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EXPLAINING THE SOCIOECONOMIC VARIATION IN INCIDENCE AND SURVIVAL OF CANCER

Analyses and multiple imputation of data from The Norwegian Women and Cancer Study and The Norwegian-Swedish Women's Lifestyle and Health Cohort Study

Tonje Braaten

Tromsø 2008

Institute of Community Medicine
University of Tromsø

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TABLE OF CONTENTS

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My patient son, *Christian*

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LIST OF PAPERS

I. Braaten T, Weiderpass E, Kumle M, Adami H-O, Lund E: Education and risk of breast cancer in The Norwegian-Swedish Women's Lifestyle and Health Cohort Study. *International Journal of Cancer 2004; 110(4): 579-83*

II. Braaten T, Weiderpass E, Kumle M, Lund E: Explaining the socio-economic variation in cancer risk in The Norwegian Women and Cancer Study. *Cancer Epidemiol Biomarkers Prev 2005; 14 (11)*

III. Braaten T, Weiderpass E, Lund E: Socioeconomic status, intergenerational change in socioeconomic status and survival of cancer. The Norwegian Women and Cancer Study. *Submitted*

IV. Braaten, T: A simulation study of simple residual multiple imputation. *Submitted*

INTRODUCTION

The concepts of social class

Within the field of sociology, various definitions of the term social class have been introduced in order to classify social position within a society. Karl Marx and Max Weber have been prominent contributors. Marx categorized class on the basis of a group's relation to the means of production, which emphasized economic inequality (1), whereas Weber considered social position to be based on three dimensions: class, status, and power (2). Various efforts have been made to develop an optimal quantification of social class, either by a single measure or by combining single measures into a composite one. Other terms have emerged, such as social status, social inequality, social stratification, and socio-economic status (SES). These terms have arisen from somewhat different theoretical formulations (2), and sociologists usually distinguish between them.

However, within epidemiological practice the terms frequently appear without distinctions, and thus they will be used interchangeably in the following. Another departure from the sociological tradition is that epidemiologists rarely rely on one unambiguous definition of social class that can only be partly assessed by a single measure, but rather use it as a variable that can be *represented* by different measures. The discussion of validity of a social class measure requires prior theoretical conceptualization, which is complex and difficult to operationalize (2). For epidemiologists this issue is not considered highly relevant, as our primary interest lies in the relationship between social class and health outcomes, and not in the concept of social class itself. Different social class measures capture different aspects of social position, and are differently related to the distribution of health outcomes.

Social inequalities in health

Social inequalities in health occur globally and universally, both within developing and developed countries (3). This persists almost through the entire life course (4). Despite a conception of living in egalitarian societies, social inequalities in health even seem to be increasing also in the industrialized world (5). According to Susser, inequalities in health are just part of the social inequalities present in our society, and are one of their most convincing indices (1).

Attention towards this field was raised after the publication of the Black Report in 1982 (4), which showed the disparity in mortality by social class after the Second World War in England and other selected European countries. The socio-economic pattern of mortality was consistent – the lower social classes had higher mortality rates than the upper classes. The report introduced four models of causation; i) The artefact explanation, ii) Theories of natural or social selection, iii) Materialist or structuralist explanations, and iv) Cultural/behavioural explanations. The first approach suggests that both health and class are artificial variables that arise from attempts to measure social phenomena and that the relationship between them may itself be an artefact of little causal significance. The selection model regards social mobility – within or between generations – as affected by health status. In this approach, health is the independent variable and social class is the dependent variable in the model. People with poor health tend to move downwards in the social hierarchy, whereas healthy people move upwards. The materialist explanation emphasizes the role of economic and associated socio-structural factors in the distribution of health. Material and environmental affluence promote health while poverty damages health. The material explanation is related to a 'top-down' approach, which starts at the population level so as to ascertain the main factors that influence health status within the population. Studies at the group or population level are more often observational than experimental, and may also involve ecological studies of 'sick populations'

rather than analytical epidemiological studies of 'sick individuals'. The last paradigm, however, concerns the impact of cultural and behavioural factors on inequalities in health, which is usually described by individual (relative) risks. The strategy of using information on a low level to gain knowledge on a higher level can be denoted as a 'bottom-up' approach.

The study of social inequalities and cancer

The study of socio-economic differences in incidence and survival of cancer primarily belongs to the 'top-down' tradition (5), with several ecological or correlation studies published the last seventy years (6-20). The use of ecological designs has even been supported by an editorial in *The Lancet* that argued for the 'need to move away from the almost exclusive focus of research on individual risk, toward the social structures and processes within which ill-health originates, and which will be more amenable to modification' (21). Besides this recommendation, an increasing number of studies have been carried out through record linkages to national registers (22-32), mainly since the early 1990s. And besides McKinlay's view, record linkage studies are also supposed to offer valuable knowledge on the association between social class and cancer through their utilization of individual data on large populations. However, an important limitation of both ecological and record linkage studies is their lack of exposure data on the individual level. The two designs may contribute to reveal occupational or other environmental differences in cancer risk and generate hypotheses about the impact of lifestyle and behavioural factors on the socio-economic variation in risk. However, identifying these factors requires survey data with individual exposure information. The majority of the surveys performed are case-control studies and cross-sectional studies with selected exposure information. Although these studies obviously have contributed to the understanding of social class and cancer, they also contain certain weaknesses. The general criticism against case-control/cross-sectional studies concerns the

validity of exposure information collected after/simultaneously with information on outcome. The only way to put emphasis on causal cultural and behavioural explanations of social inequalities in cancer is within a prospective cohort design, but unfortunately, the number of such studies is very small due to their demand in both cost and time.

The relationship between socioeconomic status (SES) and cancer

The earliest publications investigating the socio-economic distribution of cancer were based on correlation studies in different regions of the USA (7-9). Already the first studies revealed a property of the distribution of both incidence and mortality that is characteristic; the socio-economic gradient in risk can turn in opposite directions, according to cancer site. The Registrar-General of England and Wales showed that among married women aged 35 to 65 in 1930 to 1932, both breast- and ovarian cancer mortality was 1.7 times as frequent in the highest as in the lowest social class. The opposite relationship existed for mortality from cancer of the uterus (8). The finding of a positive social gradient in the risk of breast cancer has later been frequently reported over more than seventy years, regardless of the choice of SES measurement. Additionally, excesses in high socio-economic strata were also seen among women in most populations for cancers of the colon, ovary, and skin melanoma. Low-class excesses were consistently encountered for female cancers of the oesophagus, stomach, cervix uteri and, less consistently, the liver (5). The results apply to both incidence and mortality, and operate across all socio-economic groups. For the remaining cancer sites no trends were seen, or the observed trends diverged between populations. The risk of lung cancer appeared to follow a negative socio-economic gradient in most populations, while a few studies from Latin American and Mediterranean countries showed the opposite trend. The overall risk of female cancers showed a negative social trend in some societies, but no trend in others, as in Scandinavia. Where a negative overall trend was observed, it seems to have

reinforced over time (5). One more recent study of time trends in SES differences for female cancers of the breast and genital organs reported widening differences for cervical cancer, but a weakly diminishing trend for breast cancer from 1971 to 1995 (28).

According to survival of cancer, the negative socioeconomic gradient seems to be more consistent than for incidence and mortality. Several ecologic studies together with a few record linkage studies have found an improved survival by increasing SES, both overall and for specific anatomic sites. Null associations are also reported, whereas inverse associations between SES and survival are rarely observed (33).

As described, SES differences in cancer vary between populations and within populations over time. The disparity between populations is naturally greatest between developed and developing societies, but also appears within the developed ones. The reasons for both intra- and inter-societal variation in risk by SES can be explained by two different aspects: the choice of SES measurement, and the socio-economic profile in health exposures.

Measurement of SES

SES is an important variable in studies of health and is frequently included in epidemiological studies. Some studies treat SES as the variable of primary interest according to the health outcome, but the majority considers SES only as a potential confounding factor (2). However, the manner in which SES is measured may have substantial impact on the estimates (34). The three indicators most often used as single measures of social class are occupation or socio-economic group, income, and education.

Occupation-based measures

In the earliest studies of social inequalities in health in the United Kingdom, occupation was assessed according to the British Registrar General's scale (35). This classification system was developed in 1911 to allocate the occupation of the head of the household to one of five social classes: I, professional; II, intermediate; III skilled (non-manual and manual); IV, partly skilled; and V, unskilled (2). During almost hundred years, the scale has been regularly revised to take into account changes in skills and status and to incorporate new occupations, and it is still fundamental for most measures of occupational class (2).

Income

Income is usually measured as gross household income, with or without adjustment for family size. It can be recorded on a continuous scale or grouped into categories, which is most common. The variation in income level over time and between societies hampers any determination of standard categories, so the division is often based on the income range of the study subjects.

Education

The most commonly used measure of education is the number of school years completed. As with income, education can be included in the analyses as a continuous or categorical variable. The categorization may differ between studies, but usually refers to levels in the educational system of the respective countries.

Comparison of SES measures

The benefit of a certain SES measurement depends on its ability to discriminate across socio-economic strata according to the present outcome, which is conditioned by its strength of association with underlying causal factors. In addition, the categorization of the selected SES measurement affects the relative estimates of health inequalities.

Education has become a popular single indicator of social class mostly because of its association with many lifestyle characteristics and the simplicity of collecting education data (2). As a consequence of its association with lifestyle, education is strongly associated to lifestyle-related diseases. MacMahon et al. found that years of education was the measure of social class that was most closely related to breast cancer risk (36). Education has also been found to be more important than income in predicting both total mortality (37) and coronary heart disease (37;38), whereas other studies have suggested occupational class (39) and income (40) to be the strongest social class determinants of mortality.

The figures below show comparisons of education and income as SES measures according to three different health outcomes among the 80,000 participants in The Norwegian Women and Cancer Study (NOWAC).

Figure 1. Age adjusted relative risks of breast cancer by years of education. The NOWAC study.

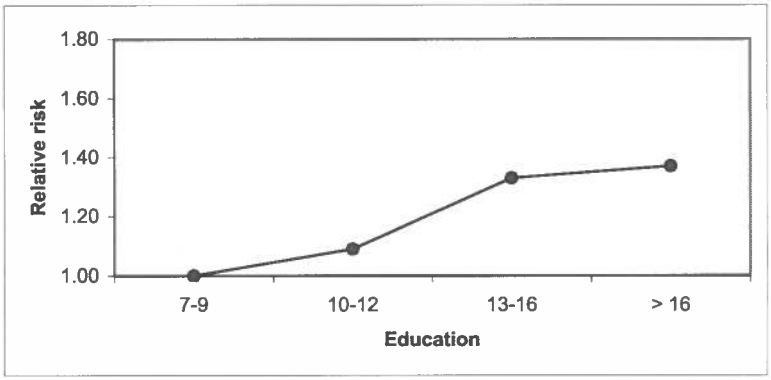


Figure 2. Age adjusted relative risks of breast cancer by level of gross household income.

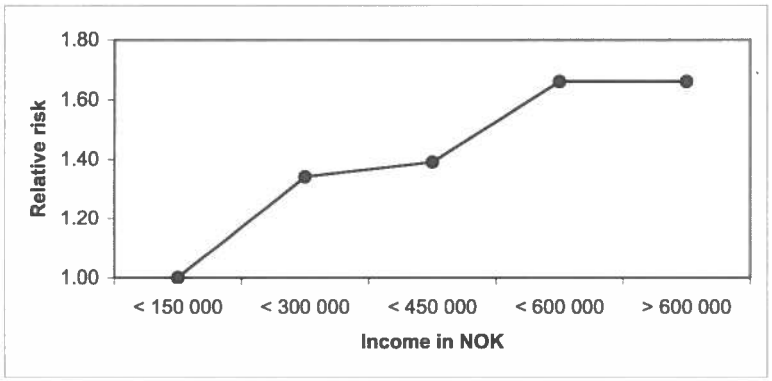


Figure 3. Age adjusted relative risks of death by years of education. The NOWAC study.

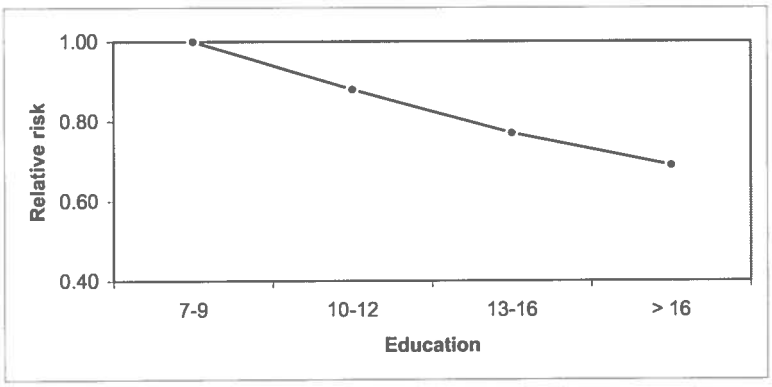


Figure 4. Age adjusted relative risks of death by level of gross household income. The NOWAC study.

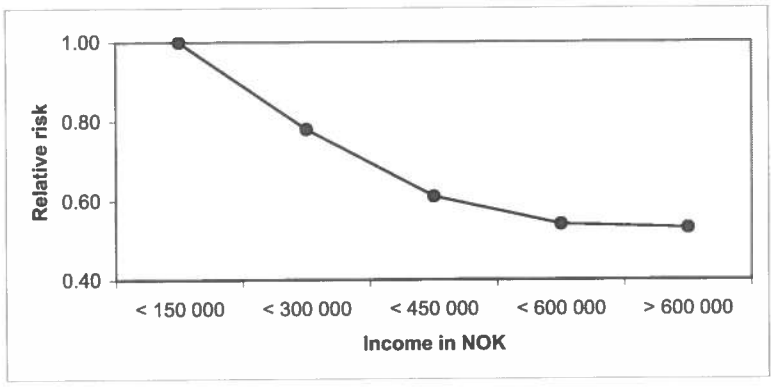


Figure 5. Age adjusted odds ratios of reporting poor health by duration of education. The NOWAC study.

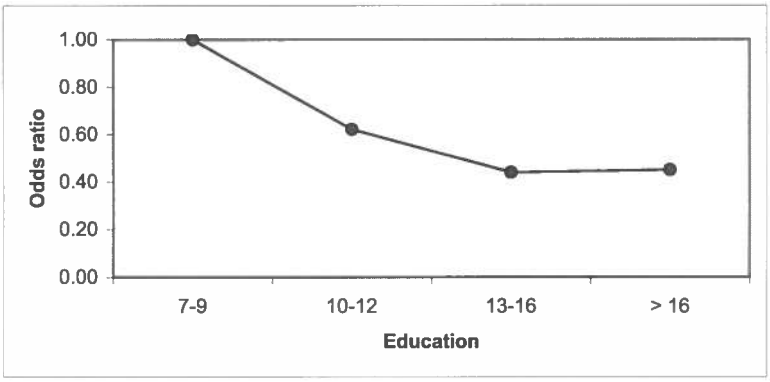
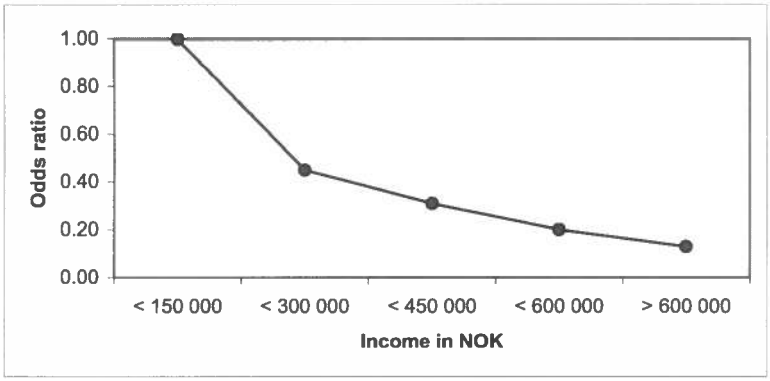


Figure 6. Odds ratio of reporting poor health by level of gross household income. The NOWAC study.



For all three outcomes, the figures reveal a wider disparity in risk by income than by education, which is verified by computing the likelihood ratio statistics for the models subject to comparison. For total mortality and perceived health the risk differences by income are

supposed to arise partly by social selection, and thus reinforce the risk differences seen by the level of education.

Socio-economic profile in health exposures

Even at a certain level of a specific SES measure, the distribution of health related lifestyle characteristics and habits varies between populations, between age cohorts within populations, and by calendar time within age cohorts. Accordingly, the distribution of disease risk by SES varies. A few examples of socio-economic variation in smoking habits are given below, as smoking is an important source of social inequalities in cancer. In developing countries, smoking prevalence is highest among socio-economic privileged groups, with high rates of growth, providing good evidence of the success of the tobacco multinationals' efforts to open new profitable markets (5). In developed countries smoking is most frequent among people with low SES, and while the overall rates decrease in many countries, the decrease is slower within the low SES groups (5). The latter is illustrated by Figure 7, which shows annual changes in smoking prevalence by education for nine European countries (41). The figure displays an increasing gap between educational groups, contributing to wider SES differences in health over time.

Figure 7. Annual change in smoking prevalence between 1985 and 2000 by country and education: women (25–79 years). Adjusted by age. L, low education group; H, high education group.

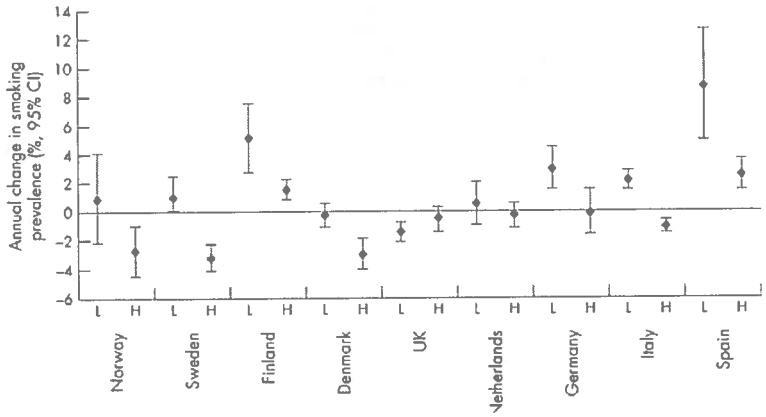


Figure 7 covers changes in smoking habits both between age cohorts and by calendar time, whereas Figure 8 gives the distribution by education of daily smokers within two age groups of women, measured contemporarily. Figure 9 shows the distribution by education of daily smokers within the same cohort of women, measured at two points of time.

Figure 8.The proportion of daily smokers within two age groups by the duration of education in years. The NOWAC Study 1996.

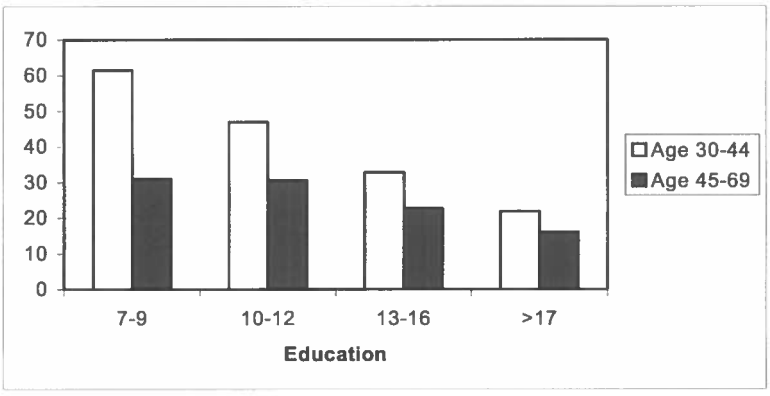
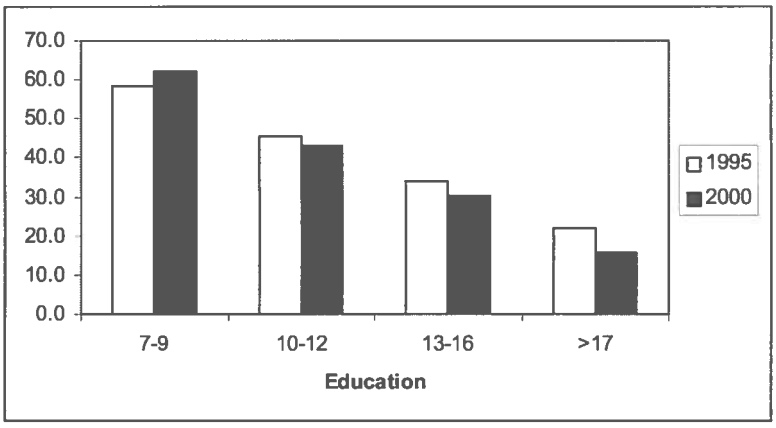


Figure 9. The proportion of daily smokers at two time points amongst 2,807 women born between 1927 and 1965 by duration of education in years. The NOWAC Study.



Multiple imputation

Usually, the questionnaires in a survey are not completely filled in by all study participants, and then missing values occur. All regression models require complete data sets, so an individual with missing information on any variable included in the model is automatically excluded from the analyses. Consequently, we are unable to utilize the remaining information on that individual.

There are several available techniques for handling missing data, among them *imputation*, which has become very popular the last decades. To impute means to replace an unobserved value with a predicted one, where the prediction is somehow based on the observed values. A proper imputation method should take into account all useful information, both from the response sample and from the individual subject to imputation. If each missing value is replaced with only one predicted value, we call it *single imputation*, which is suitable if the imputed data is used only for point estimation. On the contrary, if we need to consider the variation of the imputed data, single imputation is insufficient. The reason is that the imputed values are treated as if they were observed, and thus their true variability will be underestimated in the statistical analyses. One strategy for solving this problem is to "blow up" the estimated variance, which is possible by using *multiple imputation.* When we replace each missing value with several predicted ones, we can use the variation among these predicted values as a tool of increasing the variance estimate. The theory of multiple imputation was developed by Donald B. Rubin (42), who proposed a formula for the variance estimation which correctly reflects the true variability of imputed data. However, the requirement for this formula to be valid is that the imputed values are drawn from a Bayesian posterior distribution.

AIMS OF THE THESIS

- To examine how the risk for different cancer sites, and in particular breast cancer risk, varies with the level of education, and to identify factors that explain this variation

- To examine how the survival of cancer, both overall and for specific anatomic sites, varies with different measures of socioeconomic status, and to identify factors that explain this variation

- To develop and evaluate a simple, Non-Bayesian multiple imputation method for the accommodation of continuously scaled missing data in survey research.

MATERIALS AND METHODS

Study populations

The present thesis is based on data from The Norwegian-Swedish Women's Lifestyle and Health Study (WLH), and The Norwegian Women and Cancer Study (NOWAC). WLH was initiated in 1991/92 as a population-based cohort study, where 196 000 Norwegian and Swedish women born between 1942 and 1962 were invited to participate. Altogether 106 841 women returned a questionnaire, yielding a crude response rate of 54.5 %. In 1996, the Norwegian part of WLH expanded when additional 44 851 women born from 1927 to 1965 were included, and thus the NOWAC Study was established. In 1998, the initial subcohort received a second questionnaire, which 81.5 % responded to. Both WLH and NOWAC are described in detail previously, see (Lund), http://uit.no/21/6675/, and http://www.meb.ki.se/research/projects/.

WLH is the data source of Paper I, whereas Papers II, III, and IV are based on data from NOWAC.

The questionnaires

The initial cohort members from 1991/92 filled in and returned a four-page questionnaire[1] providing information on a wide range of lifestyle factors potentially related to cancer, with a focus on oral contraceptive use, reproductive factors, and UV light exposure. SES was measured as the total number of years attending school. The Norwegian and Swedish questionnaires were similar, but not identical. In NOWAC 1996, the questionnaires varied in length between two and eight pages, with a core set of questions retained from the original

[1] Due to a methodological sub-study, a few women received a two- or six-page questionnaire

version. The six- and eight-page questionnaires included an extensive assessment of dietary habits, following growing attention to the possible association between the consumption of fish and cancer risk. The majority of the invited women were mailed the eight-page version. The participants were also asked for total gross household income, as an additional measure of socio-economic status. The second mailing in 1998 included an eight pages questionnaire similar to the version from 1996.

Identification of cancer, death and emigration

Follow-up was achieved through linkages between the cohort data set and various population-based registries. These linkages were possible through the use of the individually unique national registration numbers present in all national registries in Norway and Sweden (43). We obtained information on the dates of death for deceased persons from the registers of deaths, and on the dates of emigration from the registers of population migration. The Cancer Registries of Norway and Sweden provided data on prevalent cancer cases at cohort enrolment and incident cancers diagnosed in the cohort during the follow-up. These registers are considered to be virtually complete.

SUMMARY OF RESULTS

Paper I. Education and Risk of Breast Cancer in The Norwegian-Swedish Women's Lifestyle and Health Cohort Study

In this article we examined the association between the level of education and the risk for breast cancer among 102,860 women enrolled in The Norwegian-Swedish Women's Lifestyle and Health Study. 1,090 incident primary invasive breast cancer cases were reported to the National Cancer Registies during the follow-up, which ended on December 31st, 1999. Self-reported number of years of education was used as the only available measure of SES. Women with more than 16 years of education had a 36 % increased risk of developing breast cancer compared to the lowest educated women (7-9 years) (Age adjusted RR=1.36, 95% CI: 1.10, 1.68). This relationship was slightly stronger among postmenopausal (RR 1.51 95% CI....) than among premenopausal (RR 1.25, 95% CI...) women. In both groups, however, the relative risk estimates turned close to the unity when adjustments for parity, age at first birth, body mass index (BMI, i.e. weight in kg divided by height in metres squared), height, age at menarche, menopausal status, use of oral contraceptives, and consumption of alcohol were made. The overall multivariate relative risk among the highest educated women was 1.04 (95% CI 0.82-1.32). The results of our study suggest a clear positive gradient in the risk of breast cancer by level of education, which can be fully explained by established breast cancer risk factors.

