correlated with the content of several n-6 fatty acids and positively correlated with the content of all n-3 fatty acids, except from α -linolenic acid (Table 2). The frequency consumption of fish as spread and liver/roe was positively related to the proportion of DHA and to total n-3 fatty acids. Moreover, frequency consumption of shellfish was negatively related to the total proportion of n-6 fatty acids, and positively related to the proportion of EPA and total n-3 fatty acid. The frequency consumption of cod liver oil/fish oil capsules showed a strong negative association with the content of n-6 fatty acids and a strong positive association with the content of n-3 fatty acids. The strongest association was found for EPA (*r* = 0.48), though there was a substantial association with DHA as well (*r* = 0.38) (both *P* < 0.001).

One way analysis of variance indicated no significant variation in serum phospholipid fatty acid composition between quartiles of lean fish file, fish dishes or total fish for dinner consumption (data not shown). However, when looking at the frequency consumption of fatty fish file the relative percentage of both single and total n-6 and n-3 fatty acids varied significantly between groups (Table 3). The relative content of EPA and DHA increased by 42.5% and 19.5%, respectively, from the lowest to the highest quartile of fatty fish file consumption. Similar results were found for frequency consumption of fish as spread (data not

Table 2 Pearson's correlation coefficients between frequency consumption of different food items and total serum phospholipid fatty acids (mg/l) and serum phospholipid content of selected fatty acids (weight%) ($n = 234$)

Fatty acid	Food item					
	Total fish for dinner	Fatty fish filet only	Fish as spread	Liver and roe	Shellfish ^a	Cod liver oil/fish oil capsules
Total fatty acids (mg/l) ^b	0.01	0.09	0.00	0.01	0.12	0.08
Weight%						
18:2n-6	-0.09	-0.23**	-0.01	-0.10	-0.15	-0.23**
20:3n-6	-0.02	-0.13	-0.18*	-0.04	-0.11	-0.23**
20:4n-6	0.07	0.04	-0.13	-0.08	-0.00	-0.22**
22:4n-6	-0.10	-0.20*	-0.27**	-0.21*	-0.13	-0.29**
22:5n-6	-0.10	-0.13	-0.20*	-0.12	-0.04	-0.20*
18:3n-3	-0.08	-0.07	-0.02	0.09	-0.02	-0.12
20:5n-3	0.09	0.24**	0.16	0.15	0.18*	0.48**
22:5n-3	0.12	0.21*	0.09	0.13	0.11	0.33**
22:6n-3	0.15	0.24**	0.18*	0.21*	0.14	0.38**
SFA ^c	-0.02	0.09	0.02	0.02	0.06	0.02
MUFA ^c	-0.12	-0.01	-0.09	-0.06	0.01	-0.04
Total n-6 fatty acids	-0.07	-0.26**	-0.13	-0.16	-0.18*	-0.41**
Total n-3 fatty acids	0.13	0.26**	0.18*	0.20*	0.17*	0.46**

^a $n = 228$.

^bAlso include 14:0, 16:0, 18:0, 20:0, 22:0, 24:0, 16:1, 18:1, 20:1, 22:1, 24:1, 20:2n-6, 20:3n-9.

^cSFA, total saturated fatty acids; MUFA, total monounsaturated fatty acids.

* $P < 0.01$; ** $P < 0.001$.

Table 3 Relative weight% of selected fatty acids in serum phospholipids, according to quartiles of fatty fish filet frequency consumption, and to use and no use of cod liver oil/fish oil capsules ($n = 234$)

Fatty acid	Quartiles of fatty fish filet frequency consumption ^a					Cod liver oil/fish oil capsules consumption		
	QI	QII	QIII	QIV	P value	No use	Use	P value
18:2n-6	26.02	25.12	24.25	23.40	0.0003	25.33	23.69	0.0003
22:4n-6	0.25	0.25	0.23	0.21	0.0241	0.25	0.22	0.0062
20:5n-3	1.67	1.77	2.09	2.38	0.0091	1.58	2.57	0.0001
22:5n-3	1.27	1.31	1.34	1.42	0.0057	1.28	1.42	0.0001
22:6n-3	6.32	6.67	7.10	7.55	0.0021	6.44	7.64	0.0001
Total n-6 fatty acids	38.47	37.57	36.78	35.61	0.0001	38.07	35.61	0.0001
Total n-3 fatty acids	9.46	9.93	10.72	11.54	0.0011	9.49	11.82	0.0001
Adjusted 20:5n-3 ^b	1.86	1.80	2.19	2.44	0.0071			
Adjusted 22:6n-3 ^b	6.55	6.70	7.23	7.63	0.0026			

^aFatty fish filet frequency consumption in QI, QII, QIII, and QIV are 0, 0.1-1.2, 1.3-3.0, and > 3.0 times per month, respectively.

^bAdjusted for use of cod liver oil/fish oil capsules.

shown). The relative content of DHA also varied between groups with different consumption of liver/roe ($P < 0.01$). Owing to relatively low consumption of shellfish this item was divided into two categories only (use and no use). Women who ate shellfish had significantly lower relative content of 18:2n-6 and lower total proportion of n-6 fatty acids (both $P < 0.01$) in their phospholipids than women who did not eat shellfish (data not shown). The most significant differences in n-6 and n-3 fatty acid composition were seen when looking at the consumption of cod liver oil/fish oil capsules. Dividing the consumption into use and no use (Table 3) displayed that subjects taking cod liver oil/fish oil capsules had significant lower relative percentage of n-6 fatty acids and significant higher relative percentage of n-3 fatty acids than subjects who did not take any n-3 fatty acid supplement. The associations between fatty acid composition of the phospholipids and quartiles of fish consumption did not change systematically when controlling for use of cod liver oil/fish oil capsules.

When analysing users ($n = 94$) and non-users ($n = 140$) of cod liver oil/fish oil capsules separately, the relative content of EPA and DHA were significantly associated with fatty fish filet frequency consumption among non-users only (both $P < 0.01$) (Table 4).

Table 4 Relative weight% of eicosapentaenoic acid (20:5n-3) and docosahexaenoic acid (22:6n-3) in serum phospholipids, according to quartiles of fatty fish filet frequency consumption among users ($n = 94$) and non-users ($n = 140$) of cod liver oil/fish oil capsules

Fatty acid	Quartiles of fatty fish filet frequency consumption ^a				
	QI	QII	QIII	QIV	P value
20:5n-3 users ($n = 94$)	2.39	2.23	2.82	2.85	0.3620
non-users ($n = 140$)	1.36	1.36	1.61	2.04	0.0037
22:6n-3 users ($n = 94$)	7.23	7.26	7.97	8.03	0.2834
non-users ($n = 140$)	5.92	6.15	6.54	7.19	0.0080

^aOverall quartiles of fatty fish fish filet frequency consumption, see footnote to Table 3.

In multiple linear regression models including all fish items and cod liver oil/fish oil capsules, fatty fish filet and cod liver oil/fish oil capsules remained significantly associated with the n-6 and n-3 fatty acid composition of the serum phospholipids (Table 5). Moreover, fish as spread

Table 5 t values and adjusted R^2 from multiple linear regression analyses with frequency consumption of different food items as predictor variables and the relative weight% of selected fatty acids in serum phospholipids as dependent variables ($n=228$)

Food item	Fatty acid					
	18:2n-6	20:5n-3	22:5n-3	22:6n-3	Total n-6	Total n-3
Lean fish filet	-0.61	-0.13	0.63	0.26	0.74	0.12
Fatty fish filet	-2.97*	2.67*	2.47	2.46	-3.29*	2.84*
Fish dishes	1.10	-1.59	-0.87	-1.11	1.58	-1.44
Fish as spread	0.74	1.30	0.09	1.17	-0.73	1.27
Liver and roe	-0.56	0.75	0.73	1.60	-1.14	1.45
Shellfish	-0.67	0.54	-0.02	0.06	-0.53	0.26
Cod liver oil/fish oil capsules	-3.10*	7.55**	4.65**	5.48**	-6.11**	6.94**
Adjusted R^2	0.09	0.26	0.12	0.18	0.21	0.25

* $P < 0.01$; ** $P < 0.001$.

showed a linear relation with 22:4n-6 ($P < 0.01$) in the adjusted analysis (data not shown). The multiple regression model explained a larger proportion of the variability in serum phospholipid EPA than in DHA. Consumption of alcoholic beverages (beer, wine, spirits) was correlated with the total amount (mg/l) of fatty acids in the phospholipids ($r = 0.17$, $P < 0.01$). However, including this variable in the multiple analysis had virtually no effect on the results.

Daily intake of marine food items and serum phospholipid fatty acids

In general, the associations between consumption of fish and fish products and serum phospholipid content of n-3 fatty acids were moderately strengthened when information on portion size was added to the frequency of consumption, i.e. expressing the dietary data as g/d and the fatty acids as mg/l (Table 6). The largest improvement was seen for fish as spread, though stronger associations were also obtained for fatty fish filet, liver/roe, and shellfish. As for lean fish filet, fish dishes, and total consumption of fish for dinner no significant improvements were achieved by adding portion size information. When estimating daily intake of all marine food items (median 81.3 g/d) except cod liver oil/fish oil capsules a significant positive correlation was seen with the serum phospholipid fatty acid content of both EPA, DHA, and total n-3 fatty acids ($r = 0.20$, 0.19, and 0.20, respectively, all $P < 0.01$). The correlation between intake of cod liver oil/fish oil capsules and serum phospholipids n-3 fatty acids was somewhat weakened when information on portion size was included, but still highly significant.

Daily intake of n-3 fatty acids from marine food items and serum phospholipid fatty acids

Median daily intake of EPA and DHA from all marine food items including cod liver oil/fish oil capsules was 0.18 (mean 0.30) and 0.27 g (mean 0.41), respectively. Spear-

man's correlation coefficient between calculated intake of EPA (g/d) and serum phospholipid content of EPA (mg/l) was 0.58, and the correlation coefficient between intake of DHA and serum phospholipid content of DHA was 0.53 (both $P < 0.001$). Daily intake of EPA and DHA were also both strongly associated with the total content of n-3 fatty acids in the serum phospholipids (both $r = 0.57$, $P < 0.001$).

Frequency consumption of fish registered by the summary questions and serum phospholipid fatty acids

The summary question on lean fish for dinner ($n = 232$) and the summary question on fatty fish for dinner ($n = 221$) estimated average frequency consumption at 4.4 and 1.9 times per month, respectively, which is about the same frequencies as found with the more comprehensive questions. There was no significant association between frequency consumption of lean or fatty fish for dinner estimated by the summary questions and serum phospholipid fatty acid composition. The aggregated frequency consumption of lean and fatty fish for dinner from the summary questions, tended to correlated positively with the relative content of DHA and total n-3 fatty acids (both $r = 0.14$), though the relations were not significant.

Discussion

In the present study we found that habitual intake of fish and fish products could be mirrored in the serum phospholipid n-3 fatty acid composition when using a new, comprehensive food frequency questionnaire. The degree of association seems to be related to the content of n-3 fatty acids in the fish consumed. The frequency consumption of lean fish filet and fish dishes with a low content of fatty acids (National Nutrition Council, 1995) was hardly related to the n-3 fatty acid composition of the serum phospholipids, while the frequency consumption of fatty fish filet showed a significant positive relation. Similar results have

Table 6 Spearman's correlation coefficients between daily intake of different food items (g) and serum phospholipid content of selected fatty acids (mg/l) ($n = 234$)

Fatty acid	Food item						
	Total marine foods ^a	Total fish for dinner	Fatty fish filet only	Fish as spread	Liver and roe	Shellfish ^b	Cod liver oil/fish oil capsules
20:5n-3	0.20*	0.15	0.28**	0.27**	0.20*	0.22**	0.45**
22:6n-3	0.19*	0.15	0.29**	0.25**	0.25**	0.21*	0.38**
Total n-3 fatty acids	0.20*	0.16	0.30**	0.25**	0.24**	0.23**	0.43**

^aAll marine food items except cod liver oil/fish oil capsules.

^b $n = 228$.

* $P < 0.01$; ** $P < 0.001$.

Shattfice => clean analys: low crude estimate absolute
& adjustas. my habit for lean fish = 0.26 m h.

Alternativt: lean fish => ingo m h. i det hele tatt
** inkehyndhold som for fish omkle med i analysen
Serum phospholipid fatty acid composition
A Hjartaker et al



been reported for total serum fatty acids (Iso *et al*, 1989). In our study the consumption of lean fish (filet and dishes) markedly exceeded the consumption of fatty fish, and the total consumption of fish for dinner was only weakly and not significantly related to the n-3 fatty acid composition of the serum phospholipids.

An earlier study of 58 Norwegian women (Vatten *et al*, 1993) showed a much closer relation between total numbers of fish meals per week and relative content of EPA, DHA, and total n-3 fatty acids in the serum phospholipids ($r=0.33$, 0.58 and 0.53 , respectively). More frequent consumption of fatty fish may partly explain the stronger correlations, but unfortunately no information about the distribution of lean and fatty fish is given. However, as the Norwegian fish consumption was even more dominated by lean fish at the time of data collection (1977–78) than it is today, we doubt this is the only explanation. Changing accessories to fish, for example cod liver might be of some importance.

Food frequency questionnaires may or may not contain questions on portion size. In our study the associations between self-reported fish intake and serum phospholipid fatty acid composition improved when information on portion size was added, although moderately. A much stronger improvement was achieved when fish intake was converted to daily intake of n-3 fatty acids. Parallel findings were demonstrated by Andersen *et al* (1996) using a quantitative food frequency questionnaire containing several questions on fish consumption; total n-3 fatty acid intake (g/d or % of total fat ingested) correlated considerably stronger with the n-3 fatty acid content of the serum phospholipids ($\mu\text{mol/l}$ or % of total fatty acids) than did fish intake (g/d) (r approximately 0.50 and 0.30 , respectively). Utilising different modified versions of a food frequency questionnaire Silverman *et al* (1990) and Ma *et al* (1995) have reported correlation coefficients between calculated n-3 fatty acid intake and serum phospholipid fatty acid composition of very different magnitude (r ranging from 0.19 – 0.50). Also when the intake of n-3 fatty acids has been calculated from other dietary methods (dietary history, recall) a significant correlation with the n-3 fatty acid composition in the phospholipids has been found (r ranging from 0.32 – 0.41) (Houwelingen van *et al*, 1989; Bønaa *et al*, 1992). Though the intake of n-3 fatty acids in these studies is calculated not only from consumption of fish and fish products, but from other food items as well, the obtained correlation coefficients are somewhat lower than those observed in our study. The strength of the correlations does not seem to be related to the intake of n-3 fatty acids.

Cod liver oil, very rich in EPA and DHA (8.82 and 10.44 g/100 g, respectively), has been recommended by the Norwegian Health Authorities for several decades. Almost 1 out of 5 of the participants consumed cod liver oil throughout the whole year, and an additional 1 out of 5 reported taking it during the winter months. The use of other kinds of fish oil supplements (capsules) was, on the other hand, negligible ($n=9$). The grouped consumption of cod liver oil/fish oil capsules was highly associated with the composition of the serum phospholipids, in particular with the content of EPA. A stronger relation to EPA than to DHA was also found for fatty fish filet consumption, but the difference was not as pronounced. This is in accordance with the higher EPA/DHA ratio found in cod liver oil compared with the ratio found in fatty fish (National Nutrition Council, 1995).

Because of the close association between consumption of cod liver oil/fish oil capsules and the composition of serum phospholipid fatty acids, separate analyses for users and non-users of cod liver oil/fish oil capsules were performed. This revealed that the relation between consumption of fatty fish filet and n-3 fatty acid composition was stronger among non-users, indicating that the influence of fatty fish is less when consuming cod liver oil/fish oil capsules. Interestingly, among non-users the content of EPA and DHA increased with 50.0% and 21.5%, respectively, from the lowest to the highest quartile of fatty fish filet consumption. According to these results, a raised content of EPA and DHA in the serum phospholipids can be obtained not only by use of cod liver oil, which is unacceptable to large groups of people because of its taste, but also by increasing the consumption of fatty fish. Roughly speaking, one portion of fatty fish for dinner (150 g) provides the same amount of EPA and DHA as one spoon of cod liver oil (11 g). In our study, women not using cod liver oil/fish oil capsules but who consumed fatty fish for dinner once a week or more often had approximately the same level of EPA and DHA in their phospholipids as women using cod liver oil/fish oil capsules but who did not eat fatty fish for dinner.

In addition to the smaller rise in serum phospholipid DHA than in serum phospholipid EPA when increasing the consumption of fish and when taking cod liver oil/fish oil capsules, we found that a lower proportion of the variability in serum phospholipid DHA than in EPA could be explained by the consumption of fish and fish products. Similar results have been published by others (Bønaa *et al*, 1992; Vatten *et al*, 1993). More rigorous homeostatic regulation of DHA than of EPA, and preferential incorporation of DHA over EPA into adipose tissue has been indicated (Leaf *et al*, 1995). The hypothesis of a stronger homeostatic regulation of DHA than of EPA is partly supported by studies comparing populations with high vs low consumption of marine foods. In a study among Greenland Eskimos and Danes the concentration of plasma phospholipid EPA was highly different in the two populations, whereas the concentration of DHA was the same (Dyerberg *et al*, 1975). Comparison of serum phospholipid fatty acid patterns in Japanese and Americans has, on the other hand, shown the largest dissimilarity for DHA (Yamori *et al*, 1985).

Like other Norwegian papers (Bønaa *et al*, 1992; Vatten *et al*, 1993) the present study shows a high serum phospholipid content of EPA and DHA compared with values reported from other Western populations (Houwelingen van *et al*, 1989; Phinney *et al*, 1991; Leaf *et al*, 1995; Ma *et al*, 1995). It is, however, lower than figures observed in Japan (Yamori *et al*, 1985; Takahashi *et al*, 1991). Likewise, the Norwegian consumption of fish and fish products is considerably higher than in most Western populations (Houwelingen van *et al*, 1989; Holst, 1991), but not as high as in Japan (Tomimaga & Kato 1992; Iso *et al*, 1989). This indicates that serum phospholipid fatty acids can reflect the intake of n-3 fatty acids, and that stronger associations might be achieved if the range of exposure is widened.

In the present study only information about sex, age, alcohol habits, and fish consumption was given in addition to the venous blood sample. Sex and age, which are the characteristics most often taken into consideration (Holman *et al*, 1979; Takahashi *et al*, 1991) were the same for all participants in our study. Other factors may influence the

serum phospholipid fatty acid composition. Adipose tissue serves as a reservoir of n-3 fatty acids (Leaf *et al*, 1995), and knowledge of body weight could be relevant. Bønaa *et al* (1992) and Ma *et al* (1995) included body mass index (kg/m²) in their analyses, but did not observe any significant influence on the results. Phinney *et al* (1991) have reported no differences in serum phospholipid n-3 fatty acids between obese and normal subjects. Chronic disease status does not seem to affect the n-3 fatty acid composition of serum phospholipids (Ma *et al*, 1995). Cigarette smoking was inversely related to serum level of phospholipid DHA in a recent paper (Simon *et al*, 1996), whereas others have found no effect (Bønaa *et al*, 1992; Ma *et al*, 1995). No association between alcohol consumption and serum phospholipid fatty acids could be detected in our study, except for a positive correlation with total amount of fatty acids (mg/l). The consumption of alcoholic beverages has been of minor importance in other studies as well (Bønaa *et al*, 1992; Ma *et al*, 1995; Simon *et al*, 1996). Finally, adjustment for n-6 fatty acid intake could affect our results as dietary intake of n-6 fatty acids inhibits n-3 fatty acid metabolism (Holman, 1986). However, the intake n-6 fatty acids could not be calculated on the basis of the fish consumption questions alone.

The summary questions on lean and fatty fish for dinner estimated average frequency consumption similarly to the comprehensive questions. However, the two summary questions were not able to relate fish intake to the serum phospholipid fatty acid composition. This is worth noticing as many questionnaires with the objective of assessing 'habitual food intake' contain only a few questions on fish consumption. When trying to elucidate the relation between diseases, for example breast cancer, and fish consumption this may not be specific enough.

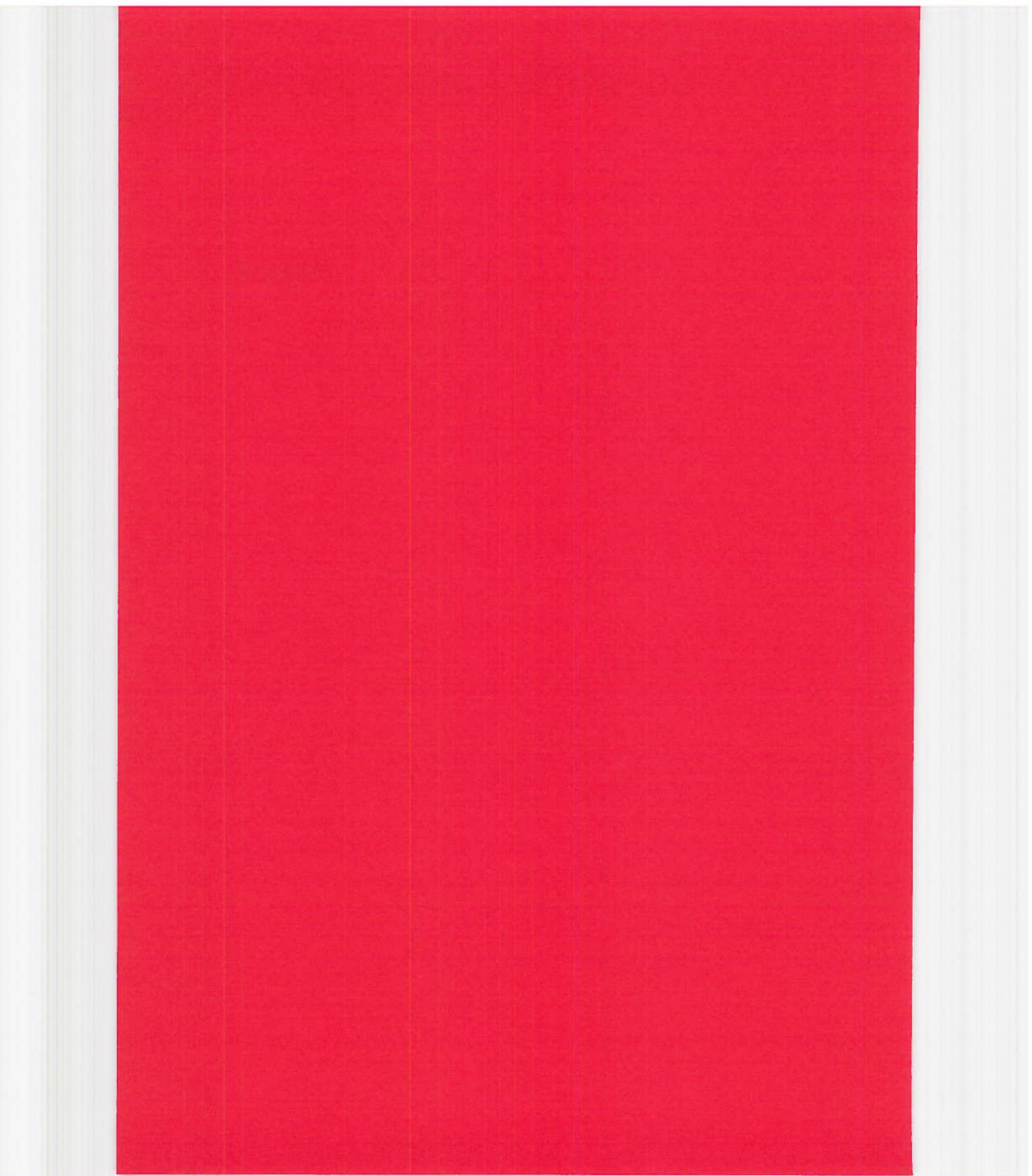
Conclusions

The present study suggests that habitual fish consumption registered by our semi-quantitative food frequency questionnaire can be reflected in the serum phospholipid fatty acid composition. However, as the fat content of fish is highly variable, consumption of lean and fatty fish should be reported separately. Information on fish species seems to be more important than information on portion size. Cod liver oil is the single item most strongly related to the serum phospholipid fatty acid composition, and should always be taken into account when studying populations where a frequent use is expected.

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Paper II





Relationship between dietary habits, age, lifestyle, and socio-economic status among adult Norwegian women. The Norwegian Women and Cancer Study

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Objective: To examine how dietary intake varies with age in a nation-wide sample of adult Norwegian women, and to evaluate the impact of lifestyle and socio-economic status on important dietary aspects.

Design: Cross-section study.

Setting and subjects: A food frequency questionnaire was mailed to a random, nation-wide sample of 20 000 women aged 45-69 y, and 9885 questionnaires were accepted for nutritional analyses.

Results: Dietary habits differed moderately with age. The oldest women reported a higher consumption of potatoes and fish, whereas the youngest reported more coffee, meat, and alcohol. The reported intake of fruit, vegetables, and potatoes was lower than recommended in all age groups. Older women had a slightly better distribution of energy yielding nutrients than younger women, although the median percentage of energy from fat was too high in all age groups. The median dietary fibre density of the diet was close to the recommended level in all age groups, yet lowest among the youngest women. Practising a healthy lifestyle and having a higher socio-economic status were associated with reporting a healthier diet. However, adjusting for lifestyle and socio-economic factors did not substantially alter the associations between diet and age.

Conclusions: Older women tend to have a healthier diet than younger women. The relationship does not seem to be strongly confounded by lifestyle and socio-economic status, although these factors are also related to dietary habits.

Sponsorship: The Norwegian Cancer Society (E96071).

Descriptors: adult nutrition; dietary recommendations; dietary survey; food frequency questionnaire

Introduction

In Norway, a national nutrition council was established in 1946. Dietary recommendations have been given since 1954 and several campaigns on healthy dietary habits have been conducted. Nation-wide information on dietary habits has been based on surveys of consumer expenditure, and dietary data at the individual level has only recently been collected (Frost Andersen *et al*, 1995; Johansson *et al*, 1997). The dietary campaigns have usually been intended for the general population. They have undergone little formal evaluation and information about dietary habits in different subgroups of the population is still inadequate.

It has been suggested that educational programs and campaigns are more successful in higher socio-economic groups and that lower socio-economic groups benefit less from these efforts (Gøransson *et al*, 1996). An association between dietary habits and demographic, social, and economic variables has been demonstrated in several studies, and generally it appears that less educated and lower income groups consume a less healthy diet (Hulshof *et al*, 1991; Smith & Baghurst, 1992; Subar *et al*, 1995; Uitenbroek *et al*, 1996). Years of education have increased markedly during the last few decades, and usually there is

an inverse association between adult age and length of the education (Roos *et al*, 1996; Johansson *et al*, 1997). In simple terms this should suggest the hypothesis that younger adults have a diet more in line with the dietary guidelines than older adults do.

The dietary habits of adolescents (Bull, 1992; Frost Andersen *et al*, 1995) and very elderly people (de Groot *et al*, 1996) usually differ from those of adults. There has been less focus on the extent to which diet also differs with age in adulthood. Studies from the UK have shown that preferred eating patterns vary with adult age (Barker *et al*, 1990; Whicelow & Prevost, 1996). Patterns containing fruit, vegetables, and other high-fibre foods were more favoured by the middle-aged, whereas soft drinks, salty snacks, and high-fat foods were favoured by younger subjects. To some extent this picture also seems to appear in other countries, including Norway (Shea *et al*, 1993; Levnedsmiddelstyrelsen, 1996; Dobson *et al*, 1997; Johansson *et al*, 1997). The picture of a healthier diet among older subjects is strengthened by their higher consumption of fish. However, a Finnish study emphasising other aspects of the diet comes to the opposite conclusion, in that older people have the least healthy diet (along with young men) (Prättälä *et al*, 1992). In terms of macro-nutrient intake expressed as proportion of energy most studies have found only little variation between age groups, whereas the micro-nutrient density seems to be highest among older subjects (Bingham *et al*, 1981; Kushi *et al*, 1988; Hulshof *et al*, 1991; Murphy *et al*, 1992).