Paper II. Explaining the Socioeconomic Variation in Cancer Risk in The Norwegian Women and Cancer Study

This article studies the association between level of education and all cancer sites, using data from The Norwegian Women and Cancer Study including 93,638 women. A total of 3,259 incident primary invasive cancer cases were diagnosed during follow-up, which ended on December 31st, 2001. Also in this study self-reported education was the only available SES measure. Besides a similar overall risk of female cancers by the level of education, we observed differing risks between educational groups for cancers of the lung, breast, cervix, kidney, and skin melanoma. Women with more than 16 years of education had an increased risk of breast cancer (RR=1.46, 95% CI: 1.19, 1.79), and a decreased risk of lung cancer (RR=0.30, 95% CI: 0.13, 0.70) and cervical cancer (RR=0.38, 95% CI: 0.17, 0.85), compared to the lowest educated women (7-9 years). The middle educated (13-16 years) had the lowest risk of kidney cancer (RR =0.24, 95% CI: 0.08, 0.71), while the risk of skin melanoma was highest among women with 10-12 years of education (RR=1.53, 95% CI: 1.05, 2.24), compared to the lowest educated women. After multivariate adjustment for potential confounders related to level of education the variation in cancer risk according to educational levels declined into non-significance for all these sites.

Paper III. Socioeconomic status, intergenerational change in socioeconomic status and survival of cancer. The Norwegian Women and Cancer Study

In this article we examined the association between different measures of SES and survival of cancer, both overall and for selected anatomic sites. We used data from The Norwegian Women and Cancer Study, a prospective cohort study including 91,814 women, of who 3,936 incident cancer cases were diagnosed during follow-up, and 968 women died within five year after the time of diagnosis. We observed an overall negative socioeconomic gradient in cancer survival when SES was measured by education or income, which was significant for ovarian cancer only in the site-specific analyses. The estimates for colorectal cancer showed increasing risk of mortality by increasing years of education. We found that the unequal socioeconomic distribution of smoking status prior to diagnosis contributed considerably to the poorer survival in low SES groups. The study of cancer survival according to intergenerational change in SES revealed the poorest survival in women who had experienced a downward change in SES, whereas women who had advanced in SES since adolescence had a higher survival than others. Tentative adjustment for both tumour stage at diagnosis and a variety of lifestyle factors did not alter the mortality estimates meaningfully.

Paper IV. A Simulation Study of Simple Residual Multiple Imputation

The fourth article is a methodological study concerning the issue of missing data in survey research. One common way of handling this problem is to use multiple imputation techniques within a Bayesian framework, as developed by Donald Rubin (42). This article proposes a Non-Bayesian approach to multiple imputation, and shows how a frequentistic, well-known procedure called simple random imputation can give valid inference of imputed data by introducing a modification of Rubin's formula for variance estimation. The evidence presented here is based on both analytic results and simulation studies, including a real data example from The Norwegian Women and Cancer Study. By executing a number of simulations we have calculated the confidence levels attained by the proposed variance estimation formula, where the indicator of statistical validity is the agreement with the chosen nominal confidence level.

Based on the satisfactory results from this study it is claimed that simple random imputation yields valid statistical inference of imputed data sets when a modified version of Rubin's variance estimation formula is applied.

GENERAL DISCUSSION

Statistical methods

The proportional hazards model

The present investigation of socio-economic status in relation to cancer incidence and survival is an example of a prospective study. Several exposures are measured at time of enrolment into the cohort, and the participants are followed over time until the event of interest occurs, or they are censored. Within this design, the proportional hazards model, proposed by D. R. Cox (44), provides efficient estimates of the effect of the explanatory variables on time-to-event.

The *hazard* for an individual *i* at time *t* refers to the probability of the event to occur, which can be expressed as

$$h_i(t) = h_0(t)\exp\{\beta_1 x_{i1} + ... + \beta_k x_{ik}\}$$

where X_1 ... X_k is the set of k explanatory variables, $\beta_1,...,\beta_k$ is the vector of regression coefficients, and $h_0(t)$ is the baseline hazard at time t, representing the hazard for a person with the value 0 for all explanatory variables.

By dividing both sides of the above equation by $h_0(t)$ and taking logarithms, we obtain:

$$\ln(\frac{h_i(t)}{h_0(t)}) = \beta_1 X_{i1} + ... + \beta_k X_{ik}$$

$h(t) / h_0(t)$ is called the *hazard ratio*.

In prospective studies, the value of a covariate may change with time, and a covariate is said to be *time-dependent* if the difference between its values for two different individuals changes with time.

In this case, the model may be written as

$$h(t) = h_0(t)\exp\{\sum_{i=1}^{k_1}\beta_i X_i + \sum_{j=1}^{k_2}\beta_j X_j(t)\}$$

where $X_1,...,X_{k_1}$ are fixed, while $X_1,...,X_{k_2}$ are time-dependent covariates.

In the present thesis, participation in mammography screening is treated as a covariate that may change value over time in the analysis of breast cancer (Paper II).

The proportional hazards assumption

The Cox proportional hazards model assumes that the hazard ratio comparing any two specifications of predictors is constant over time. Equivalently, this means that the hazard for one individual is proportional to the hazard for any other individual, where the proportionality constant is independent of time (44).

In the analyses of SES and cancer risk in Paper II, the assumption has been carefully evaluated both graphically and by a goodness-of-fit test for all explanatory variables of substantial importance. The assumption was found to be satisfied with a few exceptions, and thus, the overall model fit was considered proper.

Methodological considerations

Self-reported versus register-based measures of education

The measurement of education in The NOWAC Study and WLH is based on the participants' answer to the question of how many years they attended school. Probably, the answer includes all years they spent at school, regardless of whether the education was completed. On the contrary, the level of education recorded in the national register represents the highest

completed education, and the length of education derived from the register corresponds to expected duration, not the time virtually spent at school or in higher education. The two measures produce considerably different distributions of education, as in the following example from the sub-cohort of The NOWAC Study enrolled in 1996 (Table 1):

Table 1. Distribution of education according to register based and self-reported information. The NOWAC Study 1996 (n=46,368).

Level of education	REGISTER DATA %	SELF-REPORTED %
7-9	25,9	35,6
10-12	51,6	31,8
13-16	19,8	21,4
>=17	2,1	9,9
Unknown	0,6	1,3

The distribution of the self-reported data shows a markedly wider spread than the register based data, with both the upper and lower groups being much larger.

As the two measures of education are qualitatively different, they are also supposed to measure different effects. The register-based measure is more strongly related to educational status, whereas the self-reported one to a greater extent measures the consequences of the time spent as a student. The different nature of these two measures hampers any comparison of the distributions by education between the present studies and national figures, and therefore this is omitted in the following sections.

Validity

The validity of a study can be separated into two components; internal and external validity. Internal validity refers to the validity of the inferences drawn as they pertain to the members of the source population, whereas external validity refers to the generalizability of the results

(45). Various types of biases can detract from internal validity, where bias can be defined as the deviation of results or inferences from the truth, or processes leading to such deviation. Biases concern *systematic errors* that decrease the validity of estimates, and do not involve random variation. Biases are usually classified as selection bias, information bias, and confounding.

Selection bias

Selection bias refers to a distortion in the effect estimate resulting from the manner in which subjects are selected for the study population, or from selective losses from the study population prior to data analysis (46).

Selection of study subjects according to a certain characteristic or exposure variable does not itself cause biased estimates, unless the association of interest between exposure and outcome is affected. The following elucidates this issue regarding the present studies.

Like many other sample surveys, the NOWAC study is overrepresented by highly educated participants compared to the source population. From Statistics Norway we have received the distribution of educational level for both responders and the total invited sample of The NOWAC Study 1996, which is given in table 2:

Table 2. Distribution of education among responders and the total invited sample of The NOWAC Study 1996.

Level of education	Total sample (n=82,478) %	Responders (n=46,368) %
7-9	34,0	25,9
10-12	48,2	51,6
13-16	15,4	19,8
>=17	1,7	2,1
Unknown	0,8	0,6

The extent of selection by education is somewhat higher than previously published from another subcohort of The NOWAC Study (47), presumably due to a wider distribution of age in the present cohort. The data here show an increasing overrepresentation of highly educated women by increasing age. However, selection by education is not itself a threat against the validity of the relative risk estimates. The crucial question is whether the association between education and health behaviour varies according to response. The question is impossible to answer exhaustively due to the lack of information on non-responders, but nevertheless the attempt is made to give a superficial assessment of the possible extent of selection bias in this study.

The only available information on exposures among the total invited sample is the distribution of parity. The data is provided from the national birth register and comprises the same subcohort as described above, all women invited to The NOWAC Study in 1996 (table 3).

Table 3. Distribution of number of children among responders and the total invited sample of The NOWAC Study 1996.

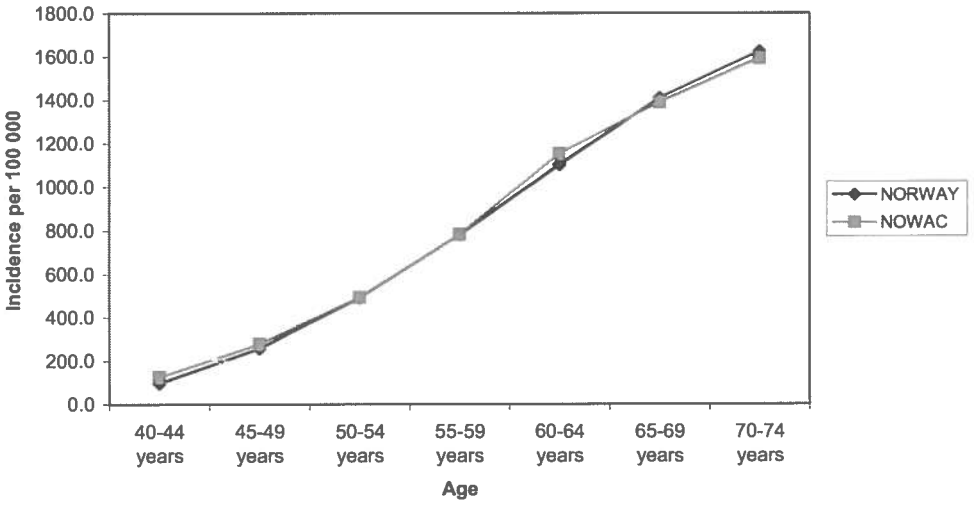
Number of children	Total sample (n=82,997) %	Responders (n=46,504) %
0	9,5	7,5
1	12,0	11,2
2	35,3	37,6
>=3	43,2	43,7

In general, parity decreases with increasing level of education, and thus we would expect fewer children among the responders if they behaved similarly to the total sample according to parity. Instead we observe a higher number of children, and in particular a lower number of nulliparous women in the response group, which is reasonable owing to the focus on reproductive history in the questionnaires. However, this example indicates the presence of a

selection bias affecting the relative risks of breast cancer according to level of education. What we need to assess is the potential magnitude of the bias based on available information. First, we can estimate the change in incidence rates by the shift in the distribution of education and parity from the total sample to the responders. If we apply the marginal incidence rates for each subgroup from The NOWAC Study we get the following results: The observed selection by education is expected to increase the overall incidence rate of breast cancer by 3 cases per 100,00 person-years, whereas the selection by parity is expected to decrease the rate by 1 case per 100,000 person-years.

Second, we can compare the observed incidence rates of breast cancer from The NOWAC Study with the expected rates from national figures, as given in Figure 10.

Figure 10. Cumulated incidence rates of breast cancer 2000-2003. The NOWAC Study and national figures

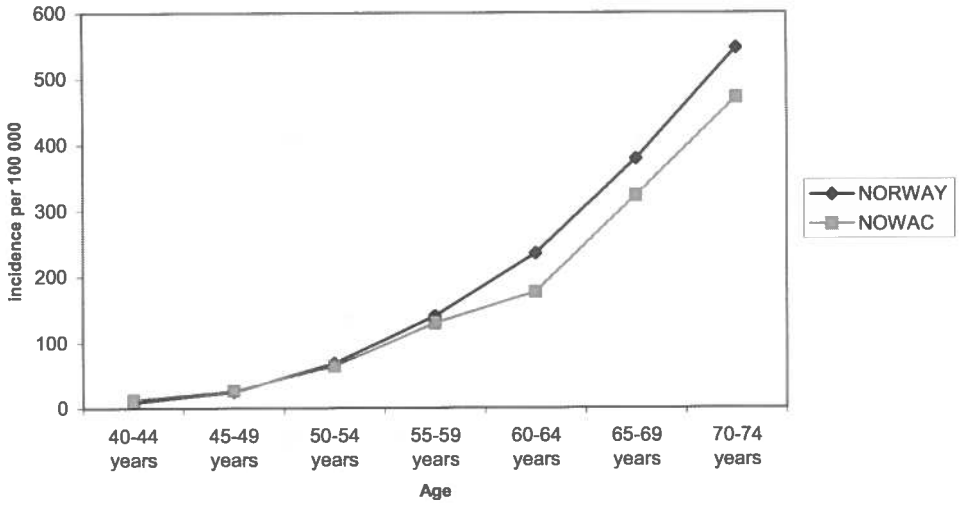


The cumulated incidence rates of breast cancer from The NOWAC Study coincide closely with national figures, which is reassuring concerning the presence of selection bias. However,

the overall agreement could potentially cover considerable alterations of risk by the level of education compared to the true parameters of the source population, but we believe this is unlikely. Moreover, a Swedish record linkage study of level of education and cancer risk found a relative risk of breast cancer of 1.37 for highly educated (>= 13 years) women compared to low educated (< 9 years) (25), which is very close to the observed RR=1.34 in The NOWAC Study.

For lung cancer, the deviance of the NOWAC incidence rates from national rates is slightly higher (Figure 11), but is significantly different only for the age group 65 to 69 years. The gap between the two rates increases with increasing age, which probably reflects an increasing under-representation of smokers by growing age.

Figure 11. Cumulated incidence rates of lung cancer 2000-2003. The NOWAC Study and national figures.



When it comes to smoking, the extent of selection is difficult to assess because of the lack of information on the true prevalence of smokers in the source population. Official statistics on

smoking habits are based on information from sample surveys, which may also be exposed to selection. Thus, if we compare the observed proportion of daily smokers in The NOWAC Study with figures from Statistics Norway, we need to keep in mind the lack of a "gold standard". The sample size of this national survey is n=5000 (in total for both genders), with a response rate of about 70 %.

The distribution of daily smokers for selected age groups is presented in Table 4. The proportions of The NOWAC Study are age standardized within the ten year age groups, using the Norwegian female population as the standard.

Table 4. Distribution of daily smokers in selected age groups. The NOWAC Study 1996 compared with figures from Statistics Norway 1996.

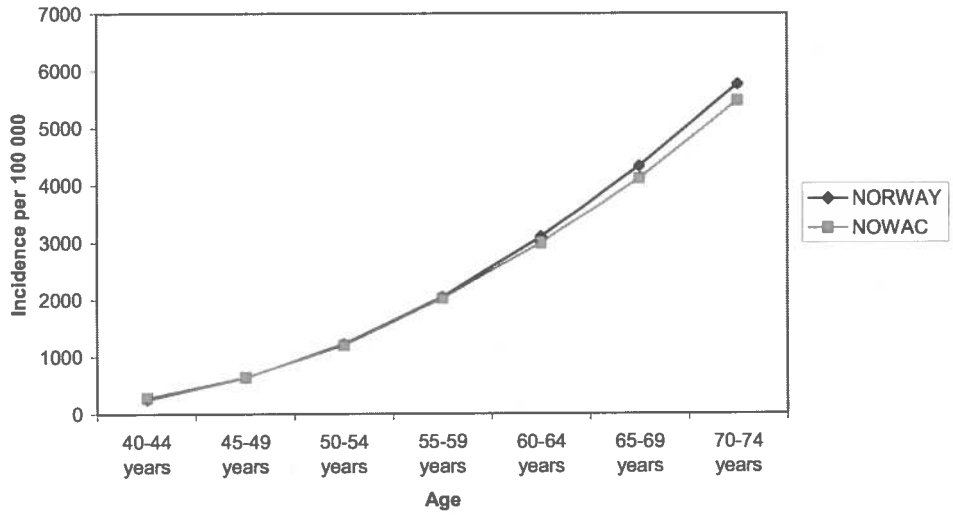
	NORWAY	The NOWAC Study
45-54 years	37 %	34.2 %
55-64 years	29 %	24.9 %

The deviation between The NOWAC Study and the national figures according to prevalence of daily smoking seems to increase with increasing age, which corresponds to the deviation in lung cancer incidence rates.

The Swedish record linkage study referred to above reported a relative risk of 0.43 of developing lung cancer among the highest educated group compared to the lowest. The corresponding estimate from The NOWAC Study was 0.37.

The overall risk of female cancer in The NOWAC Study compared to national figures is given in Figure 12.

Figure 12. Cumulated incidence rates of all cancers 2000-2003. The NOWAC Study and national figures.



Whereas the rates coincide almost completely among the younger age groups, we observe a slightly increasing gap among the elderly women. However, all deviations are non-significant. The conclusions concerning the potential impact of selection bias in the study of social inequalities and cancer in The NOWAC Study must be as follows: There is certain evidence of a present selection expressed as a difference in the socio-economic profile in health exposures according to response. Nevertheless, all material available to assess the potential resulting bias indicates no substantial effect on the relative estimates.

Information bias

Systematic error in a study can arise because the information collected on study subjects is erroneous (48). If the actual variable is measured on the categorical scale, the error implies that subjects are misclassified into wrong categories of either exposure or disease.

Misclassification of subjects may be *differential* or *non-differential*, referring to the mechanism for misclassification. For exposure misclassification, the misclassification is non-differential if it is unrelated to the occurrence or presence of disease. If the misclassification of exposure is different for those with and without disease, it is differential. Similarly, misclassification of disease is non-differential if it is unrelated to exposure; otherwise, it is differential. Non-differential misclassification of a dichotomous exposure will always bias an effect towards the null value, whereas non-differential misclassification between three or more exposure categories together with differential misclassification may either overestimate or underestimate an effect.

Misclassification of cancer diagnoses can be considered as negligible, according to the high quality of data provided by the Norwegian and Swedish cancer registries. On the other hand, potential non-differential misclassification of exposure variables cannot be ruled out. For instance, underreporting of alcohol consumption is a well known problem within sample surveys, which may lead to an overestimation of the effect.

Confounding

Confounding is the systematic error generated when another factor that causes the disease under study, or is otherwise related to it, is also related to the exposure under investigation (49).

In the present studies of social inequalities and cancer risk, the main purpose was to identify the underlying causal factors of the observed variations in risk by SES. The present data contain comprehensive information on exposures that might affect cancer risk, which offer a great opportunity to detect the influential factors. Whenever a potential causal factor was found, its aetiological relevance was evaluated according to previous studies (49), unless it

could be considered an established risk factor. Nonetheless, residual confounding cannot be completely ruled out, but we believe it is unlikely to be of significant importance.

Generalizability

The generalizability of a study depends on the study group's being of a representative subgroup of the target population (45). In the present studies of SES and cancer risk, the relative estimates of risk by socio-economic status are conditioned by the underlying relationship between SES and actual underlying exposures. Thus, the generalizability of the estimates must be restricted to populations with a similar SES profile in risk behaviour. However, though the size of the estimates of cancer risk by SES may be of limited generalizability, the existence of the identified causal factors as contributors to SES variation in risk of cancer is considered to be valid for all female populations with a socio-economic variation in the distribution of the actual exposures.

The application of multiple imputation in regression analyses

In our studies of SES and cancer, only women with complete information on all covariates were included in the respective site-specific analyses. Consequently, this prohibited the utilization of the available information on subjects with item non-response on one or more variables. This issue exemplifies a general problem in epidemiological research, and has been an important motivation to investigate the field of multiple imputation. Preliminary, the method developed in the present thesis has been applied only to univariate imputation, but the next step will be to extend it to treat imputation of several variables simultaneously. Moreover, the appropriateness of the method implemented in the Cox model will be further

examined to show that Non-Bayesian multiple imputation can offer an efficient contribution to solve the problem of missing values as experienced in the SES and cancer studies.

As an anticipation of employing the SRI multiple imputation method into the Cox model, let us consider some analyses using both imputed and non-imputed data from the Norwegian Women and Cancer Study. The association of interest is the risk of breast cancer by years of education, and we want to study the influence on the risk estimates and their corresponding confidence intervals when one covariate is subject to multiple imputation. The Non-Bayesian SRI method is applied, and the variances are estimated using the modification of Rubin's formula suggested in paper IV. The background theory of Bjørnstad (50) is developed under the MCAR (missing completely at random) assumption, but the example follows the MAR (missing at random) assumption, which is probably sufficient.

The study population of paper III comprises 83,581 women with complete information on all variables included as covariates in the analysis of breast cancer risk by education; age, parity, age at first birth, body mass index, ever use of hormonal contraceptives, current use of HRT, and consumption of alcohol. Further 5,343 women miss information on alcohol consumption only.

Table 5 A shows the relative risk estimates of the completely observed sample of 83,581 women.

Table 5 A. Relative risks (RR) with 95 % confidence intervals of developing breast cancer in relation to years of education. N=83,581, all completely observed

Adjustment	No of cases	Years of education			
		7-9	10-12	13-16	>=17
Age	1,911	1.00 (ref.)	1.11 (0.98-1.25)	1.21 (1.06-1.37)	1.32 (1.13-1.55)
Multivariate		1.00 (ref.)	1.03 (0.91-1.16)	1.07 (0.94-1.22)	1.10 (0.93-1.30)

In table 5 B, the 5,343 missing values of alcohol consumption are replaced by imputed values in the multivariate analysis, which increase the number of breast cancer cases from 1,911 to 2,014. We assume the observations of alcohol consumption to be gamma distributed.

Table 5 B. Relative risks (RR) with 95 % confidence intervals of developing breast cancer in relation to years of education. N=88,924, 6 % imputed values for alcohol consumption.

Adjustment	No of cases	Years of education			
		7-9	10-12	13-16	>=17
Age	2,014	1.00 (ref.)	1.08 (0.96-1.21)	1.19 (1.05-1.35)	1.30 (1.11-1.51)
Multivariate		1.00 (ref.)	1.00 (0.89-1.12)	1.05 (0.92-1.20)	1.08 (0.92-1.27)

In the real data example from the NOWAC study described above, the missing rate of alcohol is only 6 %. The confidence intervals for level of education become slightly shortened after imputation, and a slightly higher proportion of the variation in risk is explained after multivariate adjustment. In order to illustrate the benefit of multiple imputation more clearly, let us assume the missing rate to be considerably higher. Following the MAR assumption, we delete 40 % of the observations of alcohol consumption from the data file. High values are more likely to be deleted than low values. Subsequently, the deleted values of alcohol are

replaced by imputed values, and the resulting sample of 83,581 women are analysed as previously.

Table 5 C shows the estimates for the remaining sample of N=50,554 after exclusion of 40 % of the women. In table 5 D the original sample of 83,581 women is analysed after imputation of alcohol consumption.

Table 5 C. Relative risks (RR) with 95 % confidence intervals of developing breast cancer in relation to years of education. N=50,554, all completely observed.

Adjustment	No of cases	Years of education			
		7-9	10-12	13-16	>=17
Age	1,098	1.00 (ref.)	1.13 (0.97-1.32)	1.24 (1.05-1.46)	1.38 (1.11-1.70)
Multivariate		1.00 (ref.)	1.07 (0.91-1.25)	1.12 (0.94-1.33)	1.16 (0.93-1.45)

Table 5 D. Relative risks (RR) with 95 % confidence intervals of developing breast cancer in relation to years of education. N=83,581, 40 % imputed values for alcohol consumption.

Adjustment	No of cases	Years of education			
		7-9	10-12	13-16	>=17
Age	2,014	1.00 (ref.)	1.11 (0.98-1.25)	1.21 (1.06-1.37)	1.32 (1.13-1.55)
Multivariate		1.00 (ref.)	1.03 (0.91-1.16)	1.07 (0.94-1.23)	1.11 (0.94-1.31)

A comparison of the multivariate adjusted estimates from table 5 C and 5 D reveals a substantial shortening of the confidence intervals after imputation of one covariate. If we

compare table 5 A with 5 D we also notice that the multivariate adjusted estimates are similar for the imputed and the non-imputed sample of 83,581 women.

The relative risk of breast cancer by consumption of alcohol for the respective models is given in table 6:

Table 6. Relative risks (RR) with 95 % confidence intervals of developing breast cancer in relation to daily consumption of alcohol (per 10 grams) in different models of imputation

Cases/cohort	Proportion of imputed values	RR (95% CI)
1,098 / 50,554	0	1.09 (1.00-1.20)
1,911 / 83,581	40	1,10 (1.02-1.19)
1,911 / 83,581	0	1.10 (1.04-1.16)
2,014 / 88,924	6	1.10 (1.04-1.16)

The results can be summarized as follows:

- Multiple imputation of one covariate reduced the estimated variance of the relative risks for the variables of interest
- The estimated relative risk for the covariate itself was similar with and without multiple imputation, with a slightly reduced variance after imputation

CONCLUSIONS

The main conclusions:

- Socio-economic variation in cancer risk can be explained by known risk factors. According to the paradigms of explanation introduced in the Black report (4), the findings in these papers emphasize cultural and behavioural factors as the source of social inequalities in risk of cancer.