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The age groups defined in most previous studies are rather wide (for example, 20 y). In this paper we present the dietary intake of a population-based cohort of Norwegian women aged 45–69 y by 5 y age groups. Special emphasis is put on fat (as percentage of energy intake), dietary fibre density, and the consumption of fruit, vegetables, and potatoes, as these three areas are given special attention by the Norwegian National Nutrition Council (1996). Furthermore, as socio-economic status and health-related behaviours like smoking and level of physical activity may confound an association between age and diet (Hulshof *et al.*, 1991; Leigh & Fries, 1993) we also examined dietary habits with respect to these factors.

Methods

Subjects

A random, nation-wide sample of 20 000 female Norwegian citizens born 1927–1951 was drawn from the National Central Person Register February 1996. In July 1996 they received a mailed letter of invitation requesting informed consent and a self-instructive questionnaire. A written reminder was sent to non-responders about two months after the first invitation. Of those replying by September 1, 1997, 10 249 women agreed to participate, whereas 2201 women delivered an informed consent form answering 'No' and returned a blank questionnaire. The final response rate was therefore 51.2% (10 249 out of 20 000). Corrected for non-completion (death, emigration, severe mental handicap, unknown address) the response rate was 51.4%. The response rate declined steadily with age, ranging from 55.5% in the youngest age group (45–49 y) to 41.6% in the oldest age group (65–69 y), and women living in Northern Norway were more likely to respond than women living in Southern Norway (55.3% and 50.8%, respectively). The study was approved by the Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate.

Questionnaire and nutrient calculations

Primarily, the cohort was built for investigation of breast cancer, and the eight-page questionnaire contained questions on both established (for example, hormonal and reproductive factors) and potential risk factors for breast cancer, with a main focus on diet. The dietary part of the questionnaire had a food frequency design including both quantitative and qualitative questions. The main purpose was to assess the consumption of marine foods (fish, fish products, and shellfish), though the questionnaire was also arranged so as to record 'usual' food intake. There were 74 frequency questions on food items traditionally consumed in Norway: coffee, milk, yoghurt, cereals, bread, sandwich spreads, fruit, vegetables, potatoes, pasta, rice, rice porridge, fish and fish products, meat and meat products, eggs, cakes, ice-cream, chocolate, alcoholic beverages and dietary supplements. An evaluation of parts of the questionnaire against serum phospholipid fatty acid composition in a group of 234 middle-aged women showed correlation coefficients between calculated intake of omega-3 fatty acids and serum phospholipid omega-3 fatty acids in the order of 0.55 (Hjartåker *et al.*, 1997).

The subjects were asked to record how often, on average, they had consumed each food item during the last year, and to indicate the usual amount per consumption. For some food items consumption was elicited as frequency

consumption of a certain amount (for example, glasses of milk). Before making the final form, we conducted a pilot study to get more information about adequate food choices according to Norwegian eating habits and to obtain suitable consumption categories. Typically, six or seven frequency choices were given for each food item, with response intervals adjusted to the food item in question (for example, never/seldom, once per month, 2–3 times per month, once per week, twice per week, three times per week, four or more times per week). The portion size per consumption was asked in natural units (for example, oranges), household units (for example, spoons, pieces) or in decilitres, and weights of the portion units were derived from a Norwegian weights and measures table (National Association for Nutrition and Health, 1989). If a frequency was given without indicating portion size, the smallest portion unit was assumed. Likewise, if a portion size was given without a frequency mark, the lowest frequency option (never/seldom) in the questionnaire was chosen. If both frequency and portion size were not indicated, the food item was considered not consumed. For comparison we also estimated energy intake by replacing missing values for either frequency or amount with the median value recorded in the other questionnaires. This raised the median daily energy intake in the cohort by less than 1%, and we decided to use the first procedure throughout the analyses.

Daily intake of energy and nutrients was computed using nutrient values from the Norwegian Food Composition Table (National Nutrition Council & Norwegian Food Control Authority, 1995). This table contains data on cod liver oil but not on other vitamin and mineral supplements. Cod liver oil is therefore the only dietary supplement included in the nutrient calculations.

Information on height, weight, smoking history, physical activity, socio-economic status, and perception of diet's importance to health were also asked for in the questionnaire. Physical activity was recorded on a 10 point scale ranging from 0–10, and divided into the categories 'very low' (0–3), 'moderate' (4–7), and 'very high' (8–10). Length of education was asked as an open-ended question, and subsequently divided into categories corresponding to the Norwegian school system. Income was calculated as annual household income divided by the number of household members.

Exclusion criteria

To be included in the dietary analyses, the daily energy intake had to be in the range 2500–15 000 kJ, and the number of blank items should not exceed 35. When summarising the number of blank items, each of the frequency questions was counted as one, with the exception of three questions on different milk types, which were collapsed into one, as were three questions on different types of coffee (Kuskowska-Wolk *et al.*, 1992). In addition to the frequency questions, a qualitative question on fat used on bread was included, giving a maximum of 71 blank items. On the basis of these criteria we excluded 3.6% of the questionnaires ($n=364$), leaving 9885 questionnaires for dietary analyses. The majority of the excluded questionnaires had more than 35 blank items ($n=307$) and/or a low energy estimate ($n=102$). A daily energy intake above 15 000 kJ was computed for two questionnaires. The exclusion was done for the dietary estimates only, and did not affect the analyses of other variables.

Quality of diet

Although the questionnaire does not cover the diet completely, important aspects of the diet can be evaluated with some caution. The Norwegian National Nutrition Council focuses on the consumption of fat, dietary fibre, and fruit, vegetables, and potatoes, and we assessed the quality of diet by being 'in agreement' or 'not in agreement' with the respective guidelines. It is recommended that no more than 30% of the energy intake be derived from fat, that the dietary fibre density of the diet be of 3 g/MJ or more, and that one should eat five or more servings of fruit, vegetables, and potatoes every day ('five a day'). Therefore, the percentage of energy from fat was divided into '30%' and '>30%', and dietary fibre density into '3 g/MJ' and '<3 g/MJ'. The reported frequencies of consumption of fruit, vegetables, and potatoes were pooled and calculated as number of servings per day, and subsequently divided into '5 servings/d' and '<5 servings/d'. Unfortunately, there was no question on fruit juice in the questionnaire, and consumption of this item is therefore not included in the 'five a day' index.

Statistical analyses

Statistical analyses and nutrient calculations were done by the SAS software package, version 6.11 (SAS Institute, 1996). All reported *P*-values are two-sided, and a significance criterion of *P* < 0.05 was used. Parametric methods were used when analysing anthropometric, lifestyle, and socio-economic variables, as the distribution of these variables showed sufficient normality. The intake of food items and nutrients was, however, generally skewed to the right, and non-parametric methods were therefore used when analysing these variables. For descriptive purposes, means and standard deviations (s.d.) are given for normally distributed variables, and medians for variables with a non-normal distribution. Calculating Pearson's correlation coefficient assessed the associations between normally distributed variables. Statistical comparisons between groups were made by chi-square statistics or by Kruskal-Wallis test when appropriate. Logistic regression models were used to examine simultaneously the effects of age, body mass index, level of physical activity, smoking status, years of education, income, and perception of diet's importance to health on the quality of diet ('in agreement' vs 'not in agreement' with the recommendations). Logistic regression models were also used to examine the associations between having a diet in agreement with the recommendations on fat, dietary fibre, and the 'five a day' recommendation. The number of responders included in the individual analysis may differ somewhat, due to missing values.

Results

Characteristics of the study participants

Demographic, lifestyle, and socio-economic characteristics of the study participants are presented in Table 1. Mean age was 54.8 y (s.d. = 7.0). Body mass index (BMI) was calculated from self-reported weight (mean 67.8 kg, s.d. 11.6) and height (mean 1.66 m, s.d. 0.06) as kg/m². Average BMI was 24.6 (s.d. = 4.0), and 39% of the participants had a BMI of 25 or higher. About 16% of the study participants assessed their physical activity level to be very low, 13% considered their physical activity level as very high, while the rest of the sample said they were at an intermediate level. Today's level of physical activity was positively

Table 1 Characteristics of the study participants (n = 10249)^a

Characteristics	%
Age (y)	
45-49	28.7
50-54	25.5
55-59	18.3
60-64	14.2
65-69	13.3
BMI (kg/m ²)	
< 20	6.6
20-24.9	54.6
25-29.9	30.4
≥ 30	8.6
Physical activity	
very low	16.2
moderate	70.8
very high	13.0
Smoking status	
never	40.6
ex	30.6
current	28.8
Education (y)	
≤ 7	11.7
8-9	25.4
10-12	32.3
> 12	30.7
Income (nok, 7 nok ≈ 1 \$)	
< 75 000	12.1
75 000-124 999	39.2
125 000-199 999	29.9
≥ 200 000	18.8
Importance of diet	
little/no	2.4
some	18.4
much	54.1
very much	25.1

^aSubgroups may not total to 10 249 because of missing values.

correlated to the physical activity level both at 30 and at 14 y of age (*r* = 0.35 and 0.13, respectively) and negatively correlated with BMI (*r* = -0.18) (all *P* < 0.001). Nearly 60% of the women had ever smoked, and 29% reported daily smoking at present. Length of education (mean 11.2 y, s.d. = 3.4) was positively related to income (*r* = 0.32) and negatively related to age (*r* = -0.28) (both *P* < 0.001).

Food consumption according to age

Reported levels of consumption of selected foods and food groups are given in Table 2, which reveals that dietary habits varied somewhat with age. The reported consumption of coffee, meat, chocolate, and alcohol was highest in the youngest age groups, whereas the oldest women reported more fish, and also tended to report more cakes and potatoes. The higher intake of meat in the youngest age groups was to a large extent caused by a higher reporting of processed meat and not so much by a higher reporting of pure meat. The differences in reported fish consumption could be explained mainly by a higher reporting of lean fish fillet in the oldest age group (data not shown). In fact, the oldest women reported fish intake of the same quantity as they reported meat. Overall, the median number of hot dinner meals was 29.3 per month. The intake of bread (preferably brown bread) and cereals did not differ much between age groups. Neither did the reported milk consumption pattern vary substantially with age, though there were some differences. The youngest women preferred low fat milk to

Table 2 Reported consumption of selected food and food groups by age group (n = 9885)

	45-49y (n = 2899)	50-54y (n = 2538)	55-59y (n = 1815)	60-64y (n = 1374)	65-69y (n = 1259)	P-value
Median (mean) g/d ^a						
Milk and yoghurt	150 (207)	150 (201)	150 (215)	175 (230)	175 (228)	< 0.0001
Coffee	540 (463)	540 (460)	360 (433)	300 (404)	300 (379)	< 0.0001
Bread and cereals	140 (149)	131 (144)	131 (146)	131 (145)	131 (144)	0.003
Cakes	13 (19)	13 (20)	13 (23)	13 (25)	13 (27)	< 0.0001
Fruit	122 (147)	139 (161)	139 (166)	138 (159)	130 (154)	< 0.0001
Vegetables	92 (110)	97 (115)	93 (111)	91 (108)	92 (105)	0.003
Potatoes	150 (127)	150 (131)	150 (141)	150 (145)	150 (148)	< 0.0001
Eggs	17 (16)	17 (16)	17 (15)	17 (15)	17 (14)	0.0002
Meat and meat products	119 (125)	108 (115)	95 (100)	88 (94)	78 (85)	< 0.0001
Fish and fish products ^b	70 (78)	73 (82)	81 (91)	80 (90)	81 (87)	< 0.0001
Chocolate	3 (7)	3 (6)	2 (4)	2 (4)	2 (4)	< 0.0001
Alcoholic beverages	20 (48)	19 (42)	12 (37)	10 (31)	5 (27)	< 0.0001
Proportion using (%) ^c						
Butter as spread on bread	10	15	18	18	20	< 0.001
Cod liver oil	38	40	47	50	53	< 0.001
Fish oil capsules ^d	6	7	7	9	7	< 0.05
Vitamin/mineral supplements	39	39	38	33	30	< 0.001

^aKruskal-Wallis test.^bIncludes shellfish.^cChi² test.^dNot including cod liver oil.

skimmed milk, while in the other age groups skimmed and low fat milk were chosen in equal amounts. Full fat milk was barely used as drinking milk, but significantly more so in the oldest age groups (data not shown). The oldest women also preferred butter to margarine as spread on bread more often than the younger women. No clear age trend was observed for the intake of fruit and vegetables. Apples and pears were the most popular fruits irrespective of age, but the oldest women also reported a considerable amount of oranges (data not shown). The intake of vegetables was dominated by carrots and more so with increasing age. The largest variation in vegetable intake was found for mixed salad, for which the median intake in the youngest age group was more than three times as high as the intake in the oldest age group (data not shown). The aggregated reported consumption of fruit, vegetables and potatoes was low compared to the recently presented 'five a day' guideline. In the present cohort of adult women about 17% reported five or more servings per day; the median number of servings was 3.5 per day. There

was only modest variation in intake between the age groups; the youngest women reported 3.3 servings per day, whereas in the other age groups the median number of servings was 3.6 per day.

Cod liver oil (fluid or capsules) was used by 44% of the women, and fish oil capsules other than cod liver oil were taken by 7% of the women. The proportion of cod liver oil users increased consistently with increasing age, whereas no age trend was found for reported use of other fish oil products. Use of dietary supplements like vitamin and mineral pills were reported by 37% of the women, and the proportion of users decreased with increasing age.

Energy and nutrient intake according to age

Median daily intake of energy was 6267 kJ and there was a significant inverse trend in energy intake by age (Table 3). A similar picture was seen for the intake of protein, fat, and alcohol.