- The variation in cancer survival by socio-economic status at present seems to be related to the unequal distribution of smoking status prior to diagnosis, rather than to prognostic factors or socio-economic differences in treatment.

- Intergenerational change in SES seems to affect the likelihood of surviving from cancer

- Non-Bayesian multiple imputation can provide valid statistical inferences within any generalized linear regression model if a modification of Donald Rubin's variance formula for parameter estimates is applied.

FURTHER PERSPECTIVES

- The knowledge about both causes and health consequences of a drift from parental to own socio-economic position need to be improved.

- The role of lifestyle or behavioural factors in the progress of cancer need to be further explored.

- The method of Non-Bayesian multiple imputation should be extended to treat categorical variables, and to impute several variables simultaneously. The appropriateness of the suggested method implemented in a proportional hazards regression analysis must be verified.

Hypotese-endring
Meta-analyser

Effektforskjeller
Eksposisjon endres over tid

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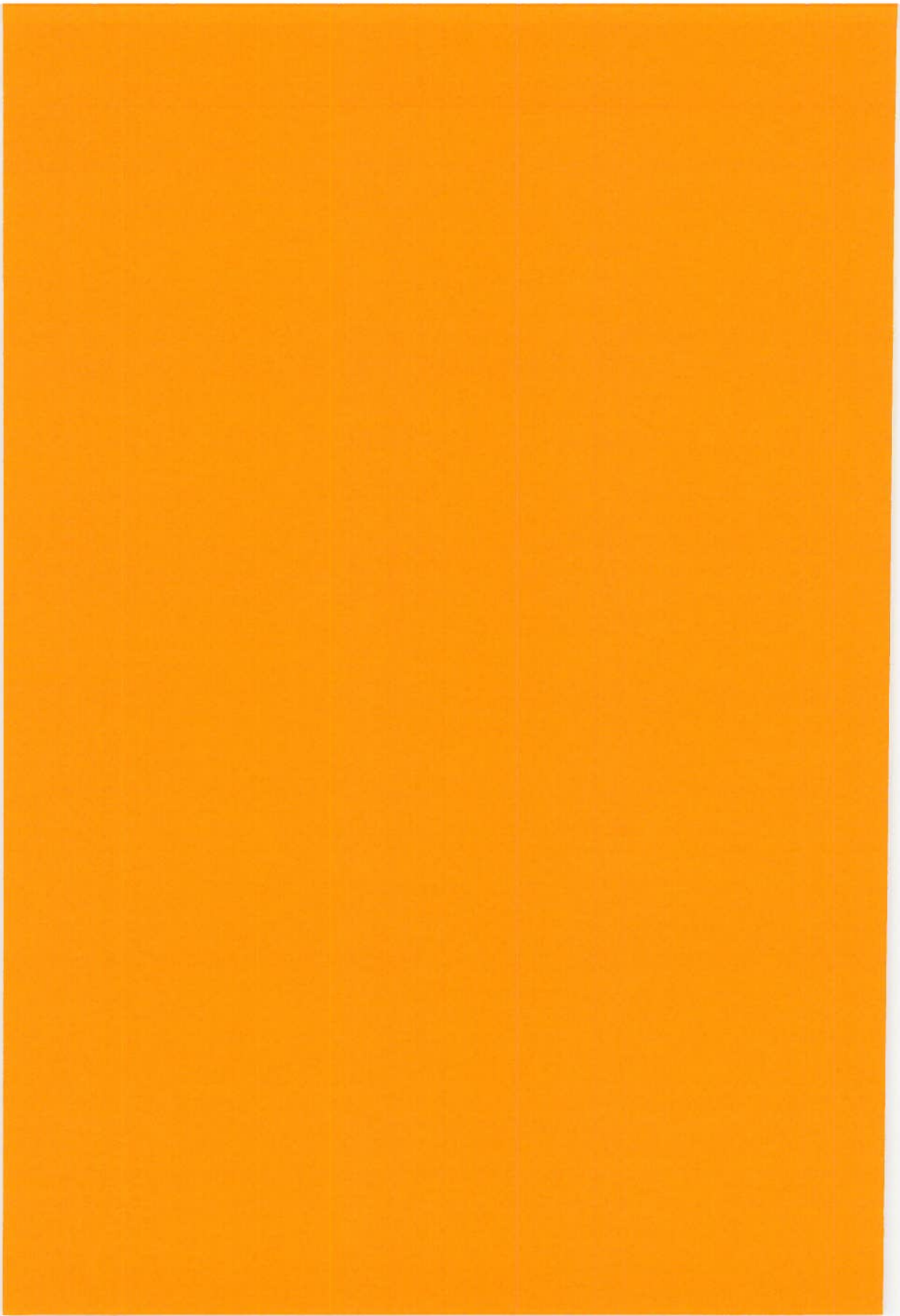
Paper I



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EDUCATION AND RISK OF BREAST CANCER IN THE NORWEGIAN-SWEDISH WOMEN'S LIFESTYLE AND HEALTH COHORT STUDY

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A positive relationship between level of education and female breast cancer risk is well supported by scientific evidence, but few previous studies could adjust for all relevant potential confounding factors. The authors' purpose was to examine how risk for breast cancer varies with level of education and to identify factors that explain this variation, using data from a prospective cohort study including 102,860 women from Norway and Sweden who responded to an extensive questionnaire in 1991/1992; 1,090 incident primary invasive breast cancer cases were revealed during follow-up, which ended in December 1999. The Cox Proportional Hazards Model was used to calculate relative risks (RR) with 95% confidence intervals (CI). Women with more than 16 years of education had a 36% increased risk compared to the lowest educated (7–9 years) (Age adjusted RR=1.36, 95% CI: 1.10, 1.68). This relationship was slightly stronger among postmenopausal (RR 1.51) than among premenopausal (RR 1.25) women. In both groups, however, the relative risk estimates turned close to unity by adjustment for parity, age at first birth, body mass index (BMI), height, age at menarche, menopausal status, use of oral contraceptives and consumption of alcohol. The overall multivariate relative risk among the highest educated women was 1.04 (95% CI 0.82–1.32). The results of our study suggest a clear positive gradient in risk for breast cancer by level of education, which can be fully explained by established breast cancer risk factors.

Key words: *education; socio-economic status; breast cancer; cohort; Sweden; Norway; epidemiology*

Socioeconomic differentials concerning a wide range of diseases, including cancer, have been frequently reported during the last decades. The direction of the socioeconomic gradient in risk differs, however, between cancer sites.[1] Among women, it tends to be negative for lung, stomach, oesophagus and cervical cancer, while a positive association has been observed for malignant melanoma and cancers of the colon, breast and ovaries. The excess risk of breast cancer among women with high socioeconomic status (SES) is confirmed by a number of epidemiological studies. Different measures of SES have been applied, but the link exists both with income,[2–8] occupation or socioeconomic group,[9–16] and level of education.[2–5,9–12,17–21] Although level of education obviously acts only as an indicator of aetiologically relevant factors, no study has fully explained the relation by multivariate adjustment for possible confounding factors. Among the few prospective studies, one found no association,[22] while two did,[2,17] one of them being restricted to postmenopausal women. However, the positive association between SES and breast cancer risk observed in these studies was explained only partially by known confounding factors. Thus, further investigation is required to increase our understanding of the correlates of education that affect risk for breast cancer.

We present here results from a large, prospective cohort study carried out in Norway and Sweden, with comprehensive information on the characteristics of a woman's life and behaviour that might affect the risk of developing breast cancer. The aim of our study was to assess how risk for breast cancer varies with level of education and to identify the underlying causal factors leading to this variation.

MATERIAL AND METHODS

The cohort

The cohort was enrolled during 1991 and 1992. In Norway, a sample of 100,000 women born between 1943 and 1957 (34–49 years of age) was randomly selected from the Central Population Register. This register records the addresses of all persons alive and residing in the country, and the dates of death or migration to or from Norway since 1960. In this register each person is identified by an individually unique national registration number; the first 6 digits encode information on the date of birth, and the last 5 digits are based on an algorithm that ensures a unique number, including information on gender. In Sweden, a sample of 96,000 women born between 1942 and 1962 (30–50 years of age), residing in the Uppsala Health Care Region (comprising about 1/6 of the Swedish population) was randomly selected from the Swedish Central Population Register at Statistics Sweden. In this register, each individual is identified by a unique 10-digit national registration number, which encodes information on date of birth and gender.

A letter of invitation to participate in the study and a health-survey questionnaire were sent to all women. In Norway, the questionnaire was mailed to 10 subgroups at regular intervals. In Sweden, 2 mailings were done: 1 in 1991 and 1 in 1992. Of the 100,000 invited women in Norway, 57,582 (57.6%) returned a completed questionnaire, as did 49,259 of the 96,000 invited women (51.3%) in Sweden. Thus, the overall crude participation rate was 54.5% (106,841 out of 196,000). The questions relevant to this analysis were identical in the 2 countries. This common set of questions included a detailed assessment of reproductive history, height and weight, contraceptive use, prevalent diseases, history of breast cancer in mother and sister(s), lifestyle habits and total number of years of education.

Follow-up

Follow-up was achieved through linkages between the cohort data set and various population-based registries. These linkages were possible through the use of the individually unique national registration numbers present in all national registries in Norway

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and Sweden.[23] We obtained information on dates of death for deceased persons from the death registers and on dates of emigration from the registers of population migration. The national cancer registries, established in the 1950s in both countries, provided data on prevalent cancer cases at cohort enrolment and incident cancers diagnosed in the cohort during the follow-up. These registers are considered to be almost complete. We excluded from the cohort 15 women who were dead or had emigrated before the start of follow-up. Another 1,663 women with a prevalent cancer diagnosis at study enrolment were also excluded, as were 2,303 women who did not state educational length in the questionnaire. Hence, the study population includes 102,860 subjects. The follow-up ended on 31 December 1999, or at emigration, death, or primary cancer diagnosis, whichever occurred first.

Classification of education

In the questionnaire, women were asked to give the total number of years they attended school. The choice of classification is yet related to levels in the educational system in Norway and Sweden, and hence the term educational level will be used in the following. In Sweden, compulsory school attendance increased from 7 to 9 years in 1959. In Norway, this happened about 7 years later. Thus 7–9 years of education means primary school with at most 2 years of additional professional education. Women with 10–12 years of education may have completed secondary school, or up to 5 years of professional training. Education lasting 13–15 years corresponds to a university bachelor degree, or, in some instances, several professional training sessions at a lower level. The highest category comprises women with more than 16 years of education, which mainly corresponds to a university master level.

Statistical analysis

The Cox Proportional Hazards Model was applied to perform the statistical analyses, using the SAS Software Package (version 8.2) to calculate hazard ratios with corresponding 95% confidence intervals. The hazard ratios are interpreted as estimates of relative risks (RR).

The relationship between years of education and breast cancer incidence was first examined in age-adjusted analyses. Subsequently, other explanatory variables were added stepwise to the model whenever they tended to confound the association of interest, which was defined as a change in the RR of at least 1%. Age at first birth (<21, 22–24, 25 years or more) and parity (0, 1, 2, 3 or more children) were considered as a set of combined indicator variables, while age at start of follow-up, BMI (weight in kilos divided by height squared), height, age at menarche and alcohol consumption were treated as continuous variables. We tested BMI as a categorical variable in the statistical models, which gave a poorer model fit than treating it as continuous variable. Information on menopausal status was obtained from the questionnaire. Only women who reported natural menopause or a bilateral oophorectomy at cohort enrolment were considered postmenopausal, regardless of hysterectomy, or use of hormonal replacement therapy (HRT). Unknown age at menopause was set to 50 in the separate analyses. Family history of breast cancer was not related to level of education in our data and hence not included in the model. Tests for linear trend were carried out by introduction of an ordinal variable obtained by assigning consecutive integers to the categories of education.

The responsible Data Inspection Boards and Ethical Committees in both countries approved the study design, and all women gave informed consent to participate in the study.

RESULTS

Characteristics of the study population by country of residence are given in Table I. A total of 1,090 incident breast cancers were diagnosed during the follow-up. The slight difference in mean age at entry among Norwegian and Swedish women is attributable to a small discrepancy in range of age. Table II shows the distribution by education of the covariates included in the analysis. Well-educated women were on average younger, had fewer children and were older at their first birth. They also had a lower BMI and were taller than the less educated. Mean alcohol consumption increased with education, as did use of hormonal contraceptives. Age at menarche was on average slightly higher for the lowest educated women in our study population.

The relative risks for the total cohort comprising both pre- and postmenopausal breast cancer cases are given in Table III. We observed a steadily increasing positive association between educational level and breast cancer risk (p for linear trend = 0.001). When we added age at first birth and number of children to the model the magnitude of the association decreased considerably. Low BMI accounted for a modest increase in risk. The slight variation in risk still left was almost completely explained by the use of hormonal contraceptives, height, age at menarche, alcohol consumption and menopausal status at cohort entry. Hence, in the ultimate multivariate model no association between education and breast cancer risk persisted (p for trend=0.66).

In Table IV, the cohort is separated by estimated menopausal status at follow-up. Among premenopausal women none of the categories of educational level showed a significantly elevated risk of breast cancer compared to the reference group, although there was a significant trend across educational groups (p=0.03). This trend levelled off by subsequent multivariate adjustment, as described above. The analysis of postmenopausal women revealed a steeper increase in risk by level of education. However, as for the total cohort, the RRs were reduced after controlling for parity in the model and turned close to unity in the multivariate analysis when other risk factors were adjusted for.

DISCUSSION

Our finding of a positive association between level of education and risk of breast cancer is consistent with most[2–5,9–12,17–21] but not all[22] previous studies. Moreover, our hypothesis that this association could be explained by known risk factors was supported. Differences in parity and age at first birth accounted for more than 50% of the difference in risk between the lower and the higher educated group of women. The remaining variation in risk was attributable to lower BMI, increased height, lower age at

TABLE I – CHARACTERISTICS OF THE STUDY POPULATION AND THE INCIDENT CASES OF BREAST CANCER ACCORDING TO COUNTRY OF RESIDENCE: THE NORWEGIAN-SWEDISH WOMEN'S LIFESTYLE AND HEALTH COHORT STUDY 1991–1999

Characteristics	Norway	Sweden	Total
Number of women	55,603	47,257	102,860
Age at entry, mean (range)	41.1 (34–49)	39.5 (30–50)	40.4
Person-years of follow-up	451,382	380,510	831,892
Number of invasive breast cancer cases	622	468	1,090
Age at diagnosis of premenopausal breast cancer, mean (range)	44.8 (36–50)	44.4 (30–50)	44.6
Age at diagnosis of postmenopausal breast cancer, mean (range)[1]	52.0 (44–56)	52.5 (38–57)	52.2

[1]Reported postmenopausal at cohort enrolment or passed age 50 at time of diagnosis.

TABLE II – CHARACTERISTICS BY EDUCATION: THE NORWEGIAN-SWEDISH WOMEN'S LIFESTYLE AND HEALTH COHORT STUDY 1991–1999

	N	Years of education			
		7–9 %	10–12 %	13–16 %	≥17 %
Total	102,860	21.7	37.8	30.2	10.3
Breast cancer cases	1,090	22.3	35.3	30.5	11.9
Characteristics					
Age at entry					
30–34 years	14,264	7.4	16.4	16.5	10.4
35–39 years	31,788	20.9	32.2	35.0	35.4
40–44 years	29,907	30.7	28.2	28.5	30.7
45–49 years	26,901	41.0	23.2	20.0	23.5
Mean age (± SD)		42.3 years (± 4.8)	39.9 years (± 5.1)	39.6 years (± 4.9)	40.4 years (± 4.8)
Age at first birth					
Less than 20 years	12,982	27.7	16.0	5.9	2.3
20–24 years	40,621	51.4	51.2	38.0	23.6
25–29 years	26,864	15.9	25.0	41.0	45.0
30 years or more	10,316	5.0	7.8	15.1	29.1
Mean age at first birth (± SD)		22.0 years (± 3.9)	23.3 years (± 4.0)	25.4 years (± 4.1)	27.4 years (± 4.3)
Parity at entry					
Nulliparous	12,072	9.0	10.1	13.1	19.5
One child	14,502	12.3	14.0	14.6	16.7
Two children	44,893	40.7	45.7	44.8	39.1
Three children or more	31,393	38.0	30.2	27.5	24.7
Mean number of children (± SD)		2.2 (± 1.2)	2.0 (± 1.1)	1.9 (± 1.1)	1.8 (± 1.2)
BMI[1]					
Less than 18.5 kg/m^2	2,148	2.1	2.0	2.3	2.4
18.5–24 kg/m^2	72,479	64.0	71.9	76.8	79.3
25–29 kg/m^2	20,247	26.4	20.8	17.0	15.3
30 kg/m^2 or more	5,112	7.5	5.3	3.9	3.0
Mean BMI (± SD)		24.0 (± 3.9)	23.3 (± 3.6)	22.8 (± 3.4)	22.5 (± 3.3)
Mean height (± SD)		165.4 cm (± 5.7)	166.1 cm (± 5.6)	166.8 cm (± 5.7)	167.3 cm (± 5.7)
Mean age at menarche (± SD)		13.2 (1.4)	13.1 (1.4)	13.1 (1.4)	13.1 (1.4)
Use of hormonal contraceptives					
Ever used	74,350	36.1	25.4	23.3	25.1
Never used	27,528	63.9	74.6	76.7	74.9
Mean alcohol consumption (± SD)		2.3 (± 5.5)	2.7 (± 5.0)	3.0 (± 4.8)	3.7 (± 5.4)

[1]Weight (kg)/height squared (m^2).

TABLE III – RELATIVE RISKS (RR) WITH 95% CONFIDENCE INTERVALS OF DEVELOPING BREAST CANCER IN RELATION TO YEARS OF EDUCATION: THE NORWEGIAN-SWEDISH WOMEN'S LIFESTYLE AND HEALTH COHORT STUDY 1991–1999

	Years of education			
	7–9	10–12	13–16	≥17
Adjustment				
Age	1.00 (ref.)	1.12 (0.95–1.32)	1.26 (1.06–1.49)	1.36 (1.10–1.68)
Age			0.001	
p for linear trend	1.00 (ref.)	1.08 (0.91–1.27)	1.13 (0.95–1.35)	1.16 (0.92–1.45)
Age, parity, age at first birth	1.00 (ref.)	1.06 (0.90–1.25)	1.11 (0.93–1.32)	1.11 (0.89–1.40)
Age, parity, age at first birth, BMI	1.00 (ref.)	1.03 (0.86–1.23)	1.05 (0.87–1.27)	1.04 (0.82–1.32)
Age, parity, age at first birth, BMI, height, age at menarche, menopausal status at entry, ever use of hormonal contraceptives, consumption of alcohol				
p for linear trend			0.66	

menarche, later age at menopause and more frequent use of both alcohol and hormonal contraceptives among the higher educated group. The association of parity and age at first birth with breast cancer risk is well established,[24] while high BMI is found to be a protective factor before but not after menopause.[25] We also observed a persisting negative linear relationship between BMI and breast cancer risk after menopause, although it weakened with increasing age. The lack of turn in effect may be due to a possible underestimation of age at menopause in our cohort, as explained below. The minor contribution to breast cancer risk by other factors included in the multivariate model is supported by previous studies,[26–29] as is the distribution of these reproductive, anthropometrical and lifestyle characteristics by level of education.[30–33]

A positive gradient in risk by level of education has been documented in one previous prospective study comprising both pre- and postmenopausal women.[2] However, even after controlling for parity, age at first birth, status of menopause, weight and height, and consumption of alcohol, a borderline significant excess risk remained among highly educated women. The lack of agreement with our study could relate to the great difference in cohort size.

Although age at menopause was unknown for most of the cohort members, we performed analyses separated by menopausal status, using age 50 as an estimate when menstrual history was unavailable.[34] This entails a possible misclassification that might have attenuated any true difference between pre- and postmenopausal women.[35]

TABLE IV – RELATIVE RISKS (RR) WITH 95% CONFIDENCE INTERVALS OF DEVELOPING BREAST CANCER IN RELATION TO YEARS OF EDUCATION, ACCORDING TO MENOPAUSAL STATUS: THE NORWEGIAN-SWEDISH WOMEN'S LIFESTYLE AND HEALTH COHORT STUDY 1991–1999

Years of education	RR (95% CI)			
	Premenopausal		Postmenopausal	
	Age adjusted	Multivariate[1]	Age adjusted	Multivariate[1]
7–9	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)	1.00 (ref.)
10–12	1.02 (0.82–1.25)	0.96 (0.77–1.21)	1.30 (1.00–1.68)	1.12 (0.85–1.48)
13–16	1.19 (0.96–1.47)	1.03 (0.81–1.31)	1.32 (0.99–1.74)	1.03 (0.75–1.40)
≥17	1.25 (0.96–1.64)	0.99 (0.74–1.34)	1.51 (1.05–2.16)	1.09 (0.74–1.61)
p for linear trend	0.03	0.81	0.02	0.80

[1]Adjusted for age, parity, age at first birth, BMI, height, age at menarche, ever use of hormonal contraceptives, and consumption of alcohol

We found indications of a slightly steeper increase in risk associated with educational level after menopause rather than before. The lack of previous published studies considering menopausal status hampers any comparison, while the few prospective studies examining only postmenopausal women show inconsistent results.[17,22]

One possible explanation for the observed lack of consistency in relative risks in pre- and postmenopausal women is that the meaning of education length varies by birth cohort. Certain occupational groups correspond to different levels of education, according to age. Compulsory school expanded during adolescence of the study population, and several professions at a middle or lower level (such as nursing and teaching) have required more years of total education during the last decades than in earlier ones. Thus, in our cohort, the younger women of a given education group may be comparable to the older women within a lower group.

Another possible explanation for the more pronounced association between educational level and breast cancer risk after menopause observed in our study may also be a birth cohort effect: the distribution of reproductive and lifestyle behaviour has changed over time according to the educational level achieved. Because the younger women in our cohort were at reproductive ages at time of cohort entry, we cannot compare their reproductive pattern according to education in all age groups, but figures from the Norwegian Population Register show a narrowing gap by birth cohort between education levels according to both average number of children and childlessness.[30] On the other hand, the disparity in age at first birth has widened between education groups during the last decades, as average age at first birth has increased in all groups.[36] However, different age at first birth seems to give smaller differentials in risk than differences in parity.[37,38] Alcohol consumption, age at menarche, menopausal status at start of follow-up and proportion of women using hormonal contraceptives increased with increasing age in our study at all levels of education.

Risk pattern for breast cancer most probably also differs according to menopausal status. Family history of breast cancer, particularly breast cancer in young first-degree relatives, is a stronger determinant of premenopausal breast cancer risk.[39] Hence, other behavioural and reproductive risk factors will be more prominent postmenopausally. Therefore, an additional reason why we were able to explain the positive relationship between education and breast cancer risk, moreso than previous studies, may be that our cohort is younger and was collected at a later time.

The strengths of our study include its prospective design, large size and complete follow-up. Our data offer sufficient variability in years of education as well as in related exposures to exhibit any differential in risk.

The use of self-reported information on education may represent a weakness of the study. Self-reported education often exceeds the number of years recorded in official statistics because the participants are likely to state both incomplete and informal training sessions. Moreover, as frequently observed in studies with volunteers, an over-representation of highly educated women as compared to the source population is present. The selection bias by education has been assessed in a part of the cohort by comparing the distribution of education among those who responded with the total invited sample using information from the Norwegian national register of education. Of the 11,600 women who responded, 26% had completed 13 or more years of education, compared to 22% in the invited sample of 18,900 women (our own unpublished data). However, since all comparisons we did in our analysis are within cohort members, we do not believe that selection bias affected any results.

Almost all studies on SES and breast cancer risk have reported a positive association irrespective of how SES was operationalised. Some of them combined education and income[2–5] or education and occupational or socioeconomic group.[10–12,40] Compared to income (measured as gross household income or poverty index ratio), years of education tends to be more strongly associated with risk.[2–4,17] Occupational class measures, however, generally provide a reinforced effect among the higher (professional) group.

There are several advantages of using years of education as a social class indicator. It applies to every adult individual, is more stable over one's lifetime than either occupation or income[41] and is easy obtainable and recordable.[40]

When the objective of a study is to estimate risks in various social strata and further explain an observed social class gradient in risk, the benefit of an indicator also depends on its ability to discriminate across strata according to the present outcome, which is conditioned by its strength of association with underlying causal factors. Education may be the most relevant measure in the analysis of social class and breast cancer, owing to its close relationship with reproductive pattern.[30,36]

The identification of the underlying factors that explain variations in risk by level of education also raises the question of whether it is still necessary to adjust for years of education in the analysis of breast cancer. We suggest that when information on reproductive factors and anthropometry is collected, it is superfluous to keep education as a covariate in the model, at least for young adults and middle-aged women. Since aetiological risk factors for breast cancer are probably similar in most populations, we believe that this statement can be applied in general.

We found a straight-line positive relationship between years of education and risk for breast cancer in a cohort of Norwegian and Swedish women at most 50 years old at enrolment, which can be fully explained by known risk factors. Dividing the analysis by pre- and postmenopausal follow-up time revealed a more pronounced relationship postmenopausally, but we were still able to identify the underlying differentials in exposure.