Table 3 Daily intake of energy and nutrients by age group (n = 9885). Figures are median (mean)^a

	45-49y (n = 2899)	50-54y (n = 2538)	55-59y (n = 1815)	60-64y (n = 1374)	65-69y (n = 1259)	P-value
Energy (kJ)	6336 (6497)	6262 (6382)	6270 (6396)	6239 (6338)	6159 (6259)	0.0005
Protein (g)	66.0 (67.4)	64.5 (66.1)	63.9 (65.7)	63.4 (64.9)	61.3 (62.9)	< 0.0001
Fat (g)	55.7 (58.2)	54.1 (57.1)	53.8 (56.6)	53.5 (55.8)	53.1 (55.3)	< 0.0001
Carbohydrate (g)	180.0 (183.2)	178.7 (180.6)	180.2 (183.3)	181.4 (183.0)	181.1 (181.8)	0.4
Sugar (g)	13.5 (15.2)	13.3 (15.4)	13.9 (15.9)	14.3 (16.0)	13.7 (15.8)	0.008
Dietary fibre (g)	18.8 (19.4)	19.2 (19.7)	19.4 (20.1)	19.5 (19.9)	19.3 (19.6)	0.01
Dietary fibre (g/MJ)	2.9 (3.0)	3.0 (3.1)	3.1 (3.2)	3.1 (3.2)	3.1 (3.2)	< 0.0001
Alcohol (g)	1.4 (2.7)	1.4 (2.5)	0.9 (2.2)	0.8 (2.0)	0.6 (1.7)	< 0.0001
Vitamin C (mg/MJ)	10.9 (12.4)	11.8 (13.5)	11.9 (13.5)	11.8 (13.4)	12.4 (13.7)	< 0.0001
Vitamin D (µg/MJ)	0.7 (1.1)	0.8 (1.3)	1.0 (1.5)	1.0 (1.6)	1.0 (1.6)	< 0.0001
% of energy intake						
Protein	17.7 (17.8)	17.6 (17.8)	17.5 (17.6)	17.4 (17.6)	17.0 (17.2)	< 0.0001
Fat	32.6 (32.8)	32.7 (32.7)	32.2 (32.4)	32.2 (32.1)	32.2 (32.3)	0.003
Carbohydrate	48.1 (48.1)	48.3 (48.2)	48.9 (48.8)	49.3 (49.3)	49.8 (49.6)	< 0.0001
Sugar	3.6 (3.9)	3.7 (4.0)	3.9 (4.2)	3.9 (4.2)	3.9 (4.2)	< 0.0001
Alcohol	0.7 (1.3)	0.6 (1.2)	0.5 (1.1)	0.4 (1.0)	0.3 (0.8)	< 0.0001

^aKruskal-Wallis test.

Table 4 Percentage of energy from fat, dietary fibre density, and servings of fruit, vegetables, and potatoes per day by lifestyle and socio-economic variables ($n = 9885$)^a. Figures are median^b

	Percentage of energy from fat	Dietary fibre density	'Five a day' ^c
BMI (kg/m ²)			
< 20	34.2	2.9	3.4
20–24.9	32.6	3.0	3.5
25–29.9	31.9	3.1	3.6
≥ 30	32.1	3.1	3.4
P-value	< 0.0001	< 0.0001	0.0003
Physical activity			
very low	33.0	3.0	3.3
moderate	32.4	3.0	3.5
very high	32.1	3.1	3.9
P-value	0.001	< 0.0001	< 0.0001
Smoking status			
never	31.9	3.1	3.6
ex	31.8	3.1	3.6
current	34.1	2.8	3.1
P-value	< 0.0001	< 0.0001	< 0.0001
Education (y)			
≤ 7	32.7	3.0	3.3
8–9	32.8	3.0	3.4
10–12	32.6	3.0	3.5
> 12	31.9	3.0	3.6
P-value	< 0.0001	0.02	< 0.0001
Income (nok)			
< 75 000	33.2	3.0	3.4
75 000–124 999	32.6	3.0	3.5
125 000–199 999	32.2	3.0	3.6
≥ 200 000	32.1	3.1	3.6
P-value	< 0.0001	0.005	< 0.0001
Importance of diet			
no/some	33.2	2.9	3.1
much	32.5	3.0	3.5
very much	31.9	3.2	3.9
P-value	< 0.0001	< 0.0001	< 0.0001

^aSubgroups may not total to 9885 because of missing values.

^bKruskal-Wallis test.

^cNumber of servings with fruit, vegetables, and potatoes per day.

The differences in nutrient intake remained after adjusting for energy intake (Table 3). In the present cohort, fat provided 32.5% of the energy intake, and more than 2 out of 3 of the women had a relative fat intake that exceeded the recommendation (maximum 30% of the energy intake derived from fat). The median dietary fibre density was close to the recommendation (minimum 3 g/MJ) in all age groups, yet lowest in the youngest group. The proportion of subjects with a less fibre dense diet than recommended ranged from 54% in the youngest age group to 43% in the oldest age group. As for micro-nutrients, higher levels (per MJ) of retinol (not shown), vitamin C, and vitamin D (Table 3) were estimated in the oldest age groups.

Quality of diet according to lifestyle factors and socio-economic status

The quality of the diet, assessed by percentage of energy from fat, dietary fibre density, and reported consumption of fruit, vegetables and potatoes was also examined in relation to lifestyle and socio-economic variables (Table 4).

Women with a higher BMI reported a relatively lower intake of fat than women with a lower BMI, and they had a more fibre dense diet. In addition to a healthier composition of their diet, women with the highest BMI also claimed to have the lowest intake of energy. Median daily intake of energy decreased steadily from 6616 kJ in the lowest BMI

category (BMI < 20) to 5938 kJ in the highest category (BMI ≥ 30) (no details shown). Controlling for age did not change the figures significantly.

Participants with a high level of physical activity reported a diet more in line with the dietary recommendations than participants exercising less. In particular, physically active women had a higher intake of fruit, vegetables and potatoes. The dietary habits of current smokers differed significantly from those of ex- and never-smokers, whereas no differences were found between the diet of ex-smokers and the diet of never-smokers. Among current smokers, fat provided 34.1% of the energy intake, compared to 31.8% and 31.9% among ex- and never-smokers, respectively. Current smokers also had a less fibre dense diet, and they reported less frequent consumption of fruit, vegetables and potatoes than did ex- and never-smokers.

Years of education and income were both significantly negatively related to percentage energy from fat, and positively related to dietary fibre density, and to intake of fruit, vegetables, and potatoes.

The quality of diet was also associated with the women's perception of diet's importance to health. Nearly 4 out of 5 of the participants regarded their diet to be of very great (25%) or great (54%) importance to their health, while 1 out of 5 regarded their diet to be of some (18%) or little/no (2%) importance. In the analyses, the categories 'some importance' and 'little/no importance' were merged because of the small number in the latter category. Women giving great emphasis to their diet followed all three dietary recommendations better than women emphasising their diet less. Still, they received too much of their energy from fat and reported too low consumption of fruit, vegetables and potatoes.

In order to account for interrelations among lifestyle and socio-economic factors, associations with quality of diet were also examined by multiple logistic regression analyses (Table 5). Percentage of energy from fat was highly significantly associated with smoking status, BMI, and perception of diet's importance to health. Moreover, percentage of energy from fat was related to income and level of physical activity, but not as strongly. Age, smoking status, BMI, level of physical activity, perception of diet's importance to health, and income were also predictors of the fibre density of the diet. Furthermore, all the independent variables in the multiple model were significantly related to reported consumption of fruit, vegetables and potatoes. The strongest relation was found with perception of diet's importance to health, for which women emphasising diet most were 2.5 times more likely to follow the recommendation than women putting only some or no emphasis on their diet.

Reporting a diet in agreement with one of the recommendations was positively associated with reporting a diet in agreement with the other recommendations. The strongest association was found between practising a diet compatible with the recommendation on dietary fibre density and the recommendation on fruit, vegetables, and potatoes (OR = 11.52, CI 9.78–13.57). Women with a fibre dense diet were also more likely to have a diet in agreement with the fat recommendation than women reporting a less fibre dense diet (OR = 7.68, CI 6.92–8.51). Likewise, there was a significant association between following the recommendation on fat and on fruit, vegetables, and potatoes (OR = 2.50, CI 2.25–2.78). Furthermore, there was a very strong association between following all three recommen-

Table 5 Odds ratio (OR)^a and 95% confidence interval (CI) of being in agreement with the guidelines on percentage of energy from fat, dietary fibre density, and servings of fruit, vegetables, and potatoes per day in relation to age, lifestyle, and socio-economic status (no = 0, yes = 1) (n = 7385)^b

	Percentage of energy from fat OR (95% CI)	Dietary fibre density OR (95% CI)	'Five a day' ^c OR (95% CI)
Age (y)			
45-49	1.00	1.00	1.00
50-54	0.95 (0.83-1.08)	1.23 (1.09-1.40)	1.34 (1.14-1.58)
55-59	1.10 (0.95-1.28)	1.39 (1.21-1.61)	1.33 (1.10-1.60)
60-64	1.08 (0.91-1.28)	1.45 (1.24-1.71)	1.45 (1.18-1.79)
65-69	1.08 (0.90-1.30)	1.60 (1.35-1.90)	1.42 (1.14-1.78)
P-value for linear trend	0.1	< 0.0001	0.0003
BMI (kg/m²)			
< 20	1.00	1.00	1.00
20-24.9	1.34 (1.08-1.67)	1.27 (1.05-1.54)	1.11 (0.85-1.43)
25-29.9	1.57 (1.25-1.98)	1.59 (1.29-1.94)	1.23 (0.94-1.62)
≥ 30	1.53 (1.16-2.01)	1.45 (1.13-1.86)	1.20 (0.86-1.67)
P-value for linear trend	< 0.0001	< 0.0001	0.03
Physical activity			
very low	1.00	1.00	1.00
moderate	1.07 (0.93-1.23)	1.09 (0.96-1.24)	1.09 (0.91-1.30)
very high	1.30 (1.07-1.56)	1.50 (1.25-1.80)	1.91 (1.53-2.39)
P-value for linear trend	0.003	< 0.0001	< 0.0001
Smoking status			
never	1.00	1.00	1.00
ex	1.01 (0.90-1.13)	0.98 (0.88-1.10)	1.07 (0.93-1.23)
current	0.51 (0.45-0.58)	0.57 (0.50-0.64)	0.66 (0.56-0.78)
Education (y)			
≤ 7	1.00	1.00	1.00
8-9	0.95 (0.78-1.16)	1.19 (0.99-1.44)	1.51 (1.15-1.98)
10-12	0.94 (0.77-1.14)	1.03 (0.86-1.24)	1.51 (1.16-1.97)
> 12	1.00 (0.82-1.22)	1.08 (0.89-1.30)	1.73 (1.31-2.27)
P-value for linear trend	0.6	0.7	0.001
Income (nok)			
< 75000	1.00	1.00	1.00
75000-124999	1.04 (0.87-1.24)	1.11 (0.94-1.31)	1.08 (0.86-1.36)
125000-199999	1.21 (1.00-1.46)	1.27 (1.07-1.52)	1.11 (0.88-1.41)
≥ 200000	1.25 (1.02-1.53)	1.23 (1.02-1.49)	1.27 (0.99-1.63)
P-value for linear trend	0.001	0.002	0.02
Importance of diet			
no/some	1.00	1.00	1.00
much	1.22 (1.07-1.40)	1.37 (1.21-1.55)	1.52 (1.26-1.83)
very much	1.43 (1.23-1.66)	1.86 (1.61-2.15)	2.49 (2.05-3.04)
P-value for linear trend	< 0.0001	< 0.0001	< 0.0001

^aOdds ratio adjusted by means of logistic regression model including all other variables.

^bSubjects for whom information on certain variables was missing are excluded.

^cNumber of servings with fruit, vegetables, and potatoes per day.

dations when following two of them. For instance, women following both the dietary fibre density recommendation and the 'five a day' recommendation were more likely to follow the fat recommendation (OR = 19.59, CI 10.27-37.40) than women not following the 'five a day' recommendation (OR = 7.05, CI 6.31-7.87). However, only 9% of the women reported a diet in agreement with all three recommendations.

Discussion

This cross-sectional study of Norwegian women indicates that dietary habits vary somewhat with adult age, and that older women tend to report the healthiest diet. Lifestyle factors such as smoking and physical activity seem to have greater impact on diet than socio-economic status.

The women initially invited to join the cohort constituted a nation-wide random sample of Norwegian women aged 45-69 y. The response rate was, however, less than optimal making the study vulnerable to non-response bias. We know that the non-responders differed from the responders with respect to age and geographical distribution, and

this could weaken the generalisability of the study. The associations between diet and age would, however, only be biased if the non-responders also have a different diet than responders of the same age. The distribution of lifestyle factors did not vary according to response rate in a corresponding study of adult Norwegian women (Lund & Gram, 1998).

When designing the questionnaire only a finite number of food items could be included in order not to make it too comprehensive and thereby decreasing the response rate further (Lund & Gram, 1998). An incomplete food list may not only affect the estimation of energy intake, but may also alter the nutrient density of the diet, which in turn reduces the ability to assess the diet according to nutrient recommendations. The low percentage of energy derived from sugar may indicate that foods rich in sugar (for example, cakes, desserts, syrup and soft drinks) are not sufficiently covered in the form. Thus, the estimated percentage of energy derived from fat may be somewhat high. The lack of information on orange juice consumption reduces the ability to make accurate calculations of vitamin C intake and of the 'five a day' index. Furthermore, if the

consumption of food items not included in the questionnaire differs with age, this could induce differential underestimation and originate spurious findings.

In addition to an **incomplete food list**, **underreporting** of food consumption may have contributed to the low median energy intake. **Underestimation of energy intake is known to be a problem especially among overweight subjects** (Lichtman *et al*, 1992; Bumann *et al*, 1995), and the present negative association between BMI and energy intake indicates that this may be the case in our study as well. Even though it was explicitly stated throughout the questionnaire that all dietary questions should be answered, some items were left blank on either the frequency or the amount indication, or on both. This does not necessarily mean that the consumption of these items is negligible (Kuskowska-Wolk *et al*, 1992). However, replacing missing values or either frequency or amount with the median value recorded in the other questionnaires barely increased the estimated energy intake compared with replacing them with the questionnaire's lowest option. Finally, the overall energy intake of the cohort is affected by the exclusion criteria, which were rather liberal in our study.

It may seem dubious that the figures for some of the items in Table 2 (for example, eggs) are exactly the same in all groups, and furthermore, that there is still a significant difference between the groups. The uniform figures may arise because the consumption of some food items was only asked for as frequency consumption of a certain amount, and because the figures given are median values. The underlying distribution of the variables may nevertheless differ. As the number of participants in this study is high, even small differences in dietary intake may turn out to be statistically significant, even though the practical significance may be negligible. More attention should therefore be paid to the estimated figures of dietary intake in the different subgroups than to the calculated *P*-values.