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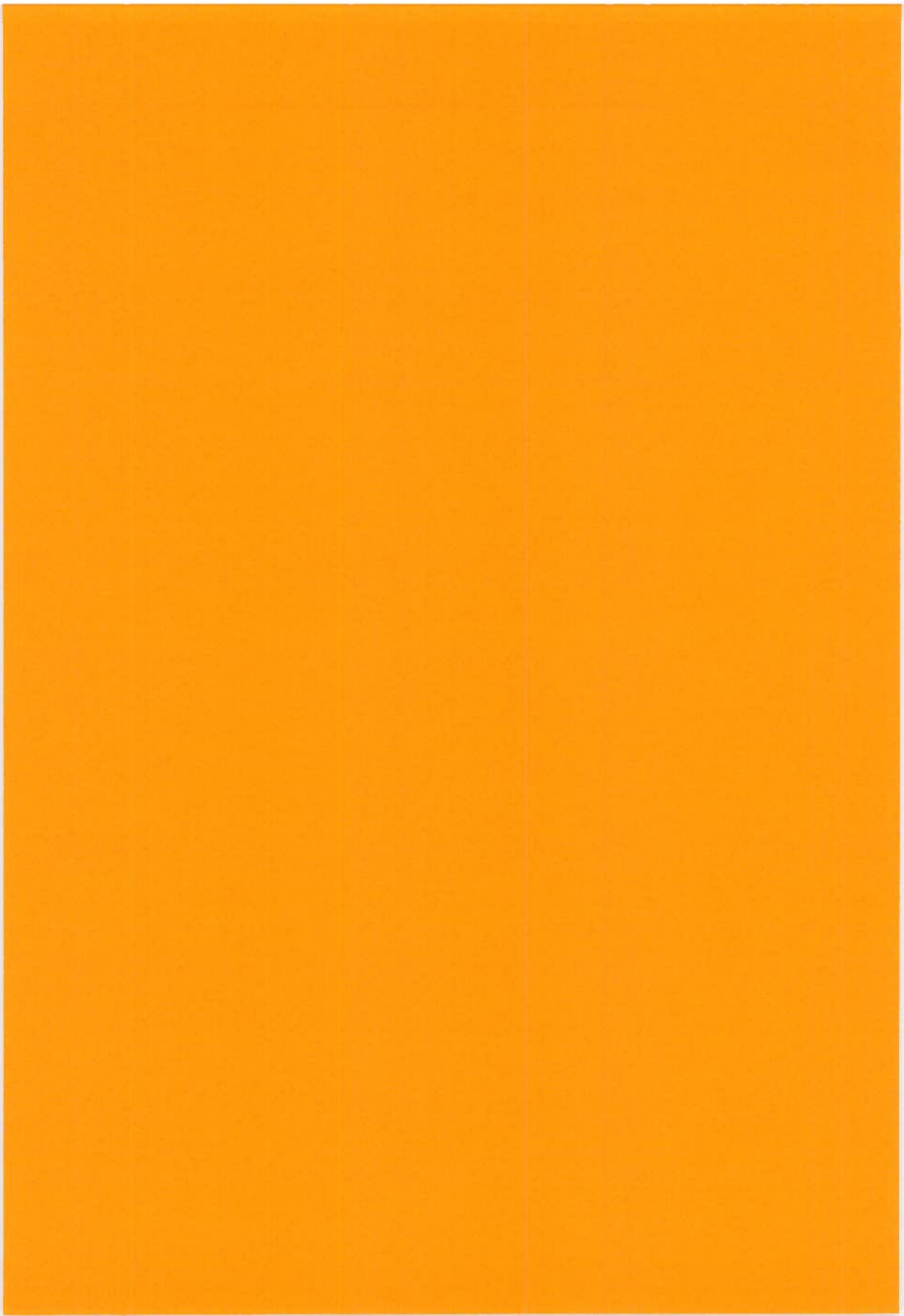
Paper II



Explaining the Socioeconomic Variation in Cancer Risk in the Norwegian Women and Cancer Study

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Abstract

Associations between level of education and cancer risk is well supported by scientific evidence, but previous studies could only partly adjust for relevant confounding factors. In this article, we examined how risk of cancer varies with level of education and identified factors that explain this variation using data from a prospective cohort study, including 93,638 Norwegian women who responded to an extensive questionnaire in 1991/1992 or 1996/1997. A total of 3,259 incident primary invasive cancer cases were diagnosed during follow-up, which ended in December 2001. We used Cox proportional hazards model to calculate relative risks (RR) with 95% confidence intervals (95% CI). Besides a similar overall risk of female cancers by level of education, we observed differing risks between educational groups for cancers of the lung, breast, cervix, kidney, and skin melanoma. Women with >16 years of education had an increased risk of breast cancer (RR, 1.46; 95% CI, 1.19-1.79) and a decreased risk of lung cancer (RR, 0.30; 95% CI, 0.13-0.70) and cervical cancer (RR, 0.38; 95% CI, 0.17-0.85) compared with the lowest educated women (7-9 years). The middle educated (13-16 years) had the lowest risk of kidney cancer (RR, 0.24; 95% CI, 0.08-0.71), whereas the risk of skin melanoma was highest among women with 10 to 12 years of education (RR, 1.53; 95% CI, 1.05-2.24) compared with the lowest educated women. After multivariate adjustment for potential confounders related to level of education, the variation in cancer risk according to educational levels declined into nonsignificance for all these sites. (Cancer Epidemiol Biomarkers Prev 2005;14(11):2591–7)

Introduction

Variation in cancer risk by socioeconomic status (SES) has been considered by several epidemiologic studies during the last decades. Among women, the socioeconomic gradient in risk tends to be negative (i.e., poorer women are more affected than richer ones) for lung, stomach, esophagus, and cervical cancer, whereas a positive association (richer women are more affected than poorer ones) has been observed for skin melanoma and cancers of the colon, breast, and ovaries (1). A variety of measures of SES have been applied in different studies, but the associations seem to be relatively consistent in Western countries with income (2-9), socioeconomic group (8, 10-19), and level of education (2-4, 7-10, 19-21). Several of these studies are large ecological or record linkage studies that have given convincing evidence of the associations between SES and cancer risk, but their lack of individual information on exposures impairs an examination of underlying causal factors related to SES in cancer causation. A few sample surveys indicated that the differences in cancer risk associated with SES reflect differences in exposures to carcinogens or lifestyles that determine cancer risk. One case-control study has investigated the effect of tobacco and alcohol consumption (known carcinogens) on 35 cancer sites (4), whereas another case-control study has considered the role of physical activity (potentially cancer preventive) on 15 sites (15). Other case-control studies have been able to control for several potential confounders in the analyses of selected cancers (7, 8, 22). However, prospective studies addressing the effect of SES on cancer risk are scarce. One prospective cohort study of colon cancer did not find any association between SES and cancer incidence (23), whereas three studies of breast cancer show contradictory results (11, 24, 25).

We present here results from a large, prospective cohort study carried out in Norway, with comprehensive information on behavior and lifestyle characteristics that might affect cancer risk among women. Our aim was to assess how risk for different cancer sites varies with level of education and to identify the underlying causal factors leading to this variation.

Materials and Methods

The Norwegian Women and Cancer Study. The present investigation is based on data from the Norwegian Women and Cancer Study (NOWAC), a prospective cohort study described in detail previously (ref. 26; see also http://www.ism.uit.no/kk/e/). A total of 179,388 women ages 30 to 69 years were randomly selected from the Central Population Register according to year of birth. This registry records the addresses of all persons alive and residing in the country and the dates of death or migration to or from Norway since 1960. Each person is identified by an individual national registration number; the first six digits encode information on date of birth and the last five digits are based on an algorithm that ensures a unique number, including information on gender (27).

A letter of invitation to participate in the study and a health survey questionnaire were mailed to 24 subgroups of women at irregular intervals between 1991 and 1997. The length of the questionnaire varied between two and eight pages, with a core set of questions, including reproductive history, height and weight, smoking history, use of oral contraceptives and hormone replacement therapy (HRT), alcohol consumption, family history of breast cancer, participation in mammography screening, physical activity, and years of education. In total, 102,433 women returned the questionnaire, giving a crude response rate of 57.1%.

Follow-up. Follow-up was achieved through linkages of the cohort data set to national registers. The cancer data were

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provided by the National Cancer Registry, and information on death and emigration was collected from the Central Population Register of Norway. These registers are considered to be almost complete. Four women with missing information on death/emigration together with 28 women who were dead or had emigrated before the start of follow-up were excluded from the cohort. Another 3,118 women with a prevalent cancer diagnosis at study enrollment were also excluded, as were 5,645 women who did not state educational length in the questionnaire. Hence, the initial study population comprised 93,638 subjects. From each site-specific analysis, we further excluded women with missing information on covariates included in the respective multivariate model. The follow-up ended on December 31, 2001 or at emigration, death, or primary cancer diagnosis, whichever occurred first.

Classification of Education. In the questionnaire, women were asked to give the total number of years they attended school. The choice of classification is related to levels in the educational system in Norway; hence, the term educational level will be used in the following. Compulsory school attendance increased from 7 to 9 years about 1965. Thus, 7 to 9 years of education means primary school with at most 2 years of additional education. Women with 10 to 12 years of education may have completed secondary school or up to 5 years of professional training. Education lasting 13 to 16 years corresponds to a university bachelor degree or, in some instances, several professional training sessions at a lower level. The highest category comprises women with >16 years of education, which mainly corresponds to a university master level.

Statistical Analysis. We applied the Cox proportional hazards model to perform the statistical analyses using the SAS Software Package (version 8.2) to calculate hazard ratios with corresponding 95% confidence intervals (95% CI). The hazard ratios are interpreted as estimates of relative risks (RR).

The relationship between years of education and cancer incidence was first examined in age-adjusted analyses. Subsequently, other explanatory variables were added stepwise to the models whenever they tended to confound the association of interest, which was defined as a change in the RR of at least 1%. To make the estimates comparable, only subjects included in the multivariate analyses were left in the corresponding age-adjusted analyses. Smoking status and history, total alcohol consumption (0, <4, 4-10, >10 g/d on average), change in body mass index (BMI; weight in kilos divided by height squared) since age 18 years, participation in cervical cancer screening (never, more or less often than every third year), number of sunburns, age at first birth (<21, 22-24, 25-29, ≥30 years), and parity (0, 1, 2, ≥3 children) were included as sets of indicator variables, whereas perceived health, total intake of fat (<50, ≥50 g/d), ever use of oral contraceptives, current use of HRT, menopausal status at entry, and region of residence were considered dichotomous. Age at start of follow-up, BMI, and height were treated as continuous variables. Participation in mammography screening was included in the analysis of breast cancer as a time-varying variable, combining information from the questionnaire with time of introduction of the national screening program in each county. Information on menopausal status was obtained from the questionnaire. Only women who reported natural menopause or a bilateral oophorectomy at cohort enrollment were considered postmenopausal, regardless of hysterectomy or use of HRT.

Tests for linear trend were carried out by the introduction of an ordinal variable obtained by assigning consecutive integers to the categories of education. The relative contribution of each confounding variable was calculated as follows: The variables were added stepwise to the model by decreasing influence, evaluated at each step. For each variable (or set of variables) included, let A be the model before inclusion and B be the model after inclusion. The relative contribution of this variable is then [RR (model A) − RR (model B)] / [RR (age-adjusted model) − 1], where RR refers to the RR for the highest educated women. RRs < 1 have to be inverted before calculation. The P of each confounding variable is derived from the analysis of the respective full model. When categorical variables were considered, the P of the most significant category is reported.

Only cancer sites counting >40 incident cases are included in the analyses.

The National Data Inspectorate and the Regional Ethical Committee for Medical Research approved the study design, and all women gave an informed consent to participate in the study.

Results

Table 1 shows characteristics by education of the study population from the NOWAC. Well-educated women were on average younger, had fewer children, and had a later age at first birth. They were also taller, had a lower BMI, and had a lower increase in weight since age 18 years. The less educated were more likely to be smokers, started smoking at a younger age, and had a higher number of pack-years. They also reported a poorer self-perceived health. Alcohol consumption increased with educational level, as did both use of oral contraceptives and HRT and participation in cancer screening programs. The average number of sunburns yearly also increased by level of education, which is an indicator of vacation trips to southern countries, popular among middle and high SES people in Norway. The proportion of well-educated women was highest in the southern part of Norway. Table 2 gives the age-adjusted RRs of developing cancer by site and level of education. Besides a similar overall risk of female cancers by level of education, we observed differing risks between educational groups for cancers of the lung, breast, cervix, kidney, and skin melanoma. After multivariate adjustment for potential confounders related to level of education, the variation in risk declined into nonsignificance for all these sites (Table 3).

Positive Associations with Education. The risk of breast cancer showed a steadily increasing positive association with level of education (age-adjusted P for linear trend < 0.0001). When we added age at first birth and number of children to the model, the magnitude of the association decreased considerably. Low BMI accounted for a modest increase in risk. The slight variation still left was almost completely explained by use of oral contraceptives and HRT, consumption of alcohol, height, menopausal status at entry, and participation in mammography screening (multivariate-adjusted P for trend = 0.29). For skin melanoma, we did not observe any linear trend (age-adjusted P for trend = 0.48), only an increased risk among the middle educated women. After adjustment for number of sunburns and region of living in Norway, the RR turned into nonsignificance.

Negative Associations with Education. The risk of lung cancer was strongly related to education and, as expected, was mostly explained by differences in smoking habits. Total intake of fat and perceived health acted as minor confounders of the association (age-adjusted P for trend < 0.0001, multivariate-adjusted P = 0.06). The negative gradient in risk of kidney cancer was also partly related to the effect of smoking. Consumption of alcohol (a habit of relatively wealthy women in Norway) seemed to be a protecting factor of kidney cancer, contributing to the decrease in risk among the highly educated women (age-adjusted P = 0.004, multivariate-adjusted P = 0.07). The variation in risk of cervical cancer

Table 1. Characteristics by level of education, the NOWAC study, 1991-2001

	n	Education (y)			
		7-9 (%)	10-12 (%)	13-16 (%)	≥17 (%)
Total	96,485	28.8	34.7	25.3	11.2
Age at entry into the cohort (y)					
30-39	26,017	14.8	28.5	35.1	35.2
40-49	45,056	42.3	48.8	48.0	48.6
50-59	15,265	21.7	14.8	11.9	12.8
60-69	10,147	21.2	7.9	5.0	3.4
Mean (SD) age at cohort enrollment (y)		50.0 (9.7)	45.1 (8.3)	43.5 (7.7)	43.3 (7.2)
Smoking status					
Current	38,350	46.0	44.5	34.2	26.2
Former	23,191	24.0	23.8	24.6	26.4
Never	33,681	30.0	31.7	41.2	47.5
Age at start smoking (y)					
<20	36,412	61.8	63.6	56.6	50.0
≥20	24,084	38.2	36.4	43.4	50.0
No. pack-years smoked					
1-19	87,200	89.5	92.0	95.1	95.8
≥20	7,074	10.5	7.8	4.9	4.2
Perceived health					
Poor or very poor	7,381	14.1	7.6	5.1	4.8
Good or very good	78,083	85.9	92.4	94.9	95.2
Total intake of fat (g/d)					
<50	60,404	69.1	77.7	79.6	78.0
≥50	19,506	30.9	22.3	20.4	22.0
Age at first birth (y)					
<20	11,871	23.3	14.5	5.2	2.9
20-24	42,331	54.8	54.0	42.1	26.7
25-29	24,202	16.8	23.9	39.3	44.7
≥30	8,825	5.1	7.6	13.4	25.7
Mean (SD) age at first birth		22.3 (3.8)	23.3 (4.0)	25.2 (4.1)	26.9 (4.4)
Parity at entry					
Nulliparous	9,222	7.1	8.0	11.0	17.5
1 child	11,540	9.7	12.2	12.7	15.3
2 children	39,414	34.3	44.3	44.0	39.8
≥3 children	36,307	49.0	35.4	32.3	27.4
Mean (SD) no. children		2.6 (1.4)	2.2 (1.1)	2.1 (1.1)	1.8 (1.2)
BMI (kg/m^2)					
<18.5	2,571	2.4	2.7	3.0	3.1
18.5-24.5	64,620	59.2	69.5	74.5	77.5
25-29.5	21,106	29.2	22.1	18.3	15.7
≥30	5,763	9.2	5.8	4.2	3.6
Mean (SD) BMI		24.6 (4.1)	23.6 (3.6)	23.1 (3.4)	22.8 (3.3)
Change in BMI since age 18 y (units)					
<0	17,302	18.5	18.3	21.1	22.6
0-4	44,714	43.0	51.2	55.0	56.8
>4	26,384	38.5	30.6	23.9	20.6
Mean (SD) height (cm)		165.1 (5.6)	166.2 (5.5)	166.9 (5.6)	167.5 (5.6)
Use of oral contraceptives					
Ever used	52,316	41.2	57.7	64.0	67.0
Never used	41,549	58.8	42.3	36.0	33.0
Ever use of HRT among women ages ≥50 y at entry					
Yes	9,390	30.6	40.7	43.6	48.0
No	16,022	69.4	59.3	56.4	52.0
Menopausal status at entry					
Premenopausal	72,670	59.0	78.2	84.8	87.1
Postmenopausal	23,815	41.0	21.8	15.2	12.9
Daily consumption of alcohol (g)					
Teetotaller	26,133	38.4	27.3	24.3	20.7
0.1-3.9	43,609	48.4	50.6	47.4	43.2
4.0-9.9	15,732	10.3	17.1	21.9	26.0
≥10	4,814	2.9	5.0	6.4	10.1
Mean (SD) alcohol consumption		1.9 (5.0)	2.8 (5.5)	3.2 (4.9)	4.0 (5.7)
Frequency of cytologic screening					
Never	3,058	5.4	3.2	2.9	3.5
Less often than every third year	21,834	31.1	24.9	25.1	28.1
Every third year or more often	55,521	63.4	71.9	72.0	68.4
Participation in mammography screening before entry among women ages ≥50 y					
Yes	9,676	31.9	43.0	45.0	42.5
No	15,736	68.1	57.0	55.0	57.5
No. sunburns yearly					
0	10,145	21.2	12.3	9.1	6.8
1	55,036	67.7	73.0	72.8	72.3
≥2	11,804	11.0	14.6	18.1	20.9
Region of living					
South or middle of Norway	75,164	65.7	81.2	85.0	83.0
Northern Norway	21,321	34.3	18.8	15.0	17.0

was explained by smoking status, change in BMI since age 18 years, age at first birth, and frequency of participation in cervical cancer screening programs (age-adjusted $P = 0.004$, multivariate-adjusted $P = 0.10$).

Discussion

Our study showed a similar overall risk of female cancers across social strata, which is consistent with most (13, 16, 17) but not all (2, 10) previous studies. However, the lack of a socioeconomic gradient in overall risk covered contradictory associations between SES and cancer incidence in the site-specific analyses.

Our initial finding (before multiple adjustment) of a positive association between SES and risk for breast cancer and skin melanoma is well confirmed, as is the negative social gradient for cancers of the lung and cervix (1). For kidney cancer, the evidence is less convincing, but some studies have found an increased risk among low educated women (28, 29) as observed in our study. Moreover, our hypothesis that socioeconomic variation in cancer risk can be explained by known risk factors was supported.

Tobacco. Differing smoking habits accounted for ~64% of the increase in risk of lung cancer among the lowest category of education compared with the highest, whereas the corresponding proportions for both cervical and kidney cancer were 32%.

Diet. Consumption of alcohol seemed to have contrary effects on cancer of the breast and kidney, respectively, and contributed to extend the variation in risk for both sites. The effect of alcohol amounted to 23% of difference in risk of breast cancer after controlling for parity and age at first birth. Total intake of fat showed a minor confounding effect on the association between education and lung cancer, as a lower intake among the well educated decreased their RR.

Anthropometric Measures. BMI did also show contrary effects between cancer sites. The higher prevalence of overweight and obesity among the less educated increased their risk of lung cancer slightly but decreased their breast cancer risk. The inverse association between BMI and breast cancer risk is considered expected, as the majority of the women were premenopausal at cohort entry. Height was positively associated with breast cancer risk, yielding a further increased RR in the well educated. Increase in BMI since age 18 years was most prevalent among the less educated and showed a negative effect on risk of cervical cancer. Its effect on socioeconomic differences in risk was slight and only involving the middle and lower educated women.

Reproductive Factors. Differences in parity and age at first birth contributed to 26% of the variation in breast cancer risk between the highest and the lowest educational groups. A young age at first birth showed a minor influence on risk of cervical cancer, probably serving as a proxy of age at first intercourse.

Participation in Screening Programs. Highly educated women were more likely to participate in mammography screening, which revealed cases that otherwise would remain undiagnosed or diagnosed at a later time. On the contrary, regular participation in cytologic screening programs reduced the risk of developing invasive cervical cancer, in favor of the well-educated women.

Hormones. Use of both oral contraceptives and HRT contributed slightly to an increasing risk of breast cancer by level of education.

Other Factors. Differences in perceived health increased the variation in lung cancer risk slightly, which may result from residual confounding of smoking or perhaps a weakened immune system. The effect on variation in breast cancer risk by menopausal status increased after controlling for HRT use, BMI, and screening participation. Number of sunburns affected difference in risk of skin melanoma, as the lowest educated women reported a lower frequency than the others. Region of living did also alter risk of skin melanoma. Women in northern Norway are on average lower educated than in the rest of the country as confirmed by national figures (30).

The strengths of our study include its prospective design, large size, and complete follow-up. Our data offer sufficient variability in years of education as well as in related exposures to exhibit any differential in risk.

The use of self-reported information on education may represent a weakness of the study. Self-reported education often exceeds the number of years recorded in official statistics because the participants are likely to state both incomplete and informal training sessions. Moreover, as frequently observed in studies with volunteers, an overrepresentation of highly educated women compared with the source population is likely. Possible selection bias by education has been assessed in a part of our cohort by comparing the educational level among those who responded the questionnaire with the total population invited to participate using information from the national register of education. Of the 9,237 women who responded the questionnaire, 26% had completed ≥13 years of education compared with 22% in the invited sample of 15,000 women (26). This excess of highly educated women may increase breast cancer rates by 5 cases per 100,000 at most, assuming that the relationship between risk behaviors and education does not vary according to response to the

Table 2. Age-adjusted RRs with 95% CIs of developing cancer in relation to years of education, the NOWAC study, 1991-2001

	No. cases	Education (y)				*P* for linear trend
		7-9	10-12	13-16	≥17	
All	3,259	1.00 (reference)	1.01 (0.93-1.10)	1.03 (0.94-1.14)	1.05 (0.92-1.19)	0.41
Colon	205	1.00 (reference)	0.86 (0.61-1.20)	0.95 (0.65-1.39)	0.81 (0.46-1.42)	0.52
Rectum	112	1.00 (reference)	1.37 (0.88-2.14)	0.80 (0.44-1.45)	1.58 (0.83-3.02)	0.60
Lung	150	1.00 (reference)	0.70 (0.48-1.00)	0.40 (0.24-0.67)	0.30 (0.13-0.70)	<0.0001
Breast	1,093	1.00 (reference)	1.13 (0.96-1.32)	1.29 (1.09-1.53)	1.46 (1.19-1.79)	<0.0001
Cervix uteri	125	1.00 (reference)	0.94 (0.62-1.43)	0.61 (0.37-1.02)	0.38 (0.17-0.85)	0.004
Corpus uteri	179	1.00 (reference)	0.89 (0.61-1.29)	1.35 (0.92-1.99)	1.06 (0.61-1.86)	0.27
Ovary	251	1.00 (reference)	1.06 (0.77-1.44)	1.13 (0.80-1.59)	0.76 (0.46-1.27)	0.73
Kidney	46	1.00 (reference)	0.61 (0.32-1.19)	0.24 (0.08-0.71)	0.29 (0.07-1.25)	0.004
Melanoma of skin	201	1.00 (reference)	1.53 (1.05-2.24)	1.42 (0.94-2.14)	1.13 (0.66-1.94)	0.48
Brain	46	1.00 (reference)	0.87 (0.43-1.78)	0.61 (0.26-1.47)	1.08 (0.41-2.83)	0.67
Thyroid gland	52	1.00 (reference)	0.99 (0.47-2.09)	1.15 (0.53-2.49)	1.41 (0.57-3.50)	0.43

Table 3. Multivariate-adjusted RRs with 95% CIs of developing cancer in relation to years of education, the *P*s, the confounding variables, and their relative contribution by stepwise inclusion, the NOWAC study, 1991-2001

Cancer site	Adjustment	Relative contribution (%)	*P*	Education (y)				*P* for linear trend
				7-9	10-12	13-16	≥17	
Lung	Smoking status, age started smoking, no. pack-years	64.4	<0.0001	1.00 (reference)	0.85 (0.59-1.23)	0.66 (0.39-1.11)	0.58 (0.25-1.34)	0.06
	Perceived health	3.4	0.01					
	Total intake of fat	1.0	0.02					
Breast	No. children, age at first birth	26.3	0.005	1.00 (reference)	1.00 (0.85-1.18)	1.07 (0.89-1.27)	1.11 (0.89-1.38)	0.29
	Consumption of alcohol	23.3	0.0002					
	Ever use of oral contraceptives	7.4	0.004					
	Height	6.5	0.002					
	Current use of HRT	3.3	<0.0001					
	BMI	2.8	0.07					
	Participation in mammography screening	2.6	<0.0001					
	Menopausal status at entry	3.9	0.001					
Cervix uteri	Smoking status	31.6	0.0001	1.00 (reference)	1.05 (0.68-1.60)	0.77 (0.46-1.31)	0.51 (0.22-1.18)	0.10
	Participation in cytologic screening	3.3	<0.0001					
	Age at first birth	6.4	0.33					
	Change in BMI since age 18 y	0.0	0.03					
Kidney	Smoking status	32.4	0.001	1.00 (reference)	0.75 (0.38-1.46)	0.36 (0.12-1.08)	0.50 (0.11-2.21)	0.07
	Consumption of alcohol	26.8	0.02					
Melanoma of skin	No. sunburns	53.0	0.001	1.00 (reference)	1.43 (0.98-2.09)	1.29 (0.85-1.95)	1.02 (0.59-1.75)	0.82
	Latitude of residence	36.0	0.006					

questionnaire. Reassuringly, the NOWAC incidence rates of breast cancer and total cancer (26) coincide closely with national figures. Furthermore, the study of the external validity of NOWAC shows only modestly diverging distributions of important exposures as parity and age at first birth according to response to the questionnaire (26). We therefore believe that the respondents in our study have a similar cancer risk profile to equally educated nonrespondents and that substantial selection bias is unlikely.

The status of human papillomavirus was unknown among the cohort members. Because human papillomavirus plays a crucial role in the etiology of squamous cell carcinoma as well as adenocarcinoma of the cervix (31), our analysis of cervical cancer is limited.

All risk factors for cancer occurring in the present study have been described previously. The effect of smoking on lung and cervical cancer risk is well known (31), although we observed a stronger effect of smoking on kidney cancer than in previous studies (32, 33).

The protecting effect of alcohol consumption on kidney cancer observed in our study has been reported by a few others (28, 34), although the adverse effect of alcohol on breast cancer is well established (35, 36). The associations between reproductive pattern, anthropometric measures, and hormones on cancer risk is well evidenced (31), as is the association between screening rates and incidence of breast and cervical cancer (37-39).

The socioeconomic profile in health exposures varies not only by ethnicity and level of development (40, 41) but also between developed countries. Smoking follows a negative social gradient in most western countries, whereas a positive gradient is generally observed for consumption of alcohol and leisure time physical activity (42-45). Nevertheless, studies of a Mediterranean population show a higher proportion of smokers among highly educated but no socioeconomic differences in alcohol consumption (46, 47). In our study, we found no significant socioeconomic variation in level of total physical activity, which may result from an offsetting of contradictory associations for occupational and leisure time physical activity. Reports on SES and diet are inconsistent (48, 49). We observed certain disparities in dietary pattern, but the only alteration of cancer risk appeared by consumption of alcohol and slightly by total intake of fat. However, reproductive pattern, anthropometry, screening behavior, and use of oral contraceptives and HRT seem to be similarly related to SES in most western populations (24, 47, 50-56).

Besides the contemporary variation between populations, the socioeconomic distribution of health exposures has changed over time within populations, as the socioeconomic distribution itself has changed. The average level of education among women has increased considerably in Norway since the late 1960s as in other western countries (30, 57). Following the development of education, the lifestyle and behavior related to a certain level has changed over time and differ between birth cohorts (58-60). Dividing our cohort into two equally spaced birth cohorts revealed a wider socioeconomic distribution of anthropometry and fat and alcohol intake among the oldest, whereas the younger had a greater disparity in parity pattern, smoking, and oral contraceptive use (data not shown).

The relationship between SES and cancer incidence may also depend on how SES is operationalized, although studies using both income and level of education have provided almost similar estimates for the two measures (2-4, 7-9, 61). However, the advantages of choosing years of education as an indicator of SES are several; it applies to every adult individual, is more stable over one's lifetime than either occupation or income (62), and is easily obtainable and recordable (63).

We found a significant relationship between level of education and risk for cancers of the lung, kidney, cervix, breast, and skin melanoma. The association was negative for lung, kidney, and cervical cancer, whereas a positive association was observed for breast cancer and skin melanoma. After multivariate adjustment for potential confounders,

all RRs turned into nonsignificance, which shows that socioeconomic variation in cancer risk can be explained by known risk factors. We believe that our ability to identify the confounders in the analyses of the NOWAC study is attributable to three aspects: the comprehensive information on exposures, a high quality of both the questionnaire information and the cancer data, and a close relationship between level of education and characteristics of a woman's life and behavior that might affect the risk of developing cancer.

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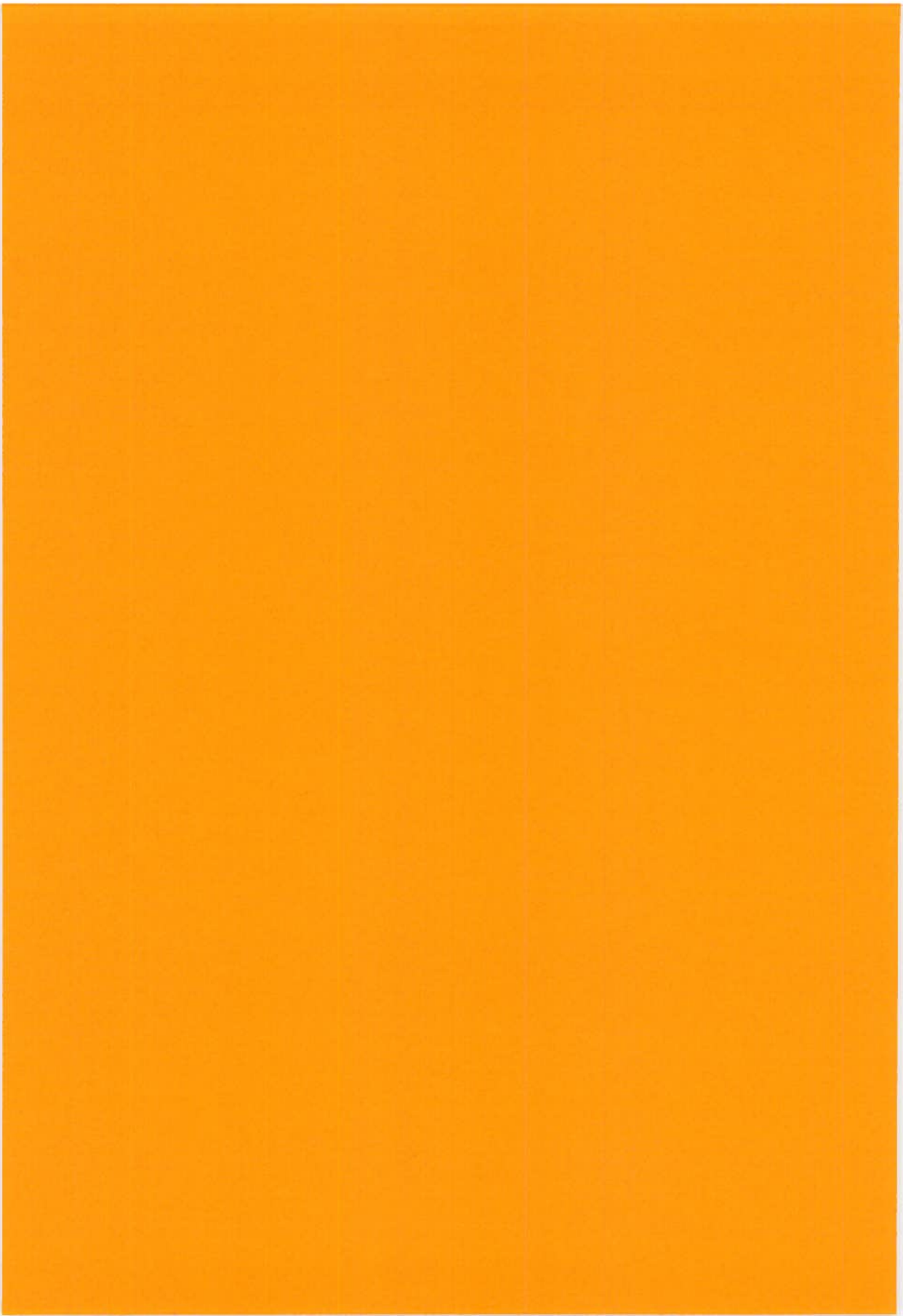
Paper III



SOCIOECONOMIC STATUS, INTERGENERATIONAL CHANGE IN SOCIOECONOMIC STATUS AND SURVIVAL OF CANCER. THE NORWEGIAN WOMEN AND CANCER STUDY

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SUMMARY/ABSTRACT (Word count 247)

Survival of cancer has been observed to be poorer in low socioeconomic groups, but the knowledge about the underlying causal factors is limited. Cancer survival according to intergenerational change in socioeconomic status (SES) has not been previously studied. The purpose of this study was to examine how survival among cancer patients varies with different measures of SES, and to identify factors that explain this variation. We used data from The Norwegian Women and Cancer Study, a prospective cohort study including 91 814 women, of whom 3 936 incident cancer cases were diagnosed during follow-up, and 968 women died within five years after the time of diagnosis. The Cox Proportional Hazards Model was used to calculate relative risks of mortality with 95% confidence intervals. We observed an overall negative socioeconomic gradient in cancer survival when SES was measured by education or income. We found that the unequal socioeconomic distribution of smoking status prior to diagnosis contributed considerably to the poorer survival in low SES groups. Cancer survival according to intergenerational change in SES revealed the poorest survival in women who had experienced a downward drift in SES, whereas women who had advanced in SES since childhood had a higher survival than others. Tentative adjustment for both tumour stage at diagnosis and a variety of lifestyle factors did not alter the mortality estimates substantially. We believe our findings may be explained by underlying factors that both induce a change in SES and affect the likelihood of surviving from cancer.

INTRODUCTION

The association between socioeconomic status (SES) and cancer survival has been examined by several epidemiologic studies within a variety of study designs. The majority of these are ecologic studies using geographical area based measures as SES indicators (comparing richer with poorer areas). Others are hospital-based or record linkage studies with individual information on socioeconomic status measured by socioeconomic group, income or level of education (1-4). Occasionally, health insurance status has been applied as a proxy of SES (5;6). Regardless of study design, a number of studies have found an improved cancer survival by increasing SES, both overall and for specific anatomic sites, especially for cancers of relatively good prognosis such as female breast, corpus uteri, and bladder cancer (7). A few studies find no association between SES and overall cancer survival, whereas site-specific null associations are more frequently reported. In general, the observed SES differences in survival seem to be lower in ecologic studies than in studies with individual assessment of SES (8).

The impact of socioeconomic conditions during childhood on adult health has been known for several decades (9). Studies have found an inverse association between parental SES and both morbidity (10) and mortality risk (11-18), also after controlling for adult SES.

Whereas the studies mentioned above have regarded SES at different stages of life, a few other studies have focused on the correlations with health outcomes of a *change* in SES from childhood to adulthood (19-23). Two studies have suggested a somewhat poorer health status among individuals with a downward change in SES (20;22), while one study disputes the hypothesis of socioeconomic conditions in childhood as important determinants of adult health (21).

To our knowledge, intergenerational change in SES and survival of cancer has not been previously studied.

We present here results from a prospective cohort study where we evaluated how socioeconomic conditions at time of recruitment and changes in SES since childhood affect the likelihood of cancer survival within five years of diagnosis. We studied both overall cancer survival, and survival for selected cancer sites, taking into consideration tumour characteristics and individual's lifestyle before diagnosis.

MATERIAL AND METHODS

The Norwegian Women and Cancer Study

The Norwegian Women and Cancer Study was initiated in 1991 as a prospective, population-based cohort study recruiting 57 600 women aged 34-49 years (response rate 57.6 %) who answered a four pages questionnaire. In 1996 the cohort expanded further and 44 843 women (56.8 % of the invited) aged 30-69 years were included by responding to an eight pages questionnaire. A similar questionnaire was mailed to the initial sub-sample in 1998, of whom 46 971 women (81.5 %) responded. The present study population is constituted by the sub-sample enrolled in 1996 together with the responders of the second questionnaire in 1998, 91 814 women in total. The questionnaires as well as other details of the cohort can be found at http://uit.no/kk/NOWAC/.

Follow-up

Follow-up was achieved through linkages of the cohort data set to national registers by the personal identification number. The cancer data was provided by the Cancer Registry of

Norway, and information on death and emigration was collected from the Central Population Register of Norway. These registers are considered to be virtually complete.

Among an initial study population of 91 814 women aged 30-69 at recruitment, a total of 3 936 incident primary invasive cancer cases were diagnosed before 1 January 2005, of whom 968 died within five years after the time of diagnosis. We excluded 51 women without any information on adult SES, leaving 3 885 incident cancer cases. The participants of the NOWAC study have been asked about one, two, or three of the SES measures, and thus the number of cases included vary between the three models. We have information on education for 3 640 women (93,7 %), on income for 3 611 (92,9 %), also parental economic conditions are known for 2 908 women (74,9 %). From each analysis of solid tumours we further excluded women with missing information on covariates included in the respective multivariate model. The follow-up started at the date of diagnosis and ended five years later (at the latest 25 April 2006), or at emigration or death, whichever occurred first.

Classification of socioeconomic status

Education

In the questionnaire, women were asked the total number of years they attended school. The choice of classification is related to levels in the educational system in Norway. Compulsory school attendance increased from seven to nine years in 1965. Thus, 7-9 years of education means primary school with at most two years of additional education. Women with 10-12 years of education may have completed secondary school, or up to five years of professional training. Education lasting 13-16 years corresponds to a university bachelor degree, or, in some instances, several professional training sessions at a lower level. The highest category

comprises women with more than 16 years of education, which mainly corresponds to a university master level.

Income

The women were asked for the gross household income per year given as five intervals equally spaced by each NOK 150 000 (18 500 EURO), with the highest category defined as more than NOK 600 000 (74 000 EURO).

Intergenerational change in SES

The indicator of intergenerational change in SES is constructed by combining the women's perception of economic conditions during childhood with gross household income at present, where childhood is defined as the period of life before puberty. The options of answer to the question of describing parental economic conditions were 'very good', 'good', 'poor' or 'very poor'. The second and third highest categories of gross household income were gathered into one in order to correspond to the number of categories for SES in childhood. The groups were ordered from 1 to 4 by increasing level, and the difference between adult and childhood income group was calculated. A value of -2 or -3 of this indicator was defined as 'downward change', the corresponding positive value as 'upward change', and the remaining individuals were assigned to 'stable low class', 'stable middle class' or 'stable high class', respectively. The indicator used here is a relative, subjective measure of change in SES, as the absolute measure of income at recruitment cannot be compared with the women's perceived level of parental economic conditions.

Statistical analysis

We applied the Cox Proportional Hazards Model to perform the statistical analyses, using the SAS Software Package (version 9.1) to calculate hazard ratios of mortality with corresponding 95% confidence intervals. The hazard ratios are interpreted as estimates of relative mortality risks (RR), and the term survival is used analogously to mortality risk.

The associations between cancer survival and different measures of SES were first examined in age adjusted analyses. Whenever a variation in risk by SES was observed, potential confounding variables were added stepwise to the models for all solid tumours and for cancer sites including at least 40 death cases. Models involving gross household income were initially adjusted for household size (number of persons) and marital status in a combined set of indicator variables. Subsequently, stage of disease (localised, regional metastasis, or distant metastasis) and smoking (current, former or never) were included in the multivariate models as a core set of covariates, regardless of their confounding effect. Other lifestyle or demographic variables such as body mass index, level of physical activity, parity, use of hormone replacement therapy (HRT) and hormonal contraceptives (HC), prevalence of certain other diseases, perceived health status, intake of alcohol and different foods, and region of living were tentatively added to each site-specific model, and included whenever they changed the association of interest by at least 5 %. Tests for linear trend were carried out by the introduction of an ordinal variable obtained by assigning consecutive integers to the categories of education. The likelihood ratio test was applied to compare different models according to the impact of certain variables on mortality risk The Wald test was used to compare risk estimates between different SES groups.

RESULTS

Table 1 shows characteristics of the study population by the three different measures of SES. Well-educated women were on the average younger and were less likely to be current smokers than the less educated. The distribution of tumour stage at diagnosis revealed a decreasing proportion of tumours with regional or distant metastasis with increasing years of education up to 13-16 years, whereas the highest educated women had a stage distribution similar to the middle educated (10-12 years of education). Increasing gross household income was associated with a lower age at cohort enrolment and a smaller proportion of current smokers, and a decreasing proportion of women with advanced metastasis. Women who had experienced a decline in SES from teenager years to adulthood were on the average older, and were more likely to be diagnosed with a distant metastasis than women who did not move between SES strata or moved upwards. Level of education was similar between the downward and also the stable low group, and between the upward and the stable high group, respectively. Alcohol consumption increased with increasing education, increasing household gross income, and was most common amongst women who moved upwards in the SES intergenerationally. Table 2 gives the relative risks of mortality among cancer patients by years of education. The age adjusted analysis shows a better overall survival (RR=0.73; 0.60-0.88) for women with 13-16 years of education compared to 7-9 years. After inclusion of stage, further adjustment for smoking status reduced the mortality risk from 0.78 to 0.91, or 64 %, among the highest educated women (more than 17 years) compared to 7-9 years. For ovarian cancer the survival was even more evident amongst well educated women (RR=0.48; 0.24-0.95 for women with 13-16 years of education compared to those with 7-9 years). On the other hand, mortality of colorectal cancer was observed to be increasing by years of education (p for linear trend = 0.02). For all solid tumours the associations declined into non-

significance by adjusting for stage, smoking status, and alcohol consumption (the latter in the analysis of colorectal cancer). The association between survival of all cancers and gross household income (Table 3) showed a similar pattern as for education, but the overall risk differed significantly only in the age adjusted analysis (RR = 0.66 (0.45-0.96 for the highest income group compared to the lowest). The observed disparity in mortality risk of all cancers between income groups declined slightly by adjusting for household size and marital status, but did still follow a significant linear trend (p=0.03). Further adjustment for stage and smoking status offset the survival trend among all solid tumours.

The values of the likelihood ratio statistic displayed a greater variation in mortality risk by education (χ_3^2 =12.3) than by income (χ_4^2 =11.5) after adjusting for age, when 3 361 individuals with non-missing information on both education and income were included. The value of the Spearman correlation coefficient between education and income was 0.40.

Table 4 shows the difference in relative mortality risk between groups according to intergenerational change in SES. We observed a linear trend of improved survival across the groups of improving SES between generations ($p < 0.0001$). These results were not substantially affected by adding potential confounding factors into the statistical models. After adjustment for household size, marital status, tumour stage, and smoking status, an excess mortality risk was still present among the group of downward change in SES. The Wald statistics displayed a significant difference in the age adjusted risk estimates for the downward group compared to the stable low group (p=0.03), and for the upward group compared to the stable high group (p=0.04). Adjustment for years of education did not alter the estimates of mortality risk by change in SES

DISCUSSION

Our study shows an inverse association between SES and five-year age adjusted overall cancer survival. The results were quite similar when different measures of SES, such as years of education or gross household income, were used. We also observed an elevated mortality risk among women with a downward drift in SES from childhood to adulthood, compared to women who remained at similar SES between the two stages of life. In the site-specific analyses by years of education the increased mortality risk among the low educated was more evident for ovarian cancer. The mortality risk among colorectal cancer patients increased with years of education. According to changes in SES, decreasing linear trends were observed for breast and ovarian cancer across the groups ordered from downward to upward change.

The opportunity of taking into account a variety of potential confounders such as tumour stage, lifestyle before diagnosis (smoking, alcohol drinking, level of physical activity, diet, anthropometry), and prevalence of certain other diseases in the analyses of SES and cancer survival is a considerable advantage of the present study. The information on lifestyle and behaviour was collected before cancer diagnosis, and therefore, is not subject to recall bias, which is advantageous according to the understanding of causality. However, we did not have information on changes in behaviour after the time of diagnosis, which may have affected survival.

All measures of SES in our study are based on self-reported information. We have no access to register data on either education or income, which hampers a validation of the SES outcomes. Self-reported education often exceeds the number of years recorded in official statistics because the participants are likely to state both incomplete and informal training sessions. We believe that the self-reported level of income can be considered valid, whereas the women's perceived level of parental economic conditions may be subject to recall bias, e.

g. if the level of household income affect an individual's perception of parents' income. However, our main interest lies in the comparison of different movements in SES within similar level of income at recruitment, and in that connection any recall bias by household income is irrelevant.

The estimates of mortality risk among all cancer patients show a significantly reduced risk by increasing level of SES at recruitment. We are aware that a part of the variation in risk may be explained by higher rates of cancers of poor prognosis (e. g. lung cancer) in individuals of low SES. In the analyses of survival by gross household income the observed variation in mortality risk of all cancers declined after adjusting for household size and marital status, whereas neither household size nor marital status affected educational differences in risk. Thus, the influence of these factors seems to be related to the importance of adjusting income measures for number of incomes in the household rather than adjusting for the potential psychosocial benefit of being married. However, for both education and income all estimates of relative risks and linear trends in risks levelled off after further adjusting for tumour stage and smoking status before diagnosis, with the exception for colorectal cancer. The educational differences in survival of this site seem to be weakly associated with consumption of alcohol. Similar differences in survival of colorectal cancer did not emerge in the age adjusted analysis by income because the unfavourable effect of alcohol among the highest income groups was counterbalanced by a favourable distribution of stage.

The values of the likelihood ratio statistic displayed a greater variation in mortality risk by education than by income. Lack of individual information on income among women in previous studies of cancer survival hampers any comparison, but studies of other health outcomes suggest that the relative magnitude of each SES measure varies with outcome (24-29). Different SES measures are dissimilarly related to underlying causal factors and cannot be used interchangeably (24). A single measure of SES does only partly explain the effect of

another single measure (30). In the present study the impact of smoking status on variation in survival is strong both for educational and income differences, but strongest for education. To understand the influence of smoking prior to diagnosis, it is crucial to assess the proportion of women dying from other diseases. We have information on cause for about 80% of the deaths, of which 94 % had cancer as the underlying cause. Thus, the contribution of deaths of other smoking related diseases to the effect of smoking on survival is almost negligible. The predominance of cancer as the cause of death does not completely rule out comorbidity as a potential mediator between smoking and case mortality, but either prevalence at recruitment of certain chronic diseases or the women's self-perceived general health status were observed to act as confounders of the variation in mortality by SES. Adjustment for lifestyle- or behavioural factors such as body mass index, level of physical activity, diet, reproductive history, use of HRT or HC did not affect the socioeconomic variation, nor the impact of smoking on SES differences. In our analyses we have not been able to explain any portion of the effect of smoking by other factors, but according to overall survival we believe the effect of smoking is partly attributable to an excess of poor prognosis cancers among smokers. However, we observed an increased case mortality of specific cancers among current smokers, which supports that smoking prior to diagnosis may play a biological role in the progress of some cancer sites, but not all.

Our analysis of cancer survival by intergenerational change in SES is novel. We find that SES in childhood alters the effect of SES in adulthood. Women who have experienced a fall in SES since childhood have a worse prognosis of cancer, whereas women who have advanced in SES have a better prognosis than other women at similar level of SES at recruitment. The overall difference in survival is recognised in the site-specific analyses of colorectal, lung, breast, and ovarian cancer. The distribution of potential mediating factors such as tumour stage and smoking status is less consistent by change in SES than by adult SES measures.

Inclusion of tumour stage alters the relative risk estimates inversely in different models, and smoking status before diagnosis contribute only modestly to explain differences in survival.

The increased mortality risk in cancer patients of low SES groups observed in our study is confirmed by several previous studies (1;2;31-35). However, our result of a poorer prognosis of colorectal cancer among highly educated women is rarely supported (7).

Survival of cancer is influenced by three factors: biological characteristics of the tumour, patient characteristics, and treatment (8). Consequently, SES differences in survival must originate from an unequal socioeconomic distribution of some of these factors. The predominant established prognostic factor of cancer survival is stage at diagnosis, as the classification of stage is derived from expected survival probability. According to SES differences in cancer survival, stage at diagnosis is an explaining factor often cited, but its influence varies by anatomic site and between populations (7). A previous study following all cancer patients in Norway from 1960 to 1991 showed persisting differences in survival still after adjusting for stage (1). The origin of social inequalities in stage distribution has also been discussed previously, but neither differences in timing of diagnosis nor differences in tumour aggressiveness have been evidenced to explain the variation (7;8). SES differences in cancer treatment have also been reported (7;8), but the role of patient characteristics has received little attention (8). A few studies have considered the potential effect of psychosocial factors (1;36), and comorbidity (37;38), and one study was able to control for smoking and alcohol consumption among men (39), finding a minor effect on crude survival. The results of our study question the distribution of tumour stage at diagnosis as the most important mediator of SES variation in survival, and indicate the influence of lifestyle factors. Indeed, in our study, smoking status explained about 64 % of mortality risk difference between the upper and lower educational groups after adjusting for age and stage.

In summary, we found an overall negative socioeconomic gradient in cancer survival when SES is measured as years of education or gross household income. The contribution of stage at diagnosis on survival differences was inconsistent, whereas smoking status prior to diagnosis was an important predictive factor for survival. After adjustment for stage and smoking status survival differences according to both education and income turned into non-significance, and thus no significant variation is left for potential differences in treatment. The policy of the public health care system in Norway is supposed to offer equal access for all citizens, which may differ from the health policy of other countries.

We also found that a downward change in SES since childhood is associated with a poorer prognosis than a stable SES, whereas an upward change relates to an improved prognosis. The disparity in survival by intergenerational change in SES observed in our study is not explained by marital status, tumour stage, smoking status, comorbidity, anthropometry, diet, level of physical activity, or other lifestyle- or behavioural factors tentatively added to the model as potential confounders. We believe there may exist underlying cultural or behavioural factors that both induce a drift in the social hierarchy and affect the likelihood of surviving from cancer.

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Table 1. Characteristics of the incident cancer cases by different measures of socioeconomic status. The Norwegian Women and Cancer Study 1996-2006.