Three important aspects of diet were given special attention in this study, namely **fat**, **dietary fibre**, and **fruit, vegetables and potatoes**. When dividing the women as to whether they are 'in agreement' or 'not in agreement' with the respective recommendations, one should not focus too strongly on the absolute number of women following the recommendations, as the distribution may be effected by the incomplete food list. More emphasis should rather be put on the relative number of women falling into the two categories in each subgroup.

Overall, dietary habits seem to vary only moderately with adult age, though some differences appeared. The higher reporting of recommended foods like potatoes and fish, and the lower reporting of meat, chocolate, and alcohol among the oldest women is consistent with findings from another Norwegian study including women aged 16–79 y (NORKOST) (Johansson *et al*, 1997). The differences in food choices contribute to a slightly healthier distribution of the energy yielding nutrients among the oldest women. Moreover, the higher consumption of oranges and cod liver oil reported by the oldest age groups might partly explain the more vitamin C and vitamin D dense diet calculated in these groups. However, if the consumption of orange juice varies with age, this could affect the conclusion regarding vitamin C density. Also, nutrient intake provided by dietary supplements, most frequently used by the youngest age groups, was not included in the nutrient calculations. The reported consumption of milk and bread does not vary substantially with age either in the present study or in

NORKOST (Johansson *et al*, 1997). However, both studies found the highest reporting of full fat milk among the oldest women.

Some of the previous studies on women's food choices in relation to adult age are in favour of the oldest women (Barker *et al*, 1990; Whichelow & Prevost, 1996; Dobson *et al*, 1997), but not all (Prättälä *et al*, 1992). However, the age span and the way of assessing a healthy diet vary between the studies. For instance, the oldest women in our study did not seem to have a more favourable consumption pattern of the indicators applied in a Finnish study (Prättälä *et al*, 1992), that is the use of full fat milk, butter on bread, vegetables, and sugar in coffee. Generally, a higher consumption of fruit and vegetables is reported by older subjects (Hulshof *et al*, 1991; Shea *et al*, 1993; Subar *et al*, 1995; Uitenbroek *et al*, 1996; Johansson *et al*, 1997), although there are exceptions (Osler, 1993). The finding of a more fibre dense diet among older women seems to be rather consistent, whereas the association between age and percentage of energy from fat is more uncertain (Kushi *et al*, 1988; Murphy *et al*, 1992; de Castro, 1993; Ghadirian & Shatenstein, 1996; Levnedsmiddelstyrelsen, 1996; Johansson *et al*, 1997).

The observed relations between diet and age could be confounded by lifestyle and socio-economic status. A relation between smoking and diet has been found in several previous studies, and generally smokers report the least healthy diet (Larkin *et al*, 1990; Leigh & Fries, 1993; Subar *et al*, 1995; Johansson *et al*, 1997). A less healthy diet among current smokers than among ex- and never-smokers was found in our study as well, and strengthens the indication that **smoking status is one of the most important predictors of the quality of diet**. Level of physical activity was also related to diet, with **physically active** women reporting a **diet more in line with the recommendations** than those who were more inactive (Leigh & Fries, 1993; Eaton *et al*, 1995). Although BMI was negatively correlated with level of physical activity, women with a high BMI reported that they consumed relatively less fat and relatively more dietary fibre than leaner women. Overweight women may consume a healthier diet than lean women, but one should keep in mind the possibility of a **positive reporting bias for desirable foods and a negative reporting bias for less desirable ones** (Pietinen *et al*, 1988). We do not know whether women with a high BMI are more disposed to such biases than other women, but it is possible, as overweight people are subject to massive social pressure to conform to today's lean body ideal (Sarlio-Lähteenkorva *et al*, 1995).

As documented in several other studies (Prättälä *et al*, 1992; Roos *et al*, 1996; Uitenbroek *et al*, 1996; Johansson *et al*, 1997), we found dietary habits to vary with socio-economic status, though the associations were not as strong as those on age and lifestyle. Women with a **higher socio-economic status** reported the **healthiest** diet with regard to fat, dietary fibre, and fruit, vegetables and potatoes. A lower intake of fat has been associated with higher socio-economic status in some (Kushi *et al*, 1988; Hulshof *et al*, 1991; Smith & Baghurst, 1992; Johansson *et al*, 1997), but not all studies (Roos *et al*, 1996). The findings on socio-economic status and consumption of fruit and vegetables seem to be more consistent, and have been found both in Denmark (Osler, 1993), Finland (Roos *et al*, 1996), Wales (Smith & Smith, 1994), Scotland (Uitenbroek *et al*, 1996), the Netherlands (Hulshof *et al*, 1991), Bulgaria (Uitenbroek

et al, 1996), the United States (Subar et al, 1995), and Australia (Smith & Baghurst, 1992).

Perception of diet's importance to health was one of the strongest predictors of a healthy diet in the present cohort. Furthermore, healthy dietary habits were strongly associated with one another, as well as being associated with other healthy lifestyle habits. However, the picture of older women having the healthiest diet persisted even after adjusting for lifestyle and socio-economic status.

Conclusions

We summarise that the dietary habits of most adult Norwegian women do not seem to be in agreement with the guidelines on fat and fruit, vegetables and potatoes, but differ less from the recommendation concerning dietary fibre density. The older women tend to report a diet more in line with the recommendations than the younger women do. The decreasing response rate with age may, however, have biased the results in favour of the older women. Although healthy dietary habits are associated with practising other healthy lifestyle habits and higher socio-economic status, there also seems to be an independent association with age.

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Paper III

1000 samples per second
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BMR factor: EI/BMR

out-of-order - blacked + by bit

Body mass index and weight change attempts among adult women

The Norwegian Women and Cancer Study

ANETTE HJARTÅKER, PETTER LAAKE, EILIV LUND*

Background: Based on concern about the widespread increase in being overweight and obesity along with a substantial demand for leanness, we wanted to estimate body mass index (BMI) and the prevalence of weight change attempts in a population-based sample of Norwegian women. Furthermore, we wanted to examine how weight loss attempts are related to BMI and to age, socioeconomic status, reproductive factors, lifestyle and diet. **Methods:** A nationwide, cross-sectional study applying a mailed questionnaire was used. Out of a random sample of 20,000 women aged 45-69 years 10,249 women participated. **Results:** Based on self-reported data, the mean BMI was 24.6 kg m^{-2} and 40% of the women had a BMI of $\geq 25 \text{ kg m}^{-2}$. More than 50% of the women were trying to lose weight and weight loss attempts were very strongly associated with BMI. Age, education, income, smoking status and perception of diet's importance to health were also significant predictors of weight loss attempts. The effect of age, education and income on weight loss attempts was modified by the level of BMI. Women trying to lose weight reported a different diet than those not trying to lose weight, irrespective of BMI. **Conclusion:** A large proportion of middle-aged women are trying to lose weight. BMI is predominant in explaining weight loss attempts. After adjusting for BMI, age, lifestyle and socioeconomic status also contribute to explaining weight loss attempts.

Keywords: body weight, health behaviour, population study, socioeconomic status, weight loss

According to a recent report by the World Health Organisation,¹ the prevalence of being overweight and obesity is increasing worldwide, particularly in many Western populations.²⁻¹⁰ Along with the increasing prevalence of being overweight and obesity there is a growing concern about leanness and fitness. Unfortunately, this concern mainly seems to enlarge the discrepancy between actual and ideal body weight. The demand for leanness is becoming more important in all segments of the population¹¹ and the number of persons considering themselves as being overweight exceeds the actual number of overweight individuals.¹²⁻¹⁴

Weight loss attempts are prevalent among both adolescents and adults and among both sexes, although considerably more common among females. Prevalence estimates range from 33 to 48% for adult women and from 20 to 29% for adult men.¹⁵⁻²¹

Not surprisingly, body mass index (BMI) is a powerful predictor of weight loss attempts.²¹⁻²⁵ However, the high prevalence of weight loss attempts, particularly among women, indicates that other factors may be important as well. One potential predictor could be age. Although the results are somewhat disparate, older people tend to be less likely to try to lose weight than younger

ones.^{13,16,21,23,25-30} Another predictor is socioeconomic status which has shown a positive relation with weight loss attempts.^{15,31,32} Weight loss attempts may also be related to lifestyles, such as level of physical activity and smoking status.^{25,29,33}

Most of the material on weight loss attempts has been generated in the USA. Some European reports have been published recently,^{21,34} but data concerning weight loss attempts in adult European populations are still scarce. Given the widespread efforts to lose weight and their potential impact on the public health problem of being overweight and obesity, more information on the topic is warranted.

In this paper we examine the relationship between weight change attempts and BMI, age, socioeconomic status, reproductive factors, lifestyle and diet in a population-based study of Norwegian women. Moreover, we examine whether the impact of such factors may vary according to BMI.

METHODS

Subjects

This paper is based on data from a subsample of the Norwegian Women and Cancer (NOWAC) study. The subsample was drawn from the National Central Person Register February 1996 and consisted of 20,000 female Norwegian citizens born 1927-1951. In July 1996 they received a mailed letter of invitation requesting informed consent and a self-instructive questionnaire. A written reminder was sent to non-responders about 2 months after the first invitation. Of those replying by 1 September

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1997, 10,249 women agreed to participate, giving a response rate of 51.2%. Corrected for non-completion (death, emigration, severe mental handicap or unknown address), the response rate was 51.4%. The response rate declined with age, ranging from 55.5% in the youngest age group (45–49 years) to 41.6% in the oldest age group (65–69 years) and women living in northern Norway were more likely to respond than women living in southern Norway (55.3 and 50.8% respectively). The study was approved by the Regional Committee for Medical Research Ethics and the Norwegian Data Protection Registrar.

Questionnaire

Primarily, the NOWAC cohort was built for investigation of breast cancer and the eight-page questionnaire contained questions on both established (e.g. hormonal and reproductive factors) and potential risk factors for breast cancer (e.g. diet).

One section of the questionnaire focused on weight history and included questions on height, body weight and weight change attempts. The latter was asked as 'Are you trying to alter your weight?' with fixed answering options 'No', 'Yes, I want to put on weight' and 'Yes, I want to lose weight'. BMI was calculated (kg m^{-2}) from self-reported weight (kg) and height (m) and the responders were assigned to one of four categories: underweight (BMI $<18.5 \text{ kg m}^{-2}$), normal weight (BMI $18.5\text{--}24.9 \text{ kg m}^{-2}$), overweight (BMI $25.0\text{--}29.9 \text{ kg m}^{-2}$) and obese (BMI $\geq 30.0 \text{ kg m}^{-2}$).¹

Information on physical activity, smoking history, socioeconomic status (education and income), reproductive factors (number of children, menopausal status and use of hormone replacement therapy) and rating of own current state of health was also requested in the questionnaire. Years of education was asked about in an open-ended question and subsequently collapsed into categories corresponding to the Norwegian school system. Income was calculated as gross annual household income divided by the number of household members.

A major part of the questionnaire was concerned with diet and designed as a semi-quantitative food frequency questionnaire recording diet during the previous year. The questionnaire included a wide range of food items (74 questions) typically consumed in Norway, but did not cover the entire diet. Daily intake of energy and nutrients was computed using nutrient values from the Norwegian Food Composition Table.³⁵ A detailed description of the dietary questions and the nutrient calculations is given elsewhere,³⁶ as are the results from an evaluation study.³⁷

Statistical analyses

Statistical analyses and nutrient calculations were performed by means of the SAS software package, version 6.12 (SAS Institute, 1996). All reported p-values were two-sided and a significance criterion of $p < 0.05$ was used. For descriptive purposes the data are presented as means and standard deviations.

The relationship between weight loss attempts (yes versus no) and a set of selected predictor variables was analysed

using simple and multiple logistic regression models. Underweight women were excluded from these analyses due to the small number of women attempting to lose weight in this category. BMI was treated as a continuous variable. All other explanatory variables were categorised and treated as dummy variables. The multivariate analyses proceeded in several steps. First, the significance of each explanatory variable was examined by the log-likelihood criterion. Then, all significant explanatory variables were included simultaneously in a multivariate model. Variables that were non-significant in the multivariate model were subsequently eliminated and a new model was fitted. Next, effect modification by BMI on other explanatory variables was investigated by introducing interaction terms. All interaction terms contributing significantly to the model were included in the final model. Model fit was assessed by Hosmer and Lemeshow goodness-of-fit statistics and found satisfactory with the exception of some deviation in the right tail of the distribution.

The nutrient variables were generally non-normally distributed (skewed to the right) and non-parametric methods were therefore applied when analysing the dietary data. Statistical comparisons between groups were made by the Wilcoxon rank sum test or χ^2 -statistics when appropriate.

The number of subjects included in the separate analyses varied somewhat due to item non-response. Information on BMI and weight change attempts was obtained for 10,081 and 10,025 participants respectively and dietary estimates could be calculated for 9,885 women.³⁶

RESULTS

The mean reported weight was 67.8 kg (SD = 11.6 kg), mean reported height was 1.66 m (SD = 0.06 m) and mean BMI 24.6 kg m^{-2} (SD = 4.0 kg m^{-2}). Approximately 59% of the women were in the normal weight category (BMI $18.5\text{--}24.9 \text{ kg m}^{-2}$), 31% were overweight (BMI $25.0\text{--}29.9 \text{ kg m}^{-2}$), 8% were obese (BMI $\geq 30.0 \text{ kg m}^{-2}$) and 2% were underweight (BMI $<18.5 \text{ kg m}^{-2}$).

More than 50% of the women (5,339 out of 10,025) stated that they were trying to alter their body weight (table 1). The vast majority were trying to lose weight ($n=5,172$), whereas less than 2% ($n=167$) were trying to put on weight. The pattern of weight change attempts was strongly related to BMI (table 1). Figure 1 presents the percentage of women trying to lose weight by BMI. The relationship shows as an S-curve with a strong increase in the percentage of weight loss practitioners with increasing BMI. Weight loss attempts were infrequent among underweight women and will not be discussed further. Within the normal weight category the percentage of women trying to lose weight increased steadily from approximately 1% at the lower end of the interval to approximately 65% at the upper end. Among overweight/obese women some 70% to more than 90% of the participants were trying to lose weight. Treating BMI as a continuous variable and expressing the relationship between BMI and weight loss attempts in terms of odds ratios (ORs),

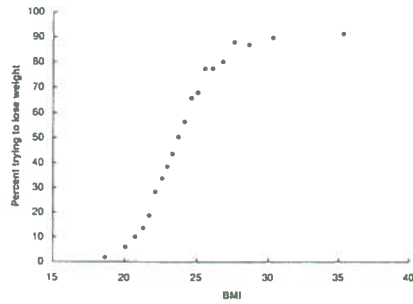


Figure 1 Percentage of women trying to lose weight by BMI (n=9,887)

gave an OR of 1.60 (95% CI: 1.57–1.64) (i.e. the OR is for one unit of change of BMI).

However, a multivariate logistic regression model with age, smoking status, importance of diet, years of education and income did reveal that there was an interaction between BMI and age ($p=0.01$), education ($p=0.001$) and income ($p<0.001$), that is the effect of BMI on weight loss attempts was dependent on age, education and income. For instance, women in the youngest age group, highest education category and highest income category had an OR of 2.00 (95% CI: 1.83–2.17) for one unit change in BMI, whereas women in the oldest age group, lowest education category and lowest income category had an OR of 1.35 (95% CI: 1.23–1.47).

In addition to the strong impact of BMI, several other characteristics of the women could predict weight loss attempts (table 2). Adjusted for BMI and all other variables in the model, smokers were less likely (OR=0.83) and ex-smokers more likely (OR=1.24) to try to lose weight compared to never smokers. Women regarding their diet to be of great (OR=1.15) or very great (OR=1.34) importance to their health were more likely to try to lose weight than women regarding their diet as less important. The effect of age, years of education and income on weight loss attempts was modified by the level of BMI (table 2). Generally, older age reduced the likelihood of trying to lose weight. However, the impact of age was considerably stronger at higher levels of BMI than at lower BMI levels. Higher income reduced the likelihood of trying to lose weight among lean women whereas it increased the likelihood among the overweight and obese. For instance, for women having a BMI of 20 kg m^{-2} , those in the highest income category had an odds which was one half of those in the lowest income

category. For women having a BMI of 30, being in the highest income category increased the odds of trying to lose weight five times compared to those of the same BMI being in the lowest category. No clear association was seen between weight loss attempts and years of education with the exception of reduced likelihood of weight loss attempts among women with less than 8 years of education.

Weight loss attempts were also examined according to level of physical activity, number of children, use of hormone replacement therapy, menopausal status and rating of own current state of health. However, none of these variables were significantly related to weight loss attempts when analysed in the multivariate model and they were therefore not included in the final model.

In order to see whether any weight loss attempts were reflected in actual food consumption, we examined some important aspects of diet. As shown in table 3, reported dietary intake seemed to be more dependent on whether a person was trying to lose weight or not than on current weight status. Significantly lower energy intakes were calculated for women stating that they were trying to lose weight than for those who did not. Furthermore, the weight loss practitioners reported a diet with less fat (as a percentage of energy intake) and more dietary fibre (g MJ^{-1}) than the women who were not trying to lose weight. In addition, they reported a slightly higher consumption of fruit and vegetables and a lower proportion of them spread fat on their bread. There were no significant differences in diet reported by normal weight and overweight/obese women when analysed stratified by weight loss attempts.

DISCUSSION

In this population-based, cross-sectional study of Norwegian women we found a considerable gap between reported and desired body weight. More than 50% of the participants were trying to lose weight. Weight loss attempts were strongly associated with BMI, but age, lifestyle and socioeconomic factors also predicted weight loss attempts to some extent.

The women initially invited to join this study constituted a nationwide random sample. However, the response rate was less than optimal, making the study vulnerable to non-response bias. We know that the non-responders

Table 1 Distribution of women by weight change attempts according to BMI category

	n	Weight change attempt		
		No weight change attempt %	Trying to put on weight %	Trying to lose weight %
Total	10,025	46.7	1.7	51.6
BMI (kg m^{-2}) ^a				
<18.5	156	64.1	35.3	0.6
18.5–24.9	5,818	66.1	1.8	32.1
25.0–29.9	3,070	19.9	0.0	80.1
≥30.0	843	8.7	0.2	91.1

a. Number of women by BMI does not total 10,025 because of missing values.

differed from the responders with respect to age and geographical distribution. However, the distribution of lifestyle factors did not vary according to response rate in another subsample of NOWAC.³⁸ Carefulness is required when interpreting data on BMI distribution and weight change attempts. As for the associations between weight loss attempts and the explanatory variables, these will only be biased if the non-responders differ from the

responders with regard to both the response and the explanatory variables.

All data in our study were self-reported and we have no information on the validity of the given body weights and heights. Compared to measured figures of heights and weights of more than 59,000 Norwegian women aged 40–42 years collected in 1991–1995 by the National Health Screening Service,⁸ our data correspond fairly

Table 2 Odds ratios^a and 95% confidence limits of trying to lose weight according to lifestyle, age and socioeconomic status among Norwegian women (no = 0 and yes = 1) (n=7,709)

	OR (95% CI)	OR (95% CI)	OR (95% CI)	p-value ^b
Smoking status				<0.001
Never (n=3,152) ^c		1.00		
Ex (n=2,415)		1.24 (1.09–1.41)		
Current (n=2,142)		0.83 (0.72–0.95)		
Importance of diet				0.002
None/some (n=1,563) ^c		1.00		
Great (n=4,200)		1.15 (1.00–1.33)		
Very great (n=1,946)		1.34 (1.14–1.58)		
	BMI = 20.0	BMI = 25.0	BMI = 30.0	
Age (years)				<0.001
45–49 (n=2,257) ^c	1.00	1.00	1.00	
50–54 (n=2,020)	0.77 (0.57–1.04)	0.88 (0.74–1.05)	1.01 (0.63–1.62)	
55–59 (n=1,432)	0.71 (0.50–1.00)	0.68 (0.56–0.82)	0.66 (0.40–1.07)	
60–64 (n=1,051)	0.78 (0.53–1.15)	0.71 (0.58–0.88)	0.66 (0.39–1.11)	
65–69 (n=949)	1.07 (0.73–1.57)	0.60 (0.49–0.73)	0.33 (0.20–0.55)	
Education (years)				<0.001
≤7 (n=796) ^c	1.00	1.00	1.00	
8–9 (n=1,872)	1.45 (0.90–2.33)	1.35 (1.10–1.67)	1.27 (0.78–2.06)	
10–12 (n=2,549)	1.98 (1.25–3.14)	1.36 (1.10–1.67)	0.93 (0.57–1.52)	
>12 (n=2,492)	1.26 (0.78–2.05)	1.65 (1.31–2.08)	2.15 (1.23–3.78)	
Income (NOK)				<0.001
<75,000 (n=877) ^c	1.00	1.00	1.00	
75,000–124,999 (n=2,953)	0.60 (0.42–0.86)	1.05 (0.87–1.25)	1.81 (1.20–2.73)	
125,000–199,999 (n=2,366)	0.60 (0.41–0.88)	1.34 (1.10–1.65)	3.00 (1.83–4.91)	
≥200,000 (n=1,513)	0.53 (0.35–0.81)	1.63 (1.29–2.07)	5.02 (2.77–9.11)	

a: Odds ratio calculated from the final multiple logistic regression model, including BMI and all other variables.

b: p-value for total significant contribution of the variables to the model.

c: Reference category.

Table 3 Intake of energy and selected nutrients and foods according to BMI and weight loss attempts (n=9,322)

	Normal-weight women BMI 18.5–24.9			Overweight/obese women BMI ≥ 25.0		
	Trying to lose weight ^a			Trying to lose weight ^a		
	No n=3,739	Yes n=1,819	p-value ^b	No n=653	Yes n=3,111	p-value ^b
Median						
Energy (kJ day ⁻¹)	6,549	6,065	<0.001	6,471	6,022	<0.001
Fat (% of energy intake)	33.2	31.6	<0.001	33.4	31.7	<0.001
Dietary fibre (g MJ ⁻¹)	2.9	3.1	<0.001	3.0	3.1	<0.001
Fruit and vegetables (g day ⁻¹)	231	251	<0.001	227	249	<0.001
Percent						
Spreading fat on bread (%)	77	63	<0.001	78	65	<0.001

a: No significant difference for normal-weight versus overweight/obese when stratified by weight loss attempts.

b: Wilcoxon rank sum test or χ^2 -test.

well. In the health screening, the mean BMI was 24.4 kg m⁻² (SD = 3.9 kg m⁻²) and 8.4% of the women had a BMI >30 kg m⁻². This is only slightly higher than the figures calculated for the youngest women in the present study. Reports from studies comparing self-reported weights and heights with measured values do usually describe rather close agreement between mean values at the group level. Typically, women underestimate their weight by an average of approximately 1 kg and overestimate their height by 0.7 cm.^{39,40} However, substantial discrepancies occur in certain subgroups.^{39,40} Subgroup differences arising from increasing under-reporting of body weight at the upper end of the weight distribution and the tendency to overestimate height more as people get older,³⁹ increases the risk of misclassification when allocating individuals to BMI categories. In our study the upper cut-off for normal weight was set at 24.9 kg m⁻² to avoid including women who were actually overweight.²⁹

The number of weight loss practitioners in NOWAC (52%) seems to be somewhat higher than estimates from other population-based studies; typically approximately 40% of women state that they are trying to lose weight.^{16,19,21,25,27} However, comparing prevalence estimates across surveys must be done cautiously as the samples (e.g. age distribution) and questionnaire design may differ.^{18,23}

As figure 1 shows, weight loss attempts were strongly related to BMI, not only among the overweight and obese, but also within the range defined as normal weight. It is noteworthy that a considerable number of middle-aged women were trying to lose weight even when not overweight. A high percentage of normal-weight females trying to lose weight has also been reported by others.^{14,17,25,28,41} It may be that these females still see themselves as overweight.¹³ However, even females who consider their weight 'right', frequently try to lose weight.^{16,27,42} In a population-based study in the USA, more than 20% of adult women who considered themselves to be the 'right weight' reported that they nevertheless tried to lose weight.²⁷

Several typical predictors of BMI such as age, socioeconomic status and lifestyle,^{13,43,44} were also independently related to weight loss attempts in our study. In most respects, greater age seems to reduce the likelihood of weight loss attempts both in the present and in previous studies,^{13,16,25-27} but the findings are somewhat inconsistent.^{23,28,30} In our study, age was of minor importance among lean women. However, with increasing level of BMI age became more important. Higher socioeconomic status on the whole increased the likelihood of trying to lose weight, although a trend was observed for income only. Moreover, the effect of income was strongly modified by BMI; higher income decreased the likelihood of weight loss attempts among lean women, but markedly increased the likelihood among the overweight and obese. Although not uniform, the literature generally describes a positive association between weight loss attempts and socioeconomic status.^{13,15,23,27,29,30,32} This may

reflect stronger social expectations to be slim in high-status groups.^{12,13,31} Our finding of current smokers being more and ex-smokers being less likely to try to lose weight compared to never smokers are consistent with the conclusion of a review paper on weight concerns and smoking.³³ Smoking cessation may motivate weight loss attempts,^{17,18} while current smoking may restrain it.^{18,25,29} No association between smoking status and weight loss attempts has also been reported.³⁰ Level of physical activity was not significantly related to weight loss attempts in our study and the literature yields conflicting results.^{25,29,30} However, the fact that increasing amounts of physical activity may be an efficient way of losing weight,⁴⁵ makes it difficult to separate the significance of physical activity as a predictor of weight loss attempts from that of being a weight loss method.

Dieting is the most commonly reported weight loss strategy and caloric restriction is very often used.^{16,17,23-25,46} The lower intake of energy calculated for those who tried to lose weight than for those who did not may indicate such action in the present study, although reporting bias (under-reporting) cannot be ruled out. Underestimation of energy intake is a problem, particularly among overweight subjects.^{19,47,48} Nevertheless, intermittent energy restriction may be a significant factor in the reduced energy intake reported by overweight women.^{49,50} Since our questionnaire did not cover diet completely it is difficult to estimate the true extent of under-reporting. Nonetheless, it is interesting that reported energy intake appears to be more strongly related to weight change attempts than to weight status. The picture is the same for intake of selected nutrients and foods. The finding of a more healthy dietary profile among women trying to lose weight than among those who were not is consistent with earlier findings.^{23,29,30,51} Moreover, it is compatible with the increased likelihood of weight loss attempts among women considering their diet to be of very great importance to their health compared to women considering their diet as less important.³⁶

The importance of being overweight¹ and its implications for several chronic diseases⁵² has recently been discussed and indicates that new strategies are needed to prevent and decrease the levels of being overweight and obese worldwide. However, the ideal BMI for middle-aged women is still debated⁵³ and health professionals should also be aware of the widespread practice of weight loss attempts even among women who may not benefit from it.