		Years of education			
		7-9	10-12	13-16	>=17
	N	%	%	%	%
Total	3640	35.4	32.8	22.5	9.3
Mean age (± SD) in years at cohort enrolment		56.8 (± 7.5)	52.3 (± 7.5)	50.9 (± 7.2)	50.0 (± 6.5)
Tumour stage at diagnosis					
Localised	1567	48.3	53.2	57.1	50.0
Regional metastasis	1063	37.1	34.1	33.0	38.3
Distant metastasis	380	14.6	12.7	9.9	11.7
Smoking status					
Never	1233	29.7	33.4	41.6	45.4
Former	1030	27.1	29.5	29.8	35.5
Current	1253	43.2	37.1	28.6	19.1
Mean alcohol consumption in grams per day		2.0 (± 3.2)	3.3 (± 4.7)	4.0 (± 4.5)	5.0 (± 5.3)

		Gross household income				
		< 150 000	150 000 – 300 000	300 000 450 000	451 000 600 000	> 600 000
	N	%	%	%	%	%
Total	3611	15.5	37.1	25.0	16.3	6.1
Mean years of education		9.2 (± 2.9)	10.9 (± 3.2)	11.6 (± 3.2)	13.3 (± 3.3)	14.4 (3.2)
Mean age (± SD) in years at cohort enrolment		58.9 (± 8.4)	54.7 (± 7.9)	51.4 (± 6.7)	50.3 (± 5.5)	49.9 (± 5.7)
Tumour stage at diagnosis						
Localised	1550	50.1	49.5	52.2	55.9	59.6
Regional metastasis	1050	36.0	35.8	36.0	33.9	29.2
Distant metastasis	385	13.9	14.7	11.8	10.2	11.2
Smoking status						
Never	1228	33.4	33.4	34.9	37.2	43.6
Former	1019	23.1	29.0	30.1	32.2	31.2
Current	1259	43.5	37.6	34.0	30.6	25.2
Mean consumption of alcohol in grams per day		1.7 (±3.5)	2.7 (±3.7)	3.3 (±4.2)	4.3 (4.7)	6.5 (7.2)

		Intergenerational change in SES				
		Down-ward change	Stable low class	Stable middle class	Stable high class	Upward change
	N	%	%	%	%	%
Total	2908	11.3	14.8	24.3	32.1	17.6
Mean years of education		10.0 (±3.5)	9.9 (±3.0)	11.1 (±3.2)	12.5 (±3.3)	12.4 (±3.8)
Mean age (± SD) in years at cohort enrolment		58.0 (±7.9)	56.5 (±7.3)	54.8 (±7.4)	51.0 (±5.7)	51.6 (±5.6)
Tumour stage at diagnosis						
Localised	1267	50.0	53.7	49.4	53.4	56.6
Regional metastasis	843	34.4	34.9	36.1	36.3	31.7
Distant metastasis	296	15.6	11.4	14.5	10.3	11.7
Smoking status						
Never	1004	36.7	32.0	34.1	36.5	37.7
Former	843	23.7	32.5	27.3	32.4	30.1
Current	981	39.6	35.5	38.6	31.1	32.2
Mean alcohol consumption in grams per day		2.2 (±3.9)	2.2 (±3.6)	2.7 (±3.7)	3.9 (±4.5)	4.1 (±4.6)

Table 2. Relative risks (RR) with 95 % confidence intervals (CI) of mortality among cancer patients within five years after diagnosis, by years of self-reported education. The Norwegian Women and Cancer Study 1996-2006.

Cancer site	Adjustment	No of deaths	Years of education				p for linear trend
			7-9	10-12	13-16	>=17	
All	Age	885	1.00 (ref.)	0.86 (0.73-1.00)	0.73 (0.60-0.88)	0.77 (0.59-1.01)	0.001
All solid tumours*	Age	701	1.00 (ref.)	0.82 (0.69-0.98)	0.73 (0.59-0.91)	0.82 (0.61-1.09)	0.009
	Age, stage		1.00 (ref.)	0.83 (0.69-0.99)	0.77 (0.63-0.95)	0.78 (0.58-1.05)	0.01
	Age, stage, smoking status		1.00 (ref.)	0.89 (0.74-1.06)	0.86 (0.69-1.06)	0.91 (0.68-1.23)	0.20
Colon and rectum*	Age	125	1.00 (ref.)	1.26 (0.81-1.96)	1.59 (0.98-2.60)	1.81 (0.99-3.32)	0.02
	Age, stage, smoking status, alcohol consumption		1.00 (ref.)	1.27 (0.82-1.99)	1.62 (0.94-2.77)	1.44 (0.76-2.69)	0.10
Lung	Age	179	1.00 (ref.)	0.90 (0.64-1.26)	1.15(0.68-1.95)	1.24(0.50-3.08)	0.77
Breast	Age	115	1.00 (ref.)	1.24 (0.76-2.01)	1.20 (0.71-2.01)	1.40 (0.74-2.66)	0.33
Ovary*	Age	64	1.00 (ref.)	0.58 (0.32-1.04)	0.48 (0.24-0.95)	0.65 (0.27-1.59)	0.07
	Age, stage, smoking status		1.00 (ref.)	0.60 (0.33-1.08)	0.66 (0.33-1.32)	0.65 (0.29-1.63)	0.20
Other solid tumours	Age	313	1.00 (ref.)	0.85 (0.65-1.12)	0.83 (0.61-1.14)	0.89 (0.56-1.42)	0.28

* Potential confounders were added stepwise to the model whenever a significant variation or a linear trend in risk by years of education was observed in the age adjusted analyses

Table 3. Relative risks (RR) with 95 % confidence intervals (CI) of mortality among cancer patients within five years after diagnosis, by self-reported gross household income.

The Norwegian Women and Cancer Study 1996-2006.

Cancer site	Adjustment	No of deaths	Gross household income in NOK					P for linear trend
			< 150 000	151 000-300 000	301 000-450 000	451 000-600 000	> 600 000	
All	Age	853	1.00 (ref.)	0.92 (0.76-1.10)	0.77 (0.62-0.96)	0.72 (0.56-0.93)	0.66 (0.45-0.96)	0.001
	Age, household size, marital status		1.00 (ref.)	0.95 (0.79-1.15)	0.84 (0.66-1.06)	0.79 (0.61-1.04)	0.73 (0.49-1.07)	0.03
All solid tumours*	Age	675	1.00 (ref.)	0.99 (0.80-1.21)	0.79 (0.62-1.01)	0.72 (0.54-0.96)	0.72 (0.47-1.09)	0.003
	Age, household size, marital status, stage, smoking status		1.00 (ref.)	0.88 (0.71-1.09)	0.86 (0.66-1.12)	0.85 (0.63-1.15)	0.83 (0.54-1.28)	0.31
Colon and rectum	Age	136	1.00 (ref.)	0.84 (0.53-1.34)	0.67 (0.37-1.20)	0.96 (0.52-1.79)	1.03 (0.46-2.32)	0.97
Lung	Age	181	1.00 (ref.)	1.25 (0.80-1.93)	1.11 (0.67-1.85)	1.53 (0.88-2.66)	1.48 (0.50-4.35)	0.25
Breast	Age	108	1.00 (ref.)	1.03 (0.56-1.91)	0.79 (0.40-1.56)	0.91 (0.44-1.87)	0.90 (0.35-2.28)	0.56
Ovary	Age	71	1.00 (ref.)	0.82 (0.42-1.59)	0.72 (0.35-1.48)	0.62 (0.25-1.51)	1.52 (0.43-5.37)	0.54
Other solid tumours	Age	304	1.00 (ref.)	0.83 (0.62-1.10)	0.77 (0.54-1.10)	0.57 (0.36-0.89)	0.67 (0.36-1.22)	0.02
	Age, household size, marital status		1.00 (ref.)	0.89 (0.66-1.19)	0.87 (0.60-1.27)	0.66 (0.41-1.06)	0.80 (0.43-1.50)	0.15

* Potential confounders were added stepwise to the model whenever a significant variation in risk by gross household income was observed in the age adjusted analyses

Imputering?

Table 4. Relative risks (RR) with 95 % confidence intervals (CI) of mortality among cancer patients within five years after the time of diagnosis, by change in SES between adolescence and adulthood.

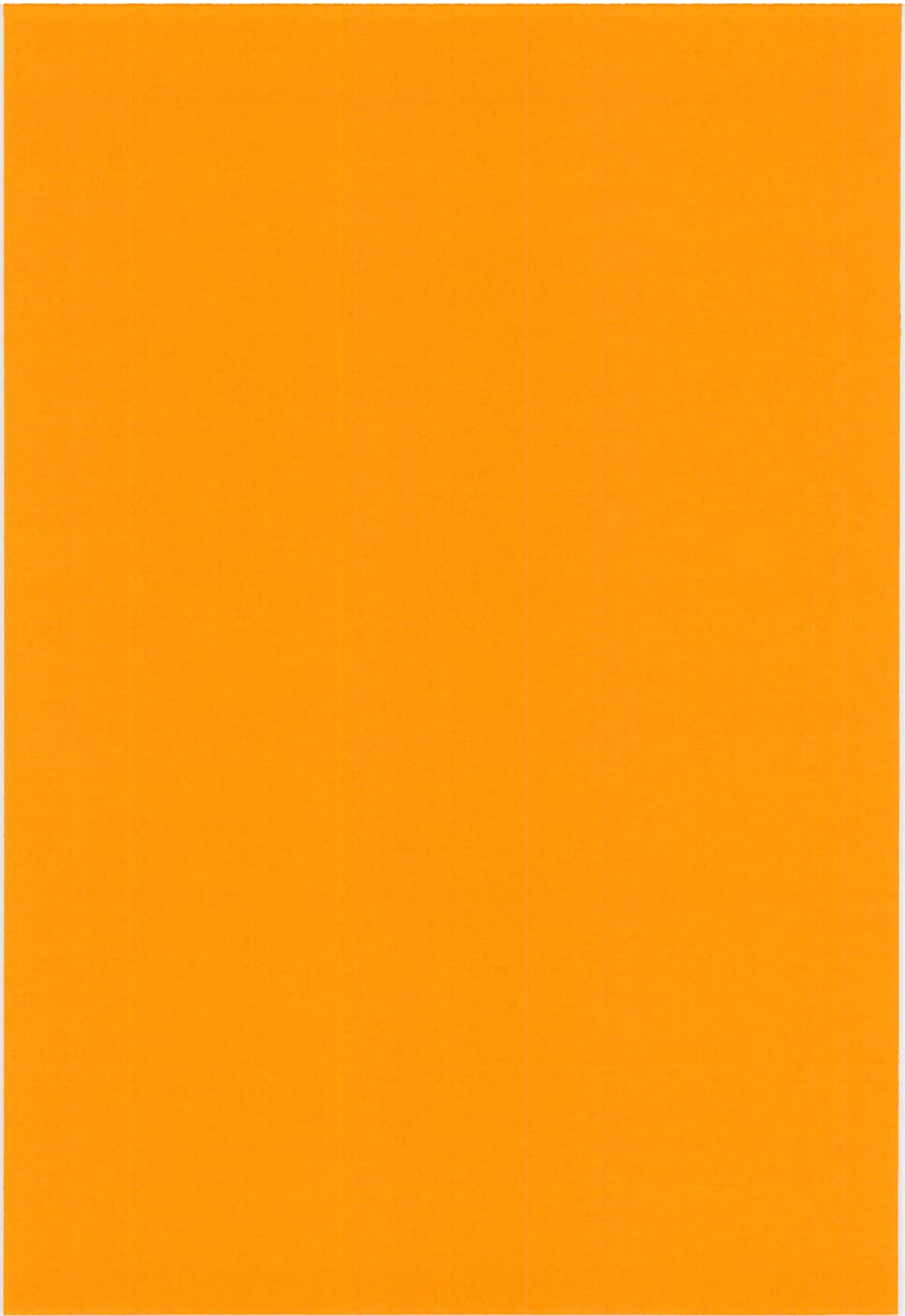
The Norwegian Women and Cancer Study 1996-2006.

Cancer site	Adjustment	No of deaths	Intergenerational change in SES					P for linear trend
			Downward change	Stable low class	Stable middle class	Stable high class	Upward change	
All	Age	637	1.32 (1.04-1.69)	0.95 (0.74-1.21)	1.00 (ref.)	0.87 (0.70-1.08)	0.68 (0.51-0.89)	<0.0001
	Age, household size, marital status		1.28 (1.00-1.64)	0.94 (0.74-1.21)	1.00 (ref.)	0.92 (0.73-1.15)	0.71 (0.54-0.94)	0.002
All solid tumours*	Age	505	1.32 (1.01-1.74)	0.89 (0.67-1.17)	1.00 (ref.)	0.84 (0.66-1.07)	0.68 (0.50-0.92)	0.0003
	Age, household size, marital status, stage, smoking status		1.53 (1.16-2.02)	1.07 (0.81-1.42)	1.00 (ref.)	1.14 (0.89-1.47)	0.87 (0.64-1.18)	0.009
Colon and rectum*	Age	98	1.65 (0.92-2.97)	0.64 (0.32-1.31)	1.00 (ref.)	1.07 (0.62-1.83)	0.59 (0.27-1.30)	0.10
	Age, household size, stage, smoking status, alcohol consumption		2.28 (1.18-4.41)	1.10 (0.53-2.29)	1.00 (ref.)	1.28 (0.71-2.41)	1.02 (0.42-2.44)	0.10

* Potential confounders were added stepwise to the model whenever a significant variation in risk by change in SES was observed in the age adjusted analyses

Lung*	Age	116	1.36 (0.72-2.56)	1.77 (1.01-3.10)	1.00 (ref.)	1.33 (0.78-2.27)	1.59 (0.87-2.88)	0.94
	Age, household size, marital status, stage, smoking status		1.40 (0.72-2.71)	1.81 (1.01-3.25)	1.00 (ref.)	1.32 (0.75-2.30)	1.35 (0.73-2.49)	0.60
Breast*	Age	75	1.16 (0.55-2.46)	0.84 (0.40-1.78)	1.00 (ref.)	0.80 (0.45-1.43)	0.40 (0.17-0.94)	0.05
	Age, household size, marital status, stage, smoking status		1.61 (0.73-3.54)	1.04 (0.49-2.21)	1.00 (ref.)	1.19 (0.62-2.27)	0.70 (0.28-1.74)	0.26
Ovary*	Age	51	4.34 (1.82-10.35)	1.50 (0.61-3.73)	1.00 (ref.)	0.90 (0.38-2.12)	1.42 (0.56-3.59)	0.01
	Age, household size, marital status, stage, smoking status		5.60 (1.96-15.95)	3.51 (1.15-10.71)	1.00 (ref.)	1.61 (0.59-4.38)	1.65 (0.57-4.76)	0.03

Paper IV



A SIMULATION STUDY OF SIMPLE RESIDUAL MULTIPLE IMPUTATION

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Short title: Simple residual multiple imputation

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SUMMARY

Simple residual imputation (SRI) is a well known method of accommodating incomplete continuous data, but as a multiple imputation method it is shown to be improper according to Rubin's combined formula for variance estimation. Like other Non-Bayesian techniques, Rubin's method using SRI provides too short confidence intervals because the imputation procedure itself does not offer any variability beyond what is present in the observed data. The present work introduces a modification of Rubin's formula inflating the variability between the imputed data sets, and by simulation studies and analytic results we show that this modification yields valid statistical inference. The study is performed using both simulated data and real data from The Norwegian Women and Cancer Study (NOWAC). The advantages of SRI are its simplicity and its applicability. The method can be implemented into any generalized linear model where residuals are computed, which allows imputation of variously distributed continuous data.

1 INTRODUCTION

Most survey data involve missing information in one or more covariates due to item non-response. A common way to handle this problem is to employ multiple imputation techniques, as developed by Rubin(1). Unlike single imputation, multiple imputation methods provide inferences that correctly reflect the variability due to unknown values, under the assumption that the imputation method is "proper" as termed by Rubin (2). The basic idea is to replace each missing datum with m values representing a distribution of likely values and combine the m imputed data sets by Rubin's formula for variance estimation. The formula comprises one term for the average variation *within* the m imputed samples, and one term for the variation *between* them. For a method to be "proper", i.e. giving a statistically valid inference based on this formula, the imputed values are required to be drawn from a posterior distribution in a Bayesian framework. Previous studies by Rubin(1), Rubin and Schenker (3), and Schenker and Welsh (4) have examined the validity of Rubin's variance formula using Non-Bayesian techniques such as hot-deck and simple residual imputation (SRI). They all conclude that the confidence intervals become too short when using Rubin's combination formula. Rubin (1) has shown that for simple random multiple imputation the expected between-imputation variability of the completed data sample mean is underestimated by the response rate for an infinite number of imputations.

Under the assumption of completely random non-response within strata, called missing at random (MAR) (5), Braaten (6) introduced a modification of Rubin's combination formula by including a term depending on the response rate, which is regarded as fixed when data is collected. This is further developed in Bjørnstad (7) to include residual imputation in regression problems. In the present paper an empirical study is presented that uses both

simulated and real data. The imputed values are generated by the SRI method, with subsequent analyses of the imputed data sets within multiple regression models where the missingness is in the explanatory variables. The purpose of this study is to assess the appropriateness of the modified combination formula for variance estimation when a classical simple random imputation procedure is applied.

2 MODELS AND METHODS

2.1 The model-based imputation method

Hot-deck and SRI are examples of procedures where values are drawn at random from an observed sample conditioned on the values of some auxiliary variables. Hot-deck imputation fits when the auxiliary variables are categorical, while the incomplete variable may be either continuous or categorical. SRI generates values on the continuous scale, while the auxiliary variables may be of both types. This study gives an example of SRI, which was essentially proposed by Kalton and Kish (8), and David, Little, Samuhel and Triest (9).

Let z be the continuous variable for which missing values are to be imputed and let $\mathbf{x} = (x_1, x_2, \ldots, x_p)$ be the set of auxiliary variables that are to be used in imputing for the missing z values. A multiple linear regression model is assumed with constant variance for the error term.

Put

$$r_i = Z_i - \mathbf{X}_i^T \hat{\theta}_r, \quad 1 \le i \le n_r$$

where $\hat{\theta}_r$ is the least-squares estimate of the regression coefficients θ based on the n_r complete $\boldsymbol{X}$, Z tuples.

Draw a sample of n-n_r residuals, $r_{(1)}, \ldots, r_{(n-n_r)}$, by sampling with replacement from the set $\{r_1, \ldots, r_{n_r}\}$, and let the imputed value be

$$Z_{(i)} = \mathbf{X}_{(i)}^{\mathrm{T}}\hat{\theta}_r + r_{(i)}, \quad 1 \le i \le n - n_r .$$

The procedure is repeated *m* times to create *m* augmented data sets, and then each of the *m* sets is the subject of the analysis of interest. All variables in the model of analysis (analyst's model) related to the imputed variable must be included in the model of imputation (imputer's model) described above. The outcome variable is included as an explanatory variable in the imputer's model, while the imputed variable acts as an explanatory variable in the analyst's model. We have examined three different combinations of imputer's and analyst's models, two with simulated data sets, and one using real data from the Norwegian Women and Cancer Study.

2.1.1. Model 1

The population of N=1 000 000 observations of four variables was generated from a multivariate normal distribution with the following arbitrary chosen mean vector $\boldsymbol{\mu}$ and variance-covariance matrix $\boldsymbol{\Sigma}$:

$$\boldsymbol{\mu} = (30, 20, 40, 50), \qquad \boldsymbol{\Sigma} = \begin{pmatrix} 8 & 2 & 3 & 2 \\ 2 & 5 & -1 & 3 \\ 3 & -1 & 6 & -2 \\ 2 & 3 & -2 & 7 \end{pmatrix}$$

The variables appear in the order Z, X_1, X_2, Y, where Z is the one subject to imputation, while Y is the outcome of the analysis of interest. The simple residual imputation was executed through a linear regression model with Z as the dependent, and X_1, X_2, Y as independent variables. A linear model was also applied for the analyses of the imputed data sets.

2.1.2 Model 2

The population of N=1 000 000 observations of the four variables Z, X_1, X_2, and Y was originally generated from a multivariate normal distribution with the following parameters:

$$\boldsymbol{\mu} = (40, 30, 20, 10), \qquad \boldsymbol{\Sigma} = \begin{pmatrix} 20 & 3.6 & 1 & 1.5 \\ 3.6 & 4 & 1.8 & 4 \\ 1 & 1.8 & 9 & 3.6 \\ 1.5 & 4 & 3.6 & 16 \end{pmatrix}$$

Subsequently, Z was transformed into a gamma distributed variable while Y was dichotomized, and X_2 was categorized into tertiles. X_1 was kept normally distributed. Hence, the imputed data was created through a generalized linear model, assuming a gamma distributed outcome. A logistic regression model was applied for the analysis.

2.1.3 Model 3

For the last model we employed real data from The Norwegian Women and Cancer Study (http://www.ism.uit.no/kk/e/), where a cohort of 72,884 women with complete information was regarded as the source population. The subject of analysis was the association between lifestyle factors and self-reported health, adjusting for years of education as an indicator of residual confounding. We chose years of education as the variable to be imputed, which was log-log transformed in order to acquire a proper fit of the linear model. The outcome self-reported health in the analyst's model was recorded as a dichotomous variable, and hence a logistic regression model was applied.

2.2 The simulation study

Under the assumption of missing completely at random (MCAR) (5), the following procedure was repeated 1000 times:

Step 1: The complete sample was drawn at random from the population.

Step 2: The response sample was drawn at random from the complete sample with a chosen response probability p_r for each observation in the complete sample

Step 3: The imputation and analysis of the data were executed m times as described in Section *2.1.*

The efficiency of the proposed variance estimator was evaluated by simulating coverages, computed as the proportion of 95 % confidence intervals including the population regression coefficients. For each model the entire procedure was run for different choices of sample size, number of imputations, and response rates.

All programming and analyses were performed by the SAS software package, version 9.1 (10;11)

2.3 The variance estimation

From Bjørnstad (7):

Let $s = (1,\ldots,n)$ denote the full sample, with $\mathbf{z} = (z_1,\ldots,z_n)$ be the planned data, values of the random variable $Z_1,\ldots,Z_n$. The objective is to estimate some parameter θ. Now, let z_{obs} be the observed part of **z**, with s_r being the response sample of size n_r,

$z_{obs} = (z_i : i \in s_r)$.

Let $\hat{\theta}$ be the estimator based on the full sample data **z**, with $Var(\hat{\theta})$ estimated by $\hat{V}(\mathbf{z})$. For $i \in s - s_r$ we impute z_i^* by some method and let **z*** denote the complete data $(z_{obs}, z_i^*, i \in s - s_r)$. Based on **z***, we have

$$\hat{\theta}^* = \hat{\theta}(\mathbf{z}^*)$$
$$\hat{V}^* = \hat{V}(\mathbf{z}^*)$$

Multiple imputation of m repeated imputations leads to m augmented data-sets with m estimates $\hat{\theta}_i^*, i = 1,...,m.$ and related variance estimates $\hat{V}_i^*, i = 1,...,m$. The combined estimate is given by

$$\bar{\theta}^* = \sum_{i=1}^{m} \hat{\theta}_i^* / m.$$

The within-imputation variance is defined as

$$\bar{V}^* = \sum_{i=1}^{m} \hat{V}_i^* / m$$

and the between-imputation component is

$$B^* = \frac{1}{m-1} \sum_{i=1}^{m} (\hat{\theta}_i^* - \bar{\theta}^*)^2$$

The total estimated variance of $\bar{\theta}^*$ is proposed to be

$$W = \bar{V}^* + (k + \frac{1}{m}) B^*.$$

That is, we need to determine k such that

$$E(W) = Var(\bar{\theta}^*). \qquad (1)$$

Rubin(1) has shown that $k = 1$ can be used when the imputed values are drawn from a Bayesian posterior distribution.

2.3.1 Estimating the variance of the population mean with simple random imputation.

Assume the missingness mechanism is MCAR, and z_i^* is imputed from z_{obs} at random by a simple random procedure or by drawing values from the estimated distribution of z_{obs}. Let $f = (n - n_r)/n$ be the rate of non-response, which can be regarded as fixed when data is collected. Then, from Braaten (6) and Bjørnstad (7), (1) is satisfied by letting

$$k = \frac{1}{1-f}$$

2.3.2 Estimating the variance of estimated regression coefficients with simple residual imputation.

In case of MCAR missingness and hot-deck imputation, Bjørnstad (7) shows that if $\hat{\theta}$ is a linear estimator in $(z_i : i \in s)$, that is, $\hat{\theta} = \sum_{i \in s} a_i(s) z_i$, and

$$E(\hat{\theta}^* \mid \mathbf{z}) = \hat{\theta},$$

then $k = 1/(1-f)$.

Consider now the multiple linear regression model with MCAR , and simple residual multiple imputation. Let $\hat{\boldsymbol{\beta}}$ be the vector of estimated regression coefficients based on the fully observed sample, and let $\hat{\boldsymbol{\beta}}^*$ be the corresponding estimates of the imputation-based data, while $\hat{\boldsymbol{\beta}}_r$ are the estimates based on the response sample.

Then

$$E(\hat{\boldsymbol{\beta}}^* \mid \mathbf{z}) = E(E(\hat{\boldsymbol{\beta}}^* \mid \mathbf{z}, z_{obs}) \mid \mathbf{z}) = E(E(\hat{\boldsymbol{\beta}}^* \mid z_{obs}) \mid \mathbf{z}) = E(\hat{\boldsymbol{\beta}}_r \mid \mathbf{z})$$

and approximately,

$$E(\hat{\boldsymbol{\beta}}_r \mid \mathbf{z}) = \hat{\boldsymbol{\beta}} \frac{p_r - \dfrac{1-p_r}{n(n-1)p_r}}{p_r - \dfrac{1-p_r}{n-1}} \approx \hat{\boldsymbol{\beta}}$$

Then one might expect that $k = 1/(1-f)$ also in this case, since the imputation method is a hot-deck method of the residuals. In fact, in a modified version of Bjørnstad (7), submitted for publication, it is shown that this is indeed the case.

3. RESULTS

The results of model 1 are given in Table 1. The linear model of analysis included three independent variables, where Z was the one subject to imputation, while X_1 and X_2 were completely observed. The coverage converged towards the nominal confidence level with increasing sample size for all choices of m, with a sufficient approximation already for $m=10$. On the other hand, increasing m did not increase the efficiency for small samples.

The study was re-run using Rubin's variance estimation formula ($k=1$) in order to assess the influence of the between-variability modification factor $k=1/(1-f)$. Table 2 shows the resulting coverages for both approaches when $m=100$ and $n=1000$, respectively. Table 3 shows the results of model 2, with an assumed gamma distributed imputed variable, and both continuous and categorical covariates, the latter dichotomized into indicator variables. Since the results for model 1 were similar for $m=100$ and $m=1000$, m>100 was omitted for model 2. For small samples ($n=100$) the confidence intervals tended to be slightly too wide, particularly for the completely observed variables. However, for $n>1000$ the coverage is proper both for $m=10$ and $m=100$, although it varies between 0.93 and 0.97. Model 3 evaluates the appropriateness of the modified variance estimator applied on real data, and the results are given in Table 4. Due to the low prevalence of the outcome poor health, the size of the complete samples must be at least $n=1000$ to give a valid estimation. The results for model 3 seem similar to model 2; proper, but occasionally with a little too high coverage for the fully observed variables.

4. DISCUSSION

A modification of Rubin's combination formula for variance estimation of multiple imputed data is introduced, and its appropriateness is examined when SRI is applied. The results of the simulation study show confidence levels close to the nominal, which support the validity of the modified variance estimator. The confidence levels of the regression coefficients for fully observed variables tend to slightly exceed the nominal level, but the difference does not increase with increasing non-response. Moreover, the comparison with Rubin's formula clearly leaves the modified formula as the preferable by SRI, also for the fully observed variables.

Initiated by Donald Rubin, several multiple imputation procedures based on Bayesian theory have been developed and further integrated in software packages such as SOLAS for Missing Data Analysis, and PROC MI in SAS. Some attention has also been paid to frequentistic, non-parametric methods like SRI and hot-deck multiple imputation; Schenker and Welsh (4) have derived the asymptotic properties of both the SRI and hot-deck multiple-imputation estimator for an incomplete outcome variable, whereas Reilly (12) has considered hot-deck multiple imputation of incomplete covariates. The present study presents a Non-Bayesian approach to multiple imputation of continuous variables providing valid inferences. The method is easy to implement and can be applied to any generalized linear model where residuals are computed, which allows imputation of variously distributed continuous data. It may also be expanded to treat imputation of categorical variables (7). What is still lacking in this approach is the opportunity to impute several variables simultaneously, which is left for further research.

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Table 1. Model 1 with simple residual multiple imputation. Coverages (in %) of 95 % confidence intervals for the regression coefficients using $k = 1/(1-f)$, where Z is the imputed variable, and X_1, X_2 are completed observed normally distributed covariates. f is the rate of non-response.

m=10									
f	*n=100*			*n=1000*			*n=10000*		
	Z	X_1	X_2	*Z*	X_1	X_2	*Z*	X_1	X_2
0.1	0.942	0.962	0.944	0.947	0.953	0.959	0.947	0.951	0.951
0.2	0.934	0.949	0.959	0.956	0.943	0.954	0.957	0.951	0.954
0.3	0.917	0.955	0.927	0.947	0.943	0.951	0.940	0.943	0.962
0.4	0.943	0.934	0.954	0.956	0.954	0.958	0.953	0.950	0.958
0.5	0.926	0.935	0.946	0.951	0.958	0.954	0.952	0.957	0.955
m=100									
f	*n=100*			*n=1000*			*n=10000*		
	Z	X_1	X_2	*Z*	X_1	X_2	*Z*	X_1	X_2
0.1	0.940	0.956	0.946	0.960	0.953	0.948	0.951	0.934	0.955
0.2	0.941	0.943	0.937	0.953	0.933	0.956	0.956	0.958	0.945
0.3	0.940	0.936	0.940	0.948	0.956	0.958	0.953	0.962	0.952
0.4	0.935	0.944	0.946	0.953	0.951	0.943	0.954	0.957	0.962
0.5	0.930	0.936	0.930	0.959	0.958	0.945	0.964	0.956	0.949
m=1000									
f	*n=100*			*n=1000*			*n=10000*		
	Z	X_1	X_2	*Z*	X_1	X_2	*Z*	X_1	X_2
0.1	0.935	0.931	0.930	0.949	0.939	0.941	0.955	0.951	0.954
0.2	0.943	0.942	0.954	0.946	0.951	0.964	0.958	0.957	0.954
0.3	0.934	0.946	0.943	0.951	0.961	0.943	0.948	0.951	0.951
0.4	0.939	0.946	0.945	0.958	0.947	0.942	0.955	0.950	0.942
0.5	0.932	0.953	0.931	0.947	0.935	0.949	0.960	0.960	0.952

Table 2. Model 1 with simple residual multiple imputation. Coverages (in %) of 95 % confidence intervals for the regression coefficients , where *Z* is the imputed variable. Comparison of Rubin's combination formula *(k=1)* with the modified formula *(k=1/(1-f))* when *m=100, n=1000*.

f	*k=1*			*k=1/(1-f)*		
	Z	X_1	X_2	*Z*	X_1	X_2
0.1	0.951	0.962	0.948	0.951	0.962	0.948
0.2	0.954	0.955	0.945	0.955	0.955	0.947
0.3	0.946	0.943	0.938	0.955	0.944	0.944
0.4	0.917	0.942	0.945	0.938	0.951	0.954
0.5	0.919	0.934	0.927	0.957	0.948	0.951

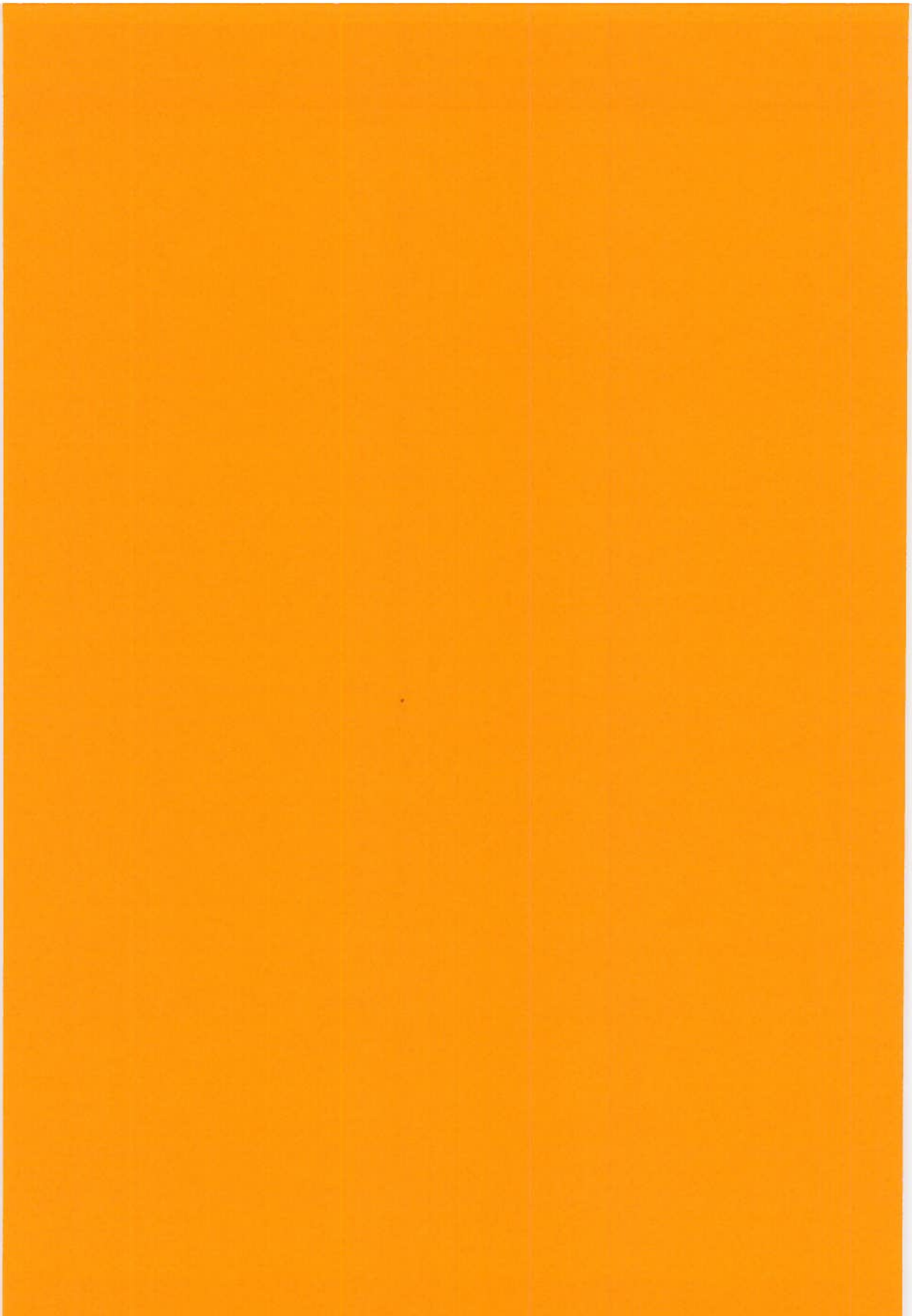
Table 3. Model 2 with simple residual multiple imputation. Coverages (in %) of 95 % confidence intervals for regression coefficients where Z is the imputed variable, and X_1, X_2 are completed observed covariates in a logistic regression model.

m=10												
f	*n=100*				*n=1000*				*n=10000*			
	Z	X_1	X_2 2nd tert	X_2 3rd tert	*Z*	X_1	X_2 2nd tert	X_2 3rd tert	*Z*	X_1	X_2 2nd tert	X_2 3rd tert
0.1	0.947	0.950	0.980	0.977	0.948	0.950	0.945	0.952	0.949	0.956	0.947	0.970
0.2	0.949	0.960	0.977	0.971	0.944	0.955	0.966	0.964	0.946	0.945	0.965	0.952
0.3	0.954	0.968	0.971	0.972	0.927	0.956	0.965	0.962	0.939	0.943	0.941	0.951
0.4	0.955	0.961	0.976	0.984	0.940	0.942	0.961	0.961	0.939	0.950	0.947	0.950
0.5	0.947	0.964	0.974	0.981	0.952	0.951	0.948	0.938	0.933	0.950	0.956	0.957
m=100												
f	*n=100*				*n=1000*				*n=10000*			
	Z	X_1	X_2 2nd tert	X_2 3rd tert	*Z*	X_1	X_2 2nd tert	X_2 3rd tert	*Z*	X_1	X_2 2nd tert	X_2 3rd tert
0.1	0.955	0.953	0.973	0.974	0.966	0.950	0.962	0.968	0.946	0.957	0.961	0.955
0.2	0.957	0.955	0.972	0.981	0.949	0.956	0.954	0.959	0.949	0.958	0.967	0.963
0.3	0.955	0.956	0.969	0.973	0.952	0.946	0.957	0.956	0.938	0.965	0.956	0.955
0.4	0.968	0.969	0.967	0.978	0.942	0.953	0.962	0.952	0.942	0.958	0.967	0.969
0.5	0.966	0.966	0.975	0.965	0.945	0.956	0.949	0.967	0.956	0.949	0.965	0.956

Table 4. Model 3 with simple residual multiple imputation Coverages (in %) of 95 % confidence intervals for regression coefficients, using data from The Norwegian Women and Cancer Study. Results for the imputed variable years of education and the selected covariates age and current smoking status (yes/no).

	m=10					
	n=1000			*n=10000*		
f	*Years of education*	*Age*	*Current smoking*	*Years of education*	*Age*	*Current smoking*
0.1	0.943	0.959	0.949	0.945	0.964	0.971
0.2	0.931	0.965	0.954	0.945	0.958	0.962
0.3	0.940	0.962	0.956	0.954	0.982	0.961
0.4	0.936	0.963	0.962	0.946	0.967	0.963
0.5	0.945	0.954	0.954	0.944	0.970	0.948
	m=100					
	n=1000			n=10000		
f	*Years of education*	*Age*	*Current smoking*	*Years of education*	*Age*	*Current smoking*
0.1	0.949	0.957	0.953	0.952	0.973	0.965
0.2	0.943	0.962	0.962	0.949	0.966	0.967
0.3	0.933	0.953	0.945	0.949	0.968	0.962
0.4	0.945	0.969	0.953	0.952	0.970	0.958
0.5	0.944	0.955	0.956	0.957	0.972	0.956

Appendix I



NSTITUTT FOR SAMFUNNSMEDISIN
NIVERSITETET I TROMSØ
000 TROMSØ
elefon 083-44 816

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.

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 å være med. Det som 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
Elliv 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;

	Ja	Nei	Hvis Ja; Hvor lenge Måneder
Spisevegring	☐	☐	
Etter slanking	☐	☐	
Etter p-pille bruk	☐	☐	
Ved stress i arbeidet (skift)	☐	☐	
Ved trening	☐	☐	
Andre årsaker	☐	☐	

Har du vanligvis før-menstruelle plager?

☐ ingen ☐ brystspreng ☐ 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? ☐
operert vekk eggstokkene? ☐
operert vekk livmoren? ☐
annet? ☐

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 år	måneder	P-pillene (se brosjyren) 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?

	Ja	Nei	Hvis Ja; Alder ved 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?

	Ja	Nei	Hvis Ja; Alder ved 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;

	Ja	Nei	Vet 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? .....cm

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

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

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.

	Antall sigaretter hver dag						
Alder	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
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 konkurranseidrett? Ja ☐ Nei ☐

Hvis Ja, hvor mange år i alt?

.....år

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 aldri
Helmelk (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 aldri
Rent kjøtt								
Oppmalt kjøtt								
Fet fisk (makrell,laks o.l)								
Mager fisk (torsk ol.)								
Ris, spaghetti								
Gulerøtter								
Kål								
Kålrot								
Salat								
Broccoli/Blomkål								

Hva slags fett blir vanligvis brukt i din husholdning?

	På brød	Til mallaging
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 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 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)?

(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 blemmer med avflassing etterpå? (Ett kryss for hver aldersgruppe)

Alder	Aldri	Høyst 1 gang pr.år	2-3 g. pr. år	4-5 g. pr. år	6 eller flere ganger
Før 10 år					
10-19 år					
20-29 år					
30-39 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!

75 Hur många oregelbundna födelsemärken, som är större än 5 mm (se sista sidan i broschyren), har Du sammanlagt på båda benen (från tår till ljumskar)?

☐ 1 Inga
☐ 2 1
☐ 3 2-3
☐ 4 4-6
☐ 5 7-12
☐ 6 13-24
☐ 7 25 eller fler

76 Hur många gånger per år har Du blivit bränd av solen med sveda i huden eller blåsor och hudflagning?

	Antal gånger per år				
Ålder	Aldrig	Högst 1	2-3	4-5	6 eller fler
10-19 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
20-29 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
30-39 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
40-49 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

77 Hur många veckor i genomsnitt per år har Du varit på badsemester, i Sverige eller utomlands?

	Antal gånger per år				
Ålder	Aldrig	1 vecka	2-3 v	4-6 v	7 v eller fler
10-19 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
20-29 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
30-39 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5
40-49 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5

78 Hur ofta har Du i genomsnitt solat i solarium?

	Antal gånger per månad					
Ålder	Aldrig	Sällan	1 gång	2 ggr	3-4 ggr	5 ggr -
före 10 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
10-19 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
20-29 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
30-39 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
40-49 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

KOSTVANOR UNDER DET SENASTE ÅRET

79 Vilka typer av mjölk brukar Du dricka eller använda till gröt, kräm, kaffe och hur mycket per dag eller per vecka (1 glas=2 dl)?

Lättmjölk/minimjölk	.....	glas/dag	.....	glas /vecka
Mellanmjölk	.....		.....	
Standardmjölk	.....		.....	
Filmjölk/yoghurt/kefir	.....		.....	
Lättfil/lättyoghurt	.....		.....	

☐ 1 Jag dricker eller använder sällan/aldrig mjölk

80 Vilka typer av bröd brukar Du äta och hur många skivor per dag eller per vecka?

Vitt bröd	.....	skivor/dag	.....	skivor /vecka
Grovt/fullkorns	.....		.....	
Limpa/skorpor	.....		.....	
Knäckebröd	.....		.....	

81 Hur många smörgåsar med smör/margarin brukar Du äta per dag eller per vecka?

..... skivor/dag ..... skivor /vecka

82 Vilka typer av matfett brukar Du använda till smörgåsar och matlagning (även bakning)?

	Smör-gåsar	Mat-lag-ning
Smör	☐ 1	☐ 2
Bregott	☐ 1	☐ 2
Bordsmargarin (t ex Flora, Vår)	☐ 1	☐ 2
Lättmargarin (t ex Lätt & Lagom, Lätta)	☐ 1	☐ 2
Hushållsmargarin (t ex Milda, TreEss)	☐ 1	☐ 2
Matolja (t ex Majs, Solros, Soja)	☐ 1	☐ 2
Rapsolja	☐ 1	☐ 2
Olivolja	☐ 1	☐ 2

☐ 1 Jag använder inget matfett till matlagning
☐ 2 Jag använder inget matfett till smörgåsar → Fortsätt med fråga 84

83 Hur brukar Du vanligen breda Dina smörgåsar?

☐ 1 Ganska tjockt lager fett
☐ 2 Tunt lager fett
☐ 3 Mycket tunt lager fett

84 Vilka typer av ost brukar Du äta och hur mycket per dag eller per vecka?

	skivor/msk/dag	skivor/msk/vecka
Ost	.....	.....
Lättost	.....	.....
Dessertost	.....	.....
Smältost	.....	.....
Lättsmältost	.....	.....
Keso, kvarg m fl	.....	.....

☐ 1 Jag äter sällan/aldrig ost

85 Hur många koppar kaffe dricker Du vanligen per dag eller per vecka? (1 kopp = 1,5 dl)

..... koppar/dag ..... koppar /vecka

☐ 1 Jag dricker sällan/aldrig kaffe

86 Hur mycket alkohol brukar Du dricka per vecka eller per månad eller per år?

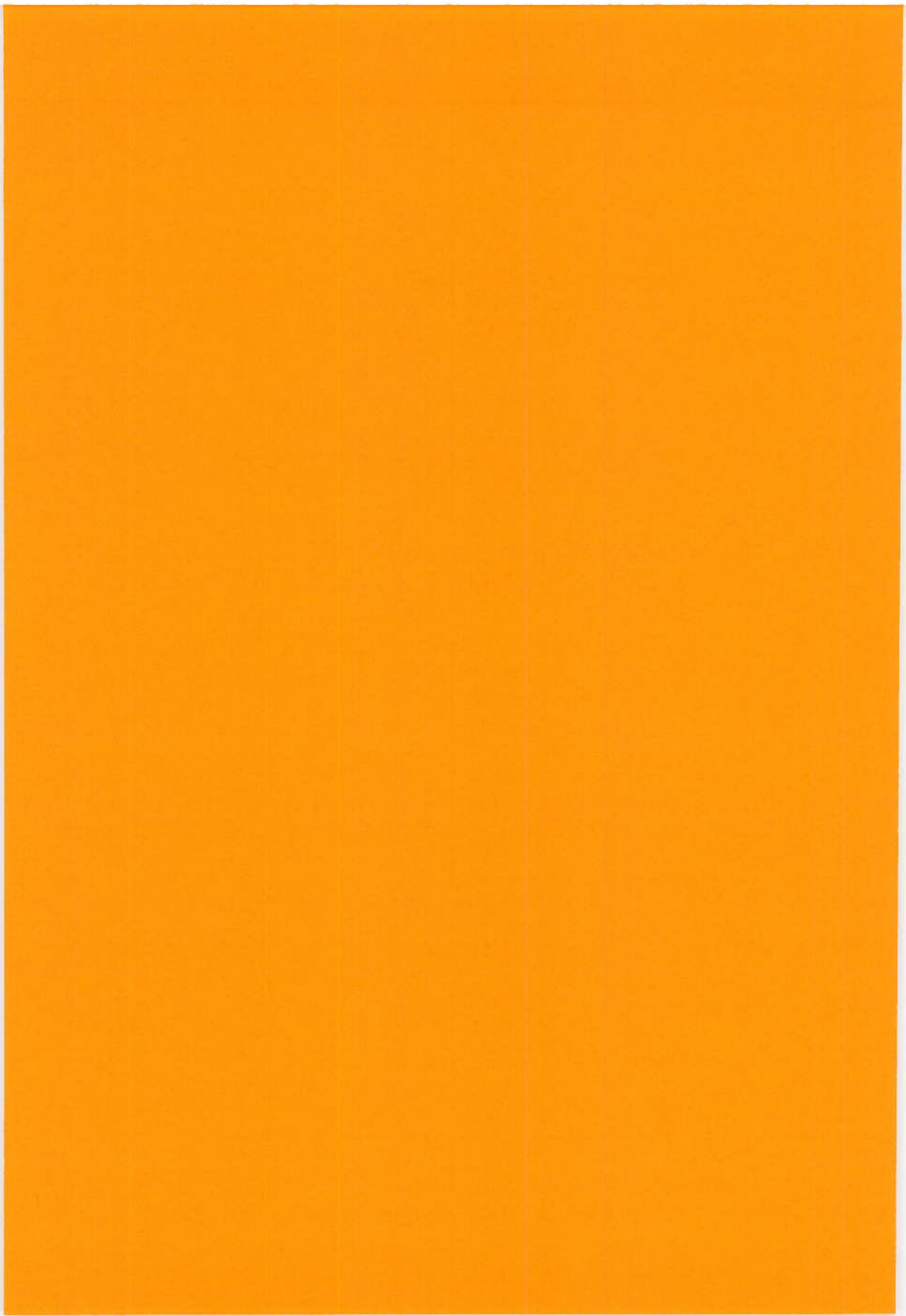
	glas/vecka	glas/månad	glas/år
Folköl, kl II (1glas=2 dl)	.....	.....	.....
Starköl (1 glas=2 dl)	.....	.....	.....
Vin (1 glas=1 dl)	.....	.....	.....
Starkvin (1 glas=4 cl)	.....	.....	.....
Starksprit (1 glas=4 cl)	.....	.....	.....

☐ 1 Jag dricker sällan alkohol
☐ 2 Jag dricker aldrig alkohol

87 Vad gör Du med fett som syns i Din köttportion och skinn på kyckling och annan fågel?

☐ 1 Jag äter allt
☐ 2 Jag äter en del
☐ 3 Jag skär bort så mycket som möjligt

Appendix II



Jag har tagit del av bifogat brev och väljer:

☐ att delta i undersökningen
☐ att inte delta i undersökningen

Kvinnors livsstil och hälsa

Vi ber Dig fylla i frågeformuläret så noga som möjligt enligt anvisningarna.

UPPVÄXT OCH UTBILDNING

Vilket land växte Du huvudsakligen upp i (0-7 år)?

1 Sverige
2 Finland
3 Norge
4 Danmark
5 Annat land.....

Ungefär hur många år har Du sammanlagt utbildat ig (räkna med den vanliga skolgången)?

..... år

Hur gammal var Din mor när Du föddes?

..... år ☐ 1 Vet ej

Hur många syskon har Du? (Ange samtliga, alltså en halvsyskon och syskon som avlidit)

..... syskon

Hur många av Dina syskon föddes före Dig?

..... syskon

Har Du någon tvillingbror/syster?

1 Ja
2 Nej

MENSTRUATION

Hur gammal var Du vid Din första menstruation?

..... år

Hur många år tog det innan menstruationen blev gelbunden?

1 Mindre än 1 år
2 1 - 3 år
3 Mer än 3 år
4 Aldrig
5 Vet ej

Hur lång tid var det mellan första dagen i en menuation och första dagen i nästa?

Menstruation Dag 1 — Menstruation Dag 1

x - - - - Hur många dagar? - - - - x

	Vet ej	Oregelbunden mens
..... dagar, vid 18 år	☐ 1	☐ 2
..... dagar, vid 30 år	☐ 1	☐ 2

10 Har menstruationen någon gång - bortsett från graviditet - uteblivit mer än sex månader?

☐ 1 Ja
☐ 2 Nej → Fortsätt med fråga 12

11 Var det i samband med/efter...

	Nej	Ja	Hur många månader
..matvägran	☐ 1	☐ 2 →	.....
..bantning	☐ 1	☐ 2 →	.....
..p-pilleranvändning	☐ 1	☐ 2 →	.....
..stress i arbetet	☐ 1	☐ 2 →	.....
..fysisk träning	☐ 1	☐ 2 →	.....
..annan orsak	☐ 1	☐ 2 →	.....

12 Har Du regelbundna menstruationer numera?

☐ 1 Ja
☐ 2 Nej, menstruationerna är oregelbundna → Fortsätt med fråga 15
☐ 3 Nej, jag är gravid
☐ 4 Nej, menstruationerna har upphört sedan mer än sex månader

13 Varför har menstruationen upphört?

☐ 1 De har upphört naturligt
☐ 2 Äggstockarna är bortopererade
☐ 3 Livmodern är bortopererad
☐ 4 Vet ej

14 Hur gammal var Du när menstruationen upphörde?

..... år

HORMONBEHANDLING

15 Har Du kommit i övergångsåldern (klimakteriet)?

☐ 1 Ja
☐ 2 Nej → Fortsätt med fråga 19

16 Tar Du nu eller har Du tidigare tagit hormontabletter mot övergångsbesvär?

☐ 1 Ja
☐ 2 Nej
☐ 3 Vet ej → Fortsätt med fråga 19

17 Hur gammal var Du när Du tog hormontabletter mot övergångsbesvär första gången?

..... år

18 Hur länge, sammanlagt, har Du tagit hormontabletter mot övergångsbesvär?

..... månader

GRAVIDITETER, FÖRLOSSNINGAR OCH AMNING

19 Har Du någon gång varit gravid?
☐ 1 Ja
☐ 2 Nej → Fortsätt med fråga 23

Om Du inte fött barn gå vidare till fråga 21

20 Ange för varje barn födelseår (även för barn som föddes döda eller som dött senare) och antal månader Du ammade. Dessutom ber vi Dig fylla i hur mycket Du gick upp i vikt under varje graviditet.