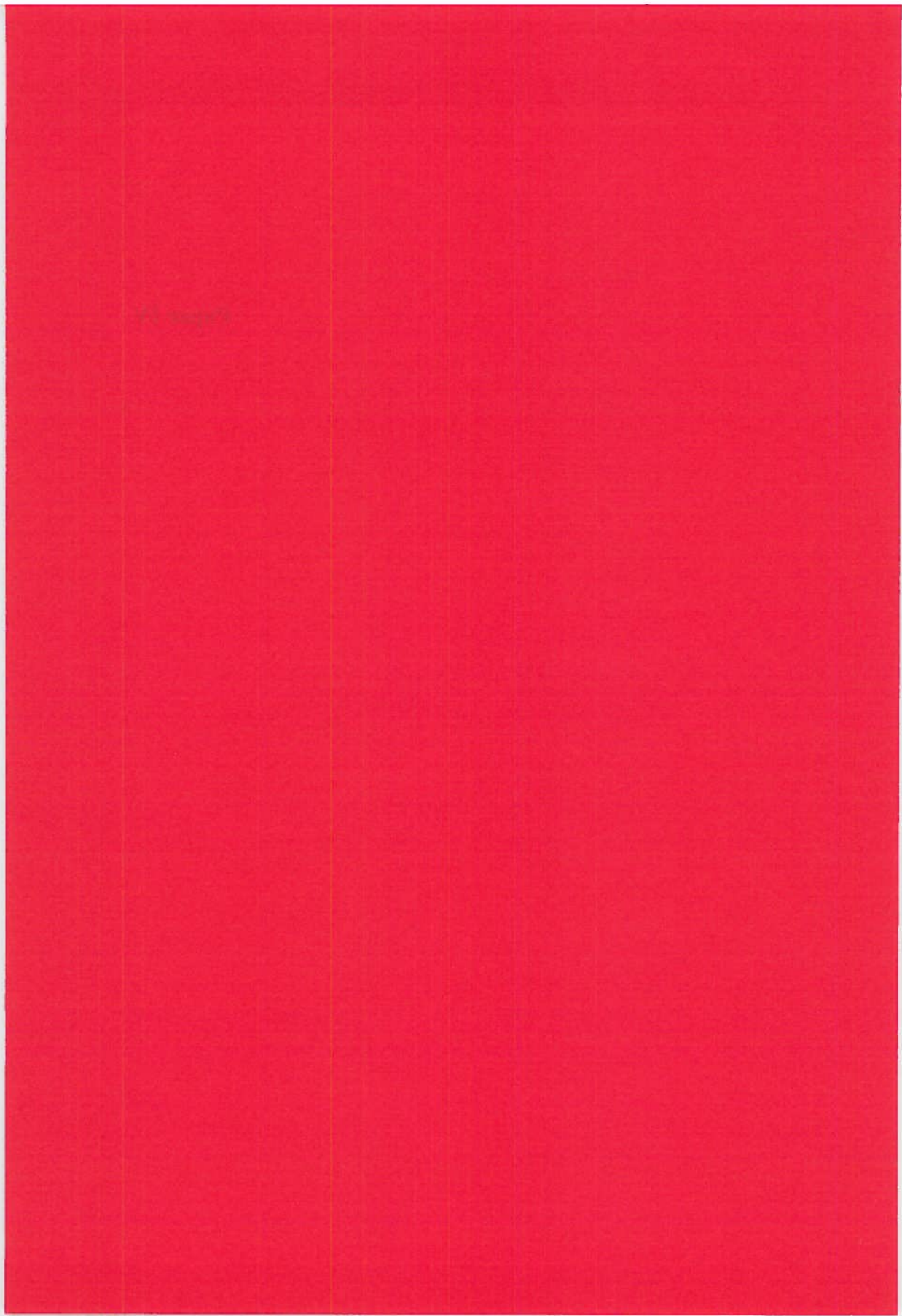
In summary, weight loss attempts are prevalent among middle-aged Norwegian women, not only among those who are overweight and obese, but also among normal-weight women. Weight loss attempts tend to be related to both age, lifestyle and socioeconomic status and the relationship may be affected by the level of BMI. It is a public health challenge to encourage and support weight loss among overweight and obese subjects on the one hand and prevent unnecessary emphasis on leanness on the other.

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Paper IV



**CHILDHOOD AND ADULT MILK CONSUMPTION AND
RISK OF BREAST CANCER IN A COHORT OF 52,592 WOMEN.
THE NORWEGIAN WOMEN AND CANCER STUDY**

Running title: Milk consumption and breast cancer

Keywords: breast cancer, milk consumption, diet, cohort study

Abbreviations: incidence rate ratio – IRR, confidence interval - CI

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SUMMARY

Analyses of dairy consumption and breast cancer incidence have yielded conflicting results. In this prospective cohort study of 52,592 Norwegian women, we examined the relationship between childhood and adult milk consumption and breast cancer incidence. During a mean follow-up time of 6.2 years, 371 incident cases of breast cancer were diagnosed. Information on childhood and adult milk consumption was obtained from frequency questions mailed to the participants in 1991/92. No association was found for milk consumption as a child and subsequent breast cancer. Adult milk consumption was negatively related to breast cancer incidence (p for trend 0.04) after adjustment for age, reproductive and hormonal factors, body mass index, education, physical activity, and alcohol consumption. Women drinking more than three glasses of milk per day had an incidence rate ratio of breast cancer of 0.64 (95% confidence interval 0.38–1.08) compared to women not drinking milk. The estimate was about the same when looking at premenopausal women only. Analyses according to type of milk consumed and milk fat consumption did not reveal any clear associations. A combination of childhood and adult milk consumption produced incidence rate ratios of the same magnitude as those of adult milk consumption only.

INTRODUCTION

Breast cancer is the most common female cancer in the world and has an age-adjusted incident rate of 71.4 per 100,000 person-years in Norway (Cancer Registry of Norway, 2000). Despite a constant search for knowledge about the biological mechanism operating behind the disease and means of preventing the disease, much is unknown and no efficient preventive methods have been revealed. Hormonal factors and reproductive history are known to influence breast cancer risk (Lund, 1991; Tavani et al., 1999), but hardly have preventive potential. Diet, on the other hand, is modifiable, but the relation to breast cancer is not as consistent.

Some of the strongest indications that diet plays a role in the aetiology of breast cancer have emerged from ecological and migration studies. Several of the migrant studies have demonstrated that the breast cancer incidence may not be substantially changed for the immigrants themselves but rather for the second- and third-generation immigrants (Ziegler et al., 1993). This delay may indicate a stronger influence of childhood diet than adult diet on breast cancer risk, and harmonises with a long latency period for breast cancer. Also, the positive association between adult height and breast cancer supports this suggestion (Tretli, 1989; Vatten et al., 1992).

Most of the research on diet and breast cancer has focused on the possible effect of fat intake, which is still hotly debated (Feldman, 1999; Holmes et al., 1999; Wu et al., 1999). The consumption of dairy products, which are important contributors to the fat intake in many Western countries, has also yielded conflicting findings regarding breast cancer incidence (Trichopoulou et al., 1995; Männistö et al., 1999). Generally, no association between milk consumption and breast cancer incidence has been found in prospective studies (Mills et al., 1989; Ursin et al., 1990; Toniolo et al., 1994), although both positive (Gaard et al., 1995) and negative (Knekt et al., 1996) findings are reported. As for any relationship between childhood or adolescent milk consumption and subsequent breast cancer, only limited data are available. A few case-control studies have, however, indicated that there may be no (Potischman et al., 1998) or an inverse association (Hislop et al., 1986; Pryor et al., 1989).

Several components of milk (e.g. growth factors, fatty acids, calcium) have been hypothesised to play a role in the development of breast cancer (Outwater et al., 1997; Visonneau et al., 1997; Lipkin and Newmark, 1999). In Norway, there is a generally high consumption of milk and milk products among both children and adults (per capita supply in 1997 was 270 kg, compared to a European average of 206 kg) (FAO, 2000), but also considerable variation in consumption. Any elucidation of the association between milk consumption, present or past, and breast cancer would be of significance. We therefore examined whether milk consumption, both as a child and as an adult, was associated with breast cancer incidence in a population-based

prospective study characterised by a high milk consumption. Furthermore, we examined the effect of a sustained high or low milk consumption. As menopausal status may interact with breast cancer risk factors (Lund, 1991; Zaridze et al., 1991), the analyses were also done for pre- and postmenopausal women separately, and all known reproductive and hormonal risk factors were adjusted for in the analyses.

MATERIAL AND METHODS

Study population

In 1991-1992, a random, nationwide sample of 100,000 Norwegian women born 1943-1957 was drawn from the National Central Person Register and invited to participate in the Norwegian Women and Cancer Study (NOWAC). A total of 61,000 women were randomly sampled in 1991, and an additional 39,000 (Norwegian citizens only) in 1992. The women received a mailed letter of invitation requesting informed consent and a self-instructive questionnaire. A written reminder was sent to non-responders about six weeks after the first invitation. Altogether 57,664 women answered the questionnaire. Sixty women answered "No" to participating in the record linkage and were excluded from the analyses, giving a crude response rate of 57.6%. Corrected for non-completion (death, severe mental handicap, unknown address), the response rate was 58.4%. Statistics Norway was responsible for sampling and for mailing of the questionnaires. The study was approved by the Regional Committee for Medical Research Ethics and the Norwegian Data Inspectorate.

Assessment of milk consumption

The dietary part of the questionnaire was designed in a food frequency manner, asking about average intake of 28 food items, including alcoholic beverages, during the last year. The question about milk consumption as a child was asked as 'How much milk did you drink as a child every day?' with fixed answering categories: 'none', '1-3 glasses', '4-6 glasses', and '7 glasses or more'. Adult milk consumption was assessed as three separate questions according to the fat content of the milk: whole milk (3.9% fat), low fat milk (1.5% fat), and skimmed milk (0.1% fat). Nine different answering categories were given, ranging from 'almost never' to '6-10 glasses per day'. Total adult milk consumption was calculated by summarising the consumption of milk from all three questions. If all three questions were left blank, the questionnaire was excluded from the analyses of adult milk consumption. If one or two of the milk questions were left blank, zero consumption of that particular type of milk was assumed. Intake of fat from milk was calculated by multiplying the number of glasses of each milk type by the respective fat content, and thereafter summarised.

Reproducibility of the milk consumption questions

A total of 555 women included in the cohort were asked to fill in the same questionnaire twice, about four months apart, and 341 women agreed to do so. Weighted kappa for milk consumption as a child was 0.54. For adult milk consumption, weighted kappa for whole milk consumption was 0.43, for low fat milk 0.55, and for skimmed milk 0.50. The kappa estimates rose to 0.80, 0.73, 0.76, respectively, when women with missing values were excluded. Most missing values on either the test or the retest corresponded to 'almost never' on the other test occasion.

Identification of breast cancer cases

Information from the questionnaire was linked to the Cancer Registry of Norway to identify incident breast cancer cases. The accuracy of the linkage was ensured by the unique 11-digit identification number which all Norwegian citizens have. In Norway, it is mandatory by law to report all incident cancer cases to the cancer registry, and the registry has an almost complete record of all cancer cases (Lund, 1981; Harvei et al., 1996). All but eight cases were histologically verified. A corresponding linkage to records at Statistics Norway provided information on death and emigration.

Person years of follow-up were calculated as the time elapsed from date of entry into the cohort (defined as three months after mailing of the invitation letter) to the time of cancer (any type), to time of death or emigration, or to the end of follow-up (31.12.1997), whichever came first.

Of the 100,000 women initially invited to participate in NOWAC, 6,000 were given a questionnaire without dietary questions (Lund and Gram, 1998). The responders of this questionnaire (n = 3,694) were not included in the present analyses. Furthermore, the following exclusions were made: six women died before the start of the follow-up; 986 women had a prior cancer diagnosis; 104 women developed cancer during the first year of follow-up; and four women were excluded as lost to follow-up due to change of identification number. Women who emigrated were followed until emigration, if their emigration date was known, otherwise they were excluded (n = 117). Finally, we excluded 101 women who did not answer any of the milk questions. A total of 52,592 women were thus available for the follow-up analyses.

Statistical analyses

Cox proportional hazards regression analyses were carried out to investigate the simultaneous effect of milk consumption and co-variables on breast cancer incidence rate. Incidence rate ratios (IRR) and 95% confidence intervals (CI) were calculated. In multivariate analyses we adjusted for age, maternal history of breast cancer, age at menarche, menopausal status, number of children, age at first birth, current use of oral

contraceptives, current use of hormone replacement therapy, body mass index ($BMI = \frac{wt(kg)}{ht(m)^2}$), body size as a child, years of education, level of physical activity, and alcohol consumption. Adjustment for total energy intake was not possible due to the restricted number of food items in the questionnaire.

Childhood milk consumption was categorised as in the questionnaire (i.e. 'none', '1-3', '4-6' and '7 or more' glasses of milk per day), with 'none' as the reference group. Adult milk consumption at baseline was divided into the categories 'none', '0.1-1.0', '1.1-3.0' and '3.1 or more' glasses of milk per day, with 'none' as the reference group. The combined effect of childhood and adult milk consumption was examined by constructing a three-level variable: 'low consumption', defined as no milk consumption on at least one of the occasions and not more than next-lowest consumption on the other occasion; 'high consumption', defined as the highest milk consumption on at least one of the occasions and not less than the next-highest consumption on the other occasions; and 'moderate consumption', defined as all other combinations. The low consumption group was used as the reference category.

In analyses stratified by menopausal status, women who were premenopausal at baseline were treated as premenopausal until they reached the age of 50 during follow-up, at which time they were considered postmenopausal. Women who reported that they were postmenopausal at baseline were treated as postmenopausal. The age of 50 as a dividing line for menopausal status was chosen based on data from an older sub-cohort of NOWAC. Because of small numbers of cases in the reference groups for postmenopausal women, the incidence rates in the postmenopausal strata were unstable and will not be pursued further.

The assumptions of proportional hazards for the exposures of interest were examined and were not found to be violated. All reported p-values are two-sided, and a significance criterion of $p < 0.05$ was used. The number of subjects included in the separate analyses varies somewhat due to item non-response. Statistical analyses were done by means of the SAS software package, version 6.12.

RESULTS

A total of 371 incident cases of breast cancer were diagnosed among the 52,592 women during follow-up. The number of person-years was 327,038, and mean follow-up time was 6.2 years (range 0.04-6.63). The mean age at diagnosis was 46.3 years (range 35.8-54.6).

Some baseline characteristics of the cohort are given in Table I. The mean age at entry was 41.1 years and about 7 percent were postmenopausal at baseline. Ten percent of the women did not have any children, while of those who had children the average number of children was 2.3. Some 7 percent of the women reported not

drinking milk as a child. Most of the women reported a moderate milk intake as a child, whilst 2 percent reported drinking 7 glasses or more per day. As for adult milk consumption (i.e. at baseline), nearly 10 percent reported not drinking milk. Low fat milk was most frequently used, followed by skimmed milk and whole milk. The women reported on average 1.7 glasses of milk per day, and the average intake of fat from milk was 3.2 grams per day.

Milk consumption as a child was not associated with breast cancer in age-adjusted analyses (Table II). Also, when adjusting for maternal history of breast cancer, age at menarche, menopausal status, number of children, age at first birth, current use of oral contraceptives, current use of hormone replacement therapy, BMI, body size as a child, years of education, level of physical activity, and alcohol intake, in addition to age, the incidence rate ratio was close to one (Table II).

Adult milk consumption tended to be negatively associated with incidence of breast cancer in age-adjusted analyses ($p = 0.09$) (Table III). After adjusting for possible confounders we observed a clear association between milk consumption and breast cancer incidence ($p = 0.04$). Among premenopausal women, those reporting drinking more than three glasses of milk per day had a 40% lower incidence rate of breast cancer (IRR = 0.58, 95% CI 0.32-1.08) than women not drinking milk at all. Also for postmenopausal women there tended to be a reduced incidence rate of breast cancer with increasing milk consumption ($p = 0.13$) (data not shown). Subgroup analyses (age at entry, number of children, BMI) did not add any further information on the relationship between milk consumption and breast cancer incident rate (data not shown). Using reference categories with larger number of cases did not alter the findings (data not shown).

Examining the relationship with incidence rate of breast cancer separately for each milk type, and using non-milk drinkers as a reference group, revealed a tendency of a negative association for low fat milk ($p = 0.08$), whereas no trend was seen for skimmed milk ($p = 0.80$) and whole milk consumption ($p = 0.34$) (data not shown). The number of cases drinking whole milk only was, however, low ($n = 34$). Nevertheless, when merging all women drinking whole milk only into one category, irrespective of amount consumed, and comparing them with non-milk drinkers, there was still no significant difference in incidence rate of breast cancer (IRR = 1.27, 95% CI 0.79-2.05) (data not shown in table).

Expressing milk consumption in quartiles of fat from milk per day, and using the lowest quartile as the reference category in a model including all the possible confounding variables, produced (non-significant) incidence rate ratios of 0.88, 0.88, and 0.85 for the 2nd, 3rd and 4th quartiles, respectively (data not shown in table).

When combining milk consumption as a child and as an adult we observed a negative trend in breast cancer incidence rate with increasing milk consumption

($p = 0.06$) (Table IV). Compared with women who reported no or low consumption of milk on both occasions, women with moderate milk consumption had a reduced incidence rate of breast cancer of about 20%, whereas women with a high milk consumption on both occasions had a reduced incidence rate of about 45%. The results were about the same when examining premenopausal women only ($p = 0.06$).

DISCUSSION

The present prospective study suggests an inverse dose-response association between adult milk consumption and breast cancer incidence in a high consumption population. No association was found between milk consumption as a child and breast cancer. A combination of milk consumption as a child and as an adult produced incidence rate ratios comparable with those of adult milk consumption.

Lately there has been a growing interest in intrauterine and childhood nutrition as risk factors for subsequent diseases, including cancer (Kemmer, 1987; Frankel et al., 1998; Henriksen, 1999). Adequate data on past diet is, however, very difficult to obtain. Based on wholesale statistics, we know that the per capita consumption of milk in Norway in the 1950's, when the women were growing up, was high: about 205 kilos, of which 195 kilos was whole milk, the rest being skimmed milk (National Council for Nutrition and Physical Activity, 1999). Our questionnaire included only a single question on childhood milk consumption, and the answering categories were rather high. We do not know how well the question reveals real differences in past consumption. No consistent associations between childhood milk consumption and breast cancer incidence were found, although one may speculate on a negative association among premenopausal women. Such an association was found in a Canadian case-control study applying childhood whole milk consumption categories ranging from 'very rarely' to 'daily' (Hislop et al., 1986). A case-control study in the US examined adolescent intake of dairy fat and breast cancer risk and found a negative trend in risks across quartiles of intake (Pryor et al., 1989), whereas no association was found in another US case-control study of dairy product consumption during adolescence (Potischman et al., 1998). Also, in our study adding information on childhood milk consumption to the analyses of adult milk consumption had only a minor effect on the association with breast cancer.

When concerning adult milk consumption and breast cancer, several case-control studies have supported no (e.g. Katsouyanni et al., 1986; Hirohata et al., 1987; La Vecchia et al., 1987; Richardson et al., 1991; Trichopoulou et al., 1995) or a positive association (e.g. Lè et al., 1986; Ewertz and Gill, 1990; Yuan et al., 1995; Witte et al., 1997; Männistö et al., 1999), although inverse associations have also been reported (Isovich et al., 1989; Pryor et al., 1989; Hirose et al., 1995; Favero et al.,

1998).

Cohort studies, regarded as the epidemiological study design least prone to bias, have generally been more focused on consumption of dietary fat and animal products than on milk consumption per se. Overall, these studies have shown no association between milk consumption and breast cancer (Mills et al., 1988, 1989; Ursin et al., 1990; Toniolo et al., 1994), apart from a positive association between whole milk consumption and breast cancer incidence in a Norwegian analysis (Gaard et al., 1995). A thorough examination of consumption of dairy products and breast cancer incidence has been done by Knekt et al. (1996) in a Finnish cohort. In accordance with our findings, their examination also revealed a reduced incidence rate of breast cancer with increasing milk consumption in a high consumption population. In the Finnish study, women in the highest tertile of milk consumption had a 50 percent reduced incidence rate compared to women in the lowest tertile.

The contradicting results may indicate that any association between milk consumption and breast cancer is not a strong one. Still, one has to remember the methodological weaknesses of dietary assessment methods. A variety of dietary methods have been applied, and we do not know how valid many of them are (including our own). The distribution of milk consumption varies greatly between the study samples, and the definition of reference group differs accordingly. Also, the possibility of sufficient adjustment for potential confounders varies between the studies.

Our study contains information on all known relevant reproductive and hormonal factors, as well as height, weight, years of education, level of physical activity and alcohol intake. Adjustment for these factors had only minor influence on the incidence rate ratios. Also, subgroup analyses indicated that the results could not be explained by residual confounding. On the other hand, our questionnaire only asked about consumption of a limited number of food items, and we chose not to include any additional dietary variables or energy intake in the multiple analyses. This may have confounded the results. However, in the cohort study by Knekt et al. (1996), adjustment for selected food items, nutrients and energy did not alter the negative association between milk consumption and breast cancer.

The strengths of the NOWAC study are the population-based approach, the large size of the cohort, the prospective design, the almost complete follow-up with regard to incidence of cancer, death, and emigration, and the opportunity to adjust for all established risk factors for breast cancer. However, due to the relatively young age of the women at entry and the short follow-up, the number of breast cancer cases in certain subgroups is small. This reduces the statistical power of the analyses and the feasibility of performing subgroup analyses.

In 1997, milk and milk products contributed 24 percent of the dietary intake of

fat in the Norwegian diet (National Council on Nutrition and Physical Activity, 1999). Dairy products contributed 40 percent of the intake of saturated fatty acids; milk alone contributed 11 percent. The issue of dietary fat and risk of breast cancer has still not been settled in spite of numerous efforts to do so. In our study, expressing milk consumption in terms of grams of fat per day produced non-significant incidence rate ratios of about 0.85-0.90 in both the 2nd, 3rd and 4th quartiles of consumption and no trend in incidence rate ratios were seen either for skimmed or whole milk consumption.

In addition to saturated fat, milk is also an important contributor of calcium, and it contains significant amounts of protein and several vitamins and minerals. Whether an association with breast cancer is connected with one or more of these factors, or even with presently unknown components in milk, are questions that are not answerable by the present analyses. However, calcium intake has previously been inversely associated with cancer risk, especially of colon cancer (Kampman et al., 2000), but also breast cancer (Negri et al., 1996). Furthermore, laboratory studies have suggested a possible protective role for calcium (together with vitamin D) in the development of breast cancer through its effect on the mammary gland (Lipkin and Newmark, 1999). Another interesting biological mechanism by which milk intake can reduce breast cancer risk is the one hypothesised for conjugated linoleic acid (CLA). CLA is mainly derived from dairy products, and has been shown to block both local growth and systematic spread of human breast cancer in animal studies (Visonneau et al., 1997). On the other hand, other researchers have hypothesised that dairy products may increase breast cancer risk through their content of oestrogen and growth factors (Outwater et al., 1997).

In summary, in this prospective population-based study we found a negative association between milk consumption and breast cancer that could not be explained by reproductive or hormonal factors. The association was not dependent on the fat content of the milk, leaving other milk components or even unmeasured lifestyle factors related to milk consumption as possible explanatory variables. The lack of association between childhood milk consumption and subsequent breast cancer may be a valid finding, although the limitations of the dietary method and difficulties in reporting remote food consumption should be borne in mind.

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TABLE I - SELECTED BASELINE CHARACTERISTICS BY AGE GROUP IN THE NOWAC STUDY

Characteristics	34-39 years (n = 21,318)	40-44 years (n = 17,119)	45-49 years (n = 14,155)	Total (n = 52,592) ¹
Age, years (mean)	36.6	42.0	46.6	41.1
Maternal history of breast cancer (%)	3.7	4.3	4.9	4.2
Age at menarche (mean)	13.2	13.3	13.4	13.3
Postmenopausal status (%)	1.5	4.9	19.0	7.3
Nulliparity (%)	12.2	8.7	7.8	9.9
Number of children, parous women only (mean)	2.2	2.4	2.5	2.3
Age at first birth, parous women only (mean)	24.1	23.7	23.7	23.9
Current use of oral contraceptives (%)	9.4	3.1	1.8	5.7
Current use of hormone replacement therapy (%)	0.0	0.6	3.3	1.1
Body mass index (mean)	22.6	23.0	23.7	23.0
Years of education (mean)	12.7	12.1	11.4	12.1
Physical activity score (min. 1- max. 10, mean)	5.7	5.7	5.6	5.7
Alcohol intake, g/day (mean)	2.8	2.9	3.1	2.9
Milk consumption as a child, glasses/day (%)				
none	6.3	6.8	7.2	6.7
1-3	61.1	60.3	61.3	60.9
4-6	30.7	30.9	29.3	30.4
≥ 7	1.9	2.0	2.1	2.0
Milk consumption as an adult, glasses/day (%)				
none	9.1	9.5	10.6	9.6
> 0.1-1.0	36.4	42.6	45.3	40.8
1.1-3.0	42.0	38.6	36.1	39.3
> 3.0	12.6	9.3	8.0	10.3
Skimmed milk, g/day (mean)	136	127	126	131
Low fat milk, g/day (mean)	161	147	140	151
Whole milk, g/day (mean)	37	40	43	39

¹Subgroups may not total 52,592 because of item non-response.

TABLE II - INCIDENCE RATE RATIOS (IRR) (95% CONFIDENCE LIMITS) OF BREAST CANCER ACCORDING TO MILK CONSUMPTION AS A CHILD IN THE NOWAC STUDY

Milk consumption as a child (glasses/day)	All women (n = 52,071) ¹			All women (n = 45,337) ²			Premenopausal only (n = 42,099) ³		
	No. of cases	IRR (95% CI)	p for trend	No. of cases	IRR (95% CI)	p for trend	No. of cases	IRR (95% CI)	p for trend
Did not drink milk	28	1		21	1		17	1	
1-3	226	0.90 (0.61-1.34)		190	0.97 (0.62-1.52)		144	0.87 (0.53-1.45)	
4-6	105	0.84 (0.56-1.28)		91	0.92 (0.57-1.49)		69	0.81 (0.48-1.39)	
7+	9	1.10 (0.52-2.33)	0.60	8	1.31 (0.58-2.95)	0.96	4	0.80 (0.27-2.37)	0.44

¹Adjusted for age.

²Adjusted for age, maternal history of breast cancer, age at menarche, menopausal status, number of children, age at first birth, current use of oral contraceptives, current use of hormone replacement therapy, body mass index, body size as a child, years of education, physical activity, and alcohol consumption.

³Adjusted for age, maternal history of breast cancer, age at menarche, number of children, age at first birth, current use of oral contraceptives, body mass index, body size as a child, years of education, physical activity, and alcohol consumption.

TABLE III - INCIDENCE RATE RATIOS (IRR) (95% CONFIDENCE LIMITS) OF BREAST CANCER ACCORDING TO MILK CONSUMPTION AS AN ADULT IN THE NOWAC STUDY

Milk consumption as an adult (glasses/day)	All women (n = 51,892) ¹			All women (n = 45,763) ²			Premenopausal only (n = 42,521) ³		
	No. of cases	IRR (95% CI)	p for trend	No. of cases	IRR (95% CI)	p for trend	No. of cases	IRR (95% CI)	p for trend
Do not drink milk	41	1		37	1		26	1	
0.1-1.0	161	0.91 (0.65-1.28)		142	0.87 (0.61-1.25)		100	0.86 (0.56-1.33)	
1.1-3.0	137	0.84 (0.60-1.20)		115	0.75 (0.52-1.09)		96	0.84 (0.54-1.29)	
3.1+	27	0.66 (0.41-1.08)	0.09	24	0.64 (0.38-1.08)	0.04	17	0.58 (0.32-1.08)	0.13

¹Adjusted for age.

²Adjusted for age, maternal history of breast cancer, age at menarche, menopausal status, number of children, age at first birth, current use of oral contraceptives, current use of hormone replacement therapy, body mass index, years of education, physical activity, and alcohol consumption.

³Adjusted for age, maternal history of breast cancer, age at menarche, number of children, age at first birth, current use of oral contraceptives, body mass index, years of education, physical activity and alcohol consumption.

TABLE IV - INCIDENCE RATE RATIOS (IRR) (95% CONFIDENCE LIMITS) OF BREAST CANCER ACCORDING TO MILK CONSUMPTION AS A CHILD AND AS AN ADULT IN THE NOWAC STUDY

Milk consumption	All women (n = 51,371) ¹			All women (n = 44,948) ²			Premenopausal only (n = 41,759) ³		
	No. of cases	IRR (95% CI)	p for trend	No. of cases	IRR (95% CI)	p for trend	No. of cases	IRR (95% CI)	p for trend
Low	47	1.0		41	1.0		31	1.0	
Moderate	299	0.87 (0.64-1.19)		252	0.82 (0.59-1.14)		190	0.78 (0.53-1.14)	
High	17	0.58 (0.33-1.01)	0.07	15	0.57 (0.32-1.03)	0.06	12	0.54 (0.28-1.06)	0.06

¹Adjusted for age.

²Adjusted for age, maternal history of breast cancer, age at menarche, menopausal status, number of children, age at first birth, current use of oral contraceptives, current use of hormone replacement therapy, body mass index, body size as a child, years of education, physical activity, and alcohol consumption.

³Adjusted for age, maternal history of breast cancer, age at menarche, number of children, age at first birth, current use of oral contraceptives, body mass index, body size as a child, years of education, physical activity, and alcohol consumption.

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