Barn	Födelseår	Antal månader med amning	Ungefärlig viktökning under graviditeten
1	.....	..... mån	..... kg
2	.....	..... mån	..... kg
3	.....	..... mån	..... kg
4	.....	..... mån	..... kg
5	.....	..... mån	..... kg
6	.....	..... mån	..... kg
7	.....	..... mån	..... kg

21 Har Du haft någon graviditet som varat mindre än sex månader, dvs slutat med missfall eller abort?
☐ 1 Ja
☐ 2 Nej

22 Har Du haft något utomkvedshavandeskap?
☐ 1 Ja
☐ 2 Nej

23 Har Du någon gång försökt att bli gravid under mer än 1 år utan framgång?
☐ 1 Ja
☐ 2 Nej → Fortsätt med fråga 26

24 Hur gammal var Du då?
..... år

25 Under hur lång period försökte Du?
..... år

P-PILLER

26 Har Du någon gång använt p-piller, inberäknat minipiller? (Kontrollera gärna i den bif. broschyren)
☐ 1 Ja
☐ 2 Nej → Fortsätt med fråga 34

27 Hur länge har Du sammanlagt använt p-piller?
..... år

28 Hur gammal var Du när Du första gången använde p-piller?
..... år

29 Om Du har fött barn; använde Du p-piller före första barnets födelse?
☐ 1 Ja
☐ 2 Nej

30 Använder Du p-piller för närvarande?
☐ 1 Ja
☐ 2 Nej

31 Har Du någon gång fått p-piller av andra skäl än för att förhindra graviditet?
☐ 1 Ja
☐ 2 Nej

32 Har Du blivit rekommenderad av läkare att sluta med p-piller av medicinska skäl?
☐ 1 Ja
☐ 2 Nej

33 Vi ber Dig att nedan besvara frågorna om p-pilleranvändning mera i detalj.

För varje period som Du använt samma slags p-piller hoppas vi att Du kan tala om vad det hette, vid vilken ålder Du började använda p-piller och hur länge Du använde dem.

Om Du inte minns vilket märke det var, ange "osäker". För att hjälpa Dig att minnas namnen ber vi Dig att titta i den bifogade broschyren med bilder av alla p-piller som sålts i Sverige. Uppge namn och det nummer som står i broschyren.

	Ålder när Du började	Användningstid	P-piller Nr	P-piller Namn
1	.....år	.....år..... mån	.....	.....
2	.....år	.....år..... mån	.....	.....
3	.....år	.....år..... mån	.....	.....
4	.....år	.....år..... mån	.....	.....
5	.....år	.....år..... mån	.....	.....
6	.....år	.....år..... mån	.....	.....
7	.....år	.....år..... mån	.....	.....
8	.....år	.....år..... mån	.....	.....
9	.....år	.....år..... mån	.....	.....
10	.....år	.....år..... mån	.....	.....

ANDRA PREVENTIVMETODER

34 Hur ofta har Du eller Din partner använt något av följande preventivmedel, och i hur många år?

	Aldrig	Ibland	Ofta	Alltid	Antal år
Kondom	☐ 1	☐ 2	☐ 3	☐ 4	.....år
Pessar	☐ 1	☐ 2	☐ 3	☐ 4	.....år

35 Använder Du nu eller har Du tidigare använt spiral?
☐ 1 Ja
☐ 2 Nej → Fortsätt med fråga 38

36 Hur gammal var Du första gången Du fick en spiral insatt?
..... år

37 Hur många år, sammanlagt, har Du haft spiral?
..... år

SJUKDOMAR

38 Har eller har Du haft någon av följande sjukdomar?

	Ja	Nej	Ungefärlig ålder vid diagnos
Högt blodtryck	☐ 1	☐ 2	..... år
Sockersjuka (diabetes)	☐ 1	☐ 2	..... år
Blodpropp i vad eller lår	☐ 1	☐ 2	..... år
Hjärnblödning	☐ 1	☐ 2	..... år
Hjärtinfarkt	☐ 1	☐ 2	..... år
Reumatoid arthrit	☐ 1	☐ 2	..... år
Crohns sjukdom	☐ 1	☐ 2	..... år
Ulcerös kolit	☐ 1	☐ 2	..... år
Psoriasis	☐ 1	☐ 2	..... år
MS (multipel skleros)	☐ 1	☐ 2	..... år
Cancer	☐ 1	☐ 2	..... år

39 Har Du någon gång sökt läkare för godartad knöl eller cysta i bröstet?

☐ 1 Ja
☐ 2 Nej

40 Har Du någon gång opererats för knöl, tumör eller cysta i bröstet?

☐ 1 Nej → Fortsätt med fråga 43
☐ 2 Ja

41 Ange senaste år .....

42 Ange vilket sjukhus .....

ALLERGI

43 Har Du någon eller några av följande allergiska sjukdomar?

	Ja	Nej	Ungefär vid vilken ålder började den
Eksem.....	☐ 1	☐ 2	..... år
Hösnuva.....	☐ 1	☐ 2	..... år
Astma.....	☐ 1	☐ 2	..... år

44 Är Du allergisk mot....

	Ja	Nej
....gluten	☐ 1	☐ 2
....annan mat	☐ 1	☐ 2
....pollen	☐ 1	☐ 2
....husdjur	☐ 1	☐ 2
....annat	☐ 1	☐ 2

EGEN UPPFATTNING OM HÄLSAN

45 Uppfattar Du Din egen hälsa som...

☐ 1 ...mycket god
☐ 2 ...god
☐ 3 ...dålig
☐ 4 ...mycket dålig

CANCER INOM DEN NÄRMASTE FAMILJEN

46 Har någon av Dina närmaste släktingar drabbats av cancer? (kryssa för samtliga, alltså även de som avlidit)

	Nej	Vet ej	Bröstcancer	Mag/tarmcancer	Underlivscancer	Malignt melanom	Annan cancer
Egna syskon	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
Mor	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
Far	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
Mors syskon	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
Fars syskon	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
Mormor	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
Morfar	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
Farmor	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
Farfar	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7

47 Har någon av Dina närmaste släktingar drabbats av cancer före 45 års ålder?

☐ 1 Ja
☐ 2 Nej
☐ 3 Vet ej

48 Hur många syskon har/hade Dina föräldrar? (Ange samtliga, alltså även halvsyskon och syskon som avlidit)

Din mor ..... syskon ☐ 1 Vet ej

Din far ..... syskon ☐ 1 Vet ej

UNDERSÖKNINGAR FÖR CANCER

49 Hur ofta undersöker Du själv Dina bröst?

☐ 1 Aldrig
☐ 2 Ibland, oregelbundet
☐ 3 Regelbundet

50 Går Du regelbundet till mammografiundersökning av brösten?

☐ 1 Nej
☐ 2 Ja, med mer än 2 års mellanrum
☐ 3 Ja , med 2 års mellanrum eller oftare

51 Går Du regelbundet på gynekologisk hälsokontroll?

☐ 1 Aldrig
☐ 2 Mindre än vart 3:e år
☐ 3 Vart 3:e år eller oftare

LÄNGD OCH VIKT

52 Hur mycket vägde Du vid födseln?

☐ 1 Mindre än 2 500 g
☐ 2 2 500 - 3 000 g
☐ 3 Mer än 3 000 g
☐ 4 Vet ej

53 Nuvarande längd:.....cm

54 Nuvarande vikt:.....kg

55 Midjemått:.....cm

56 Stussmått (över bredaste delen):.....cm

57 Ungefär hur mycket vägde Du vid 18 års ålder?

Vikt i kg .....

58 Hur många gånger har Du gått ner 5 kg eller mer i vikt?
Antal gånger .....

59 När Du gick i 1:a klass var Du.....
- ☐ 1 Mycket smal
- ☐ 2 Smal
- ☐ 3 Normal
- ☐ 4 Tjock
- ☐ 5 Mycket tjock

ROKVANOR

60 Har Du rökt regelbundet någon gång?
- ☐ 1 Ja
- ☐ 2 Nej → Fortsätt med fråga 62

61 Kryssa i för varje 5-årsperid hur många cigarretter Du rökte per dag i genomsnitt?

	Antal cigarretter per dag						
Ålder	0	1-4	5-9	10-14	15-19	20-24	25+
10-14 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
15-19 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
20-24 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
25-29 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
30-34 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
35-39 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
40-44 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7
45-49 år	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6	☐ 7

62 Bor Du tillsammans med någon som röker i hemmet?
- ☐ 1 Ja
- ☐ 2 Nej → Fortsätt med fråga 64

63 Hur många cigaretter röker den Du bor tillsammans med i hemmet?

..... st / per dag

64 Rökte någon i Ditt hem när Du var barn?
- ☐ 1 Ja
- ☐ 2 Nej → Fortsätt med fråga 66

65 Vilka rökte i Ditt hem?
- ☐ 1 Far
- ☐ 2 Mor
- ☐ 3 Andra

FYSISK AKTIVITET

66 Vi ber Dig att i tabellen nedan ange Din fysiska aktivitet vid 14 års ålder, vid 30 års ålder och idag, enligt en skala från 1 till 5, från mycket låg till mycket hög. Med fysisk aktivitet menar vi både arbete i hemmet och i yrkeslivet samt träning, promenader, cykling, skidåkning o dyl.

Sätt ett kryss i den ruta som motsvarar Din fysisk aktivitet. Med mycket låg fysisk aktivitet menar vi nästan bara stillasittande. Med normal menar vi t ex några längre promenader i veckan, och med mycket hög menar vi t ex idrott/jogging flera ggr i veckan.

Ålder	Mycket låg		Normal		Mycket hög
	1	2	3	4	5
14 år	☐	☐	☐	☐	☐
30 år	☐	☐	☐	☐	☐
idag	☐	☐	☐	☐	☐

67 Har Du bedrivit tävlingsidrott?
- ☐ 1 Ja
- ☐ 2 Nej → Fortsätt med fråga 69

68 Hur många år sammanlagt?

..... år

SOLVANOR

69 Vilken är Din naturliga hårfärg?
- ☐ 1 Mörkbrun/svart
- ☐ 2 Ljusbrun
- ☐ 3 Blond, gul
- ☐ 4 Röd

70 Vilken färg har Dina ögon?
- ☐ 1 Bruna
- ☐ 2 Grå/gröna
- ☐ 3 Blå

71 Har Du några fräknar på armarna (året om)?
- ☐ 1 Nej
- ☐ 2 Ja, enstaka
- ☐ 3 Ja, många

72 Hur blir Din hud om Du solar kraftigt i början av sommaren?
- ☐ 1 Huden blir brun utan att först bli röd
- ☐ 2 Huden blir röd
- ☐ 3 Huden blir röd med sveda
- ☐ 4 Huden blir röd med sveda och blåsor

73 Hur blir Din hud efter långvarigt solande?
- ☐ 1 Huden blir mörkt brun
- ☐ 2 Huden blir brun
- ☐ 3 Huden blir ljust brun
- ☐ 4 Huden blir aldrig brun

74 Hur ofta använder Du solskyddskräm vid solbad?
- ☐ 1 Aldrig
- ☐ 2 Någon enstaka gång
- ☐ 3 Varannan gång
- ☐ 4 Nästan alltid

88 Hur ofta och hur mycket av följande livsmedel har Du i genomsnitt ätit **under det senaste året?**
Sätt ett kryss för hur ofta och ett kryss för hur mycket (om Du aldrig, sällan äter ett livsmedel behöver Du inte kryssa för hur mycket).

LITEN portion innebär ca hälften av MEDEL-portionen eller mindre.
STOR portion innebär ca 1,5 ggr av MEDEL-portionen eller mer.

	HUR OFTA									HUR MYCKET			
Livsmedel	Aldrig, sällan	Per mån	Per vecka				Per dag			Medel-portion	Din portion under det senaste året		
		1-3	1	2	3-4	5-6	1	2	3		Liten	Medel	Stor
Exempel: Havregrynsgröt	1	2	3	4	5	6	7	8	9	2,5 dl	1	2	3
Havregrynsgröt										2,5 dl			
Annan gröt/välling										1 dl			
Flingor/müsli										2 dl			
Spagetti/makaroner	1	2	3	4	5	6	7	8	9	2 dl	1	2	3
Ris										2 dl			
Vete-/havrekli										1 msk			
Kokt potatis										2 dl/2 st			
Stekt potatis	1	2	3	4	5	6	7	8	9	2 dl	1	2	3
Morötter										1 dl/1 st			
Kålrötter/rödbetor										1 dl			
Korv/köttpålägg										2 skivor			
Leverpastej	1	2	3	4	5	6	7	8	9	2 skivor/msk	1	2	3
Korvrätter (ej pålägg)										100 g			
Fläskkött (ej färs)										100 g			
Nöt/kalvkött (ej färs)										100 g			
Viltkött (ej färs)	1	2	3	4	5	6	7	8	9	100 g	1	2	3
Köttfärsrätter										100 g			
Kyckling/annan fågel										100 g			
Lever/njure										100 g			
Blodpudding/blodpalt	1	2	3	4	5	6	7	8	9	150 g	1	2	3
Sill/strömming/makrill										100 g			
Laxfiskar										100 g			
Torsk/sej/gädda m fl										100 g			
Kaviar	1	2	3	4	5	6	7	8	9	1 msk	1	2	3
Skaldjur (räkor m fl)										1 dl			
Ägg/omelett										2 ägg			
Vitkål/rödkål										1 dl			
Blomkål	1	2	3	4	5	6	7	8	9	1 dl	1	2	3
Broccoli/brysselkål										1 dl			
Tomat										1 st			
Spenat/grönkål										1 dl			
Gröna ärtor	1	2	3	4	5	6	7	8	9	1 dl	1	2	3
Ärtsoppa/ärtpuré										2,5 dl			
Bönor/soja/linser										1 dl			
Lök/purjolök										1 msk			
Dressing med olja	1	2	3	4	5	6	7	8	9	1 msk	1	2	3
Majonnäs										1 msk			
Grädde/creme fraiche										1 msk			
Såser/sky										1/2 dl			

Var snäll och kontrollera att Du kryssat i två rutor på varje rad (hur ofta + hur mycket).
Sätt ett kryss för "aldrig, sällan"-svar.

Livsmedel	HUR OFTA									HUR MYCKET			
	Aldrig, sällan	Per mån	Per vecka				Per dag			Medel-portion	Din portion under det senaste året		
		1-3	1	2	3-4	5-6	1	2	3		Liten	Medel	Stor
Apelsin/citrusfrukt	1	2	3	4	5	6	7	8	9	1 st	1	2	3
Äpple/päron										1 st			
Banan										1 st			
Juice										1 dl			
Sylt/marmelad/mos	1	2	3	4	5	6	7	8	9	1 msk	1	2	3
Fruktkräm/fruktsoppor										2 dl			
Pannkakor/plättar/våfflor										1 portion			
Vetebröd/bullar mm										1 st			
Wienerbröd	1	2	3	4	5	6	7	8	9	1 st	1	2	3
Kex/rån										1 st			
Småkakor										1 st			
Tårta/konditoribit										1 bit			
Choklad	1	2	3	4	5	6	7	8	9	1 st/50 g	1	2	3
Glass										2 dl			
Socker/honung										2 tsk/bitar			
Chips/popcorn										2 dl			
Nötter/mandel	1	2	3	4	5	6	7	8	9	10 st	1	2	3
Te										1 kopp			
Saft/läskedryck										1 glas			
Lättöl										1 glas			

Var snäll och kontrollera att Du kryssat i två rutor på varje rad (hur ofta + hur mycket).
Sätt ett kryss för "aldrig, sällan"-svar.

89 Hur ofta äter Du stekt mat?

	gånger/ vecka	gånger/ månad	sällan/ aldrig
Kött	.....	.....	☐ 1
Korv	.....	.....	☐ 1
Fisk	.....	.....	☐ 1
Ägg / omelett	.....	.....	☐ 1

90 Vilken stekyta har vanligen den mat Du brukar äta?

☐ 1 Hårdstekt
☐ 2 Medelstekt
☐ 3 Lättstekt (ljus)

91 Hur ofta äter Du i genomsnitt...

	gånger/ vecka	gånger/ månad	sällan/ aldrig
..Frukt och bär	.....	.....	☐ 1
..Grönsaker och rotfrukter (utom potatis)	.....	.....	☐ 1
..Kött och korv (maträtter)	.....	.....	☐ 1
..Fisk	.....	.....	☐ 1
..Matfett/matolja i matlagning/såser	.....	.....	☐ 1

92 Använder Du vitaminer, mineraler eller annat kosttillskott?

☐ 1 Nej, aldrig → Fortsätt med fråga 94
☐ 2 Ja, regelbundet eller ibland

93 Vilken (vilka) sort(er) använder Du och hur myck

Namn:	Antal tabl/kapsel per vecka	Antal veckor per år
Multivitamin:	.....	.....
Vitamin C:	.....	.....
Vitamin A:	.....	.....
Vitamin E:	.....	.....
B-vitaminer:	.....	.....
Kalcium:	.....	.....
Magnesium:	.....	.....
Selen:	.....	.....
Zink:	.....	.....
Järn:	.....	.....
Karoten:	.....	.....
Fiskolja:	.....	.....
Annan, vad:	.....	.....

ARBETSMILJÖ OCH PRIVATLIV

94 Har Du det senaste året varit yrkesverksam som..

	Ja	Nej
....Sekreterare.....	☐ 1	☐ 2
....Sjuksköterska.....	☐ 1	☐ 2
....Annat vårdyrke.....	☐ 1	☐ 2
....Handelsanställd.....	☐ 1	☐ 2
....Lärare.....	☐ 1	☐ 2
....Lokalvårdare.....	☐ 1	☐ 2
....Annat.....		

Vilken är Din nuvarande arbetsituation?

1 Hemarbetande → Fortsätt med fråga 98
2 Deltidsarbetande utanför hemmet → ..... antal tim/veckan
3 Heltidsarbetande utanför hemmet
4 Arbetslös → Fortsätt med fråga 98

	Ja, ofta	Ja, ibland	Nej, sällan	Nej, så gott som aldrig
äver Ditt arbete att Du arbetar mycket fort?	☐ 1	☐ 2	☐ 3	☐ 4
äver Ditt arbete att Du arbetar mycket hårt?	☐ 1	☐ 2	☐ 3	☐ 4
äver Ditt arbete en för stor arbetsinsats?	☐ 1	☐ 2	☐ 3	☐ 4
ır Du tillräckligt med tid för att hinna med betsuppgifterna?	☐ 1	☐ 2	☐ 3	☐ 4
ırekommer det ofta motstridiga krav i Ditt arbete?	☐ 1	☐ 2	☐ 3	☐ 4
r Du lära Dig nya saker i Ditt arbete?	☐ 1	☐ 2	☐ 3	☐ 4
äver Ditt arbete skicklighet?	☐ 1	☐ 2	☐ 3	☐ 4
äver Ditt arbete påhittighet?	☐ 1	☐ 2	☐ 3	☐ 4
nebär Ditt arbete att man gör samma sak om och om igen?	☐ 1	☐ 2	☐ 3	☐ 4
ır Du frihet att bestämma hur Ditt arbete skall utföras?	☐ 1	☐ 2	☐ 3	☐ 4
ir Du frihet att bestämma vad som skall utföras i Ditt arbete?	☐ 1	☐ 2	☐ 3	☐ 4

7	Stämmer helt och hållet	Stämmer ganska bra	Stämmer inte särskilt bra	Stämmer inte alls
et är en lugn och behaglig stämning på min arbetsplats	☐ 1	☐ 2	☐ 3	☐ 4
et är god sammanhållning	☐ 1	☐ 2	☐ 3	☐ 4
lina arbetskamrater ställer upp för mig	☐ 1	☐ 2	☐ 3	☐ 4
lan har förståelse för att jag kan ha en dålig dag	☐ 1	☐ 2	☐ 3	☐ 4
ıg kommer bra överens med mina överordnade	☐ 1	☐ 2	☐ 3	☐ 4
ıg trivs bra med mina arbetskamrater	☐ 1	☐ 2	☐ 3	☐ 4

	Antal personer					
	Ingen 0 pers.	1-2 pers.	3-5 pers.	6-10 pers.	11-15 pers.	Fler än 15 pers.
3 Hur många människor känner Du och har kontakt med, om har samma intressen som Du? (Det gäller kontakter både i arbetet och på fritiden)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
9 Hur många människor, som Du känner , träffar Du ller samtalar Du med under en vanlig vecka? Räkna inte med människor som Du träffar tillfälligtvis och som Du ıappast kommer att återse, t ex kunder i en affär!)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
00 Hur många vänner har Du som kan komma hem till ıig när som helst och känna sig hemma? De skulle inte bry sig om, om det var ostädat eller om Du höll på att äta. ära släktingar skall inte räknas med)	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6
01 Hur många finns det i Din familj och bland vänner, om Du kan tala öppet med utan att behöva tänka Dig för?	☐ 1	☐ 2	☐ 3	☐ 4	☐ 5	☐ 6

102 Bortsett från de därhemma, finns det någon som ıu kan vända Dig till om Du är i svårigheter? Någon om Du lätt kan träffa och som Du litar på och kan få erklig hjälp av när Du har det besvärligt?

☐ 1 Nej
☐ 2 Ja → Antal personer: .....

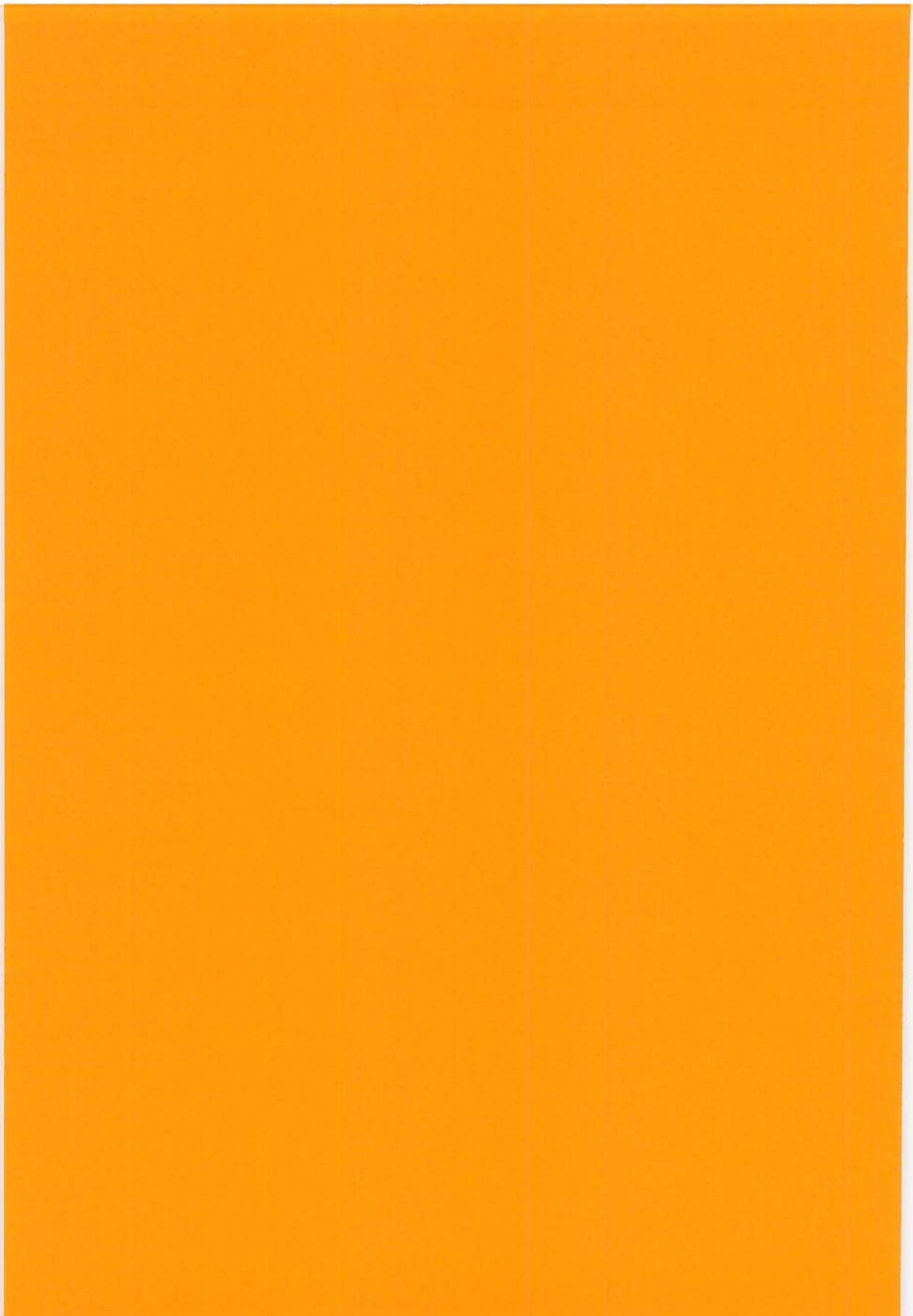
103 Hur många människor finns det i Din omgivning som Du lätt kan be om saker? Till exempel människor som Du känner så väl att Du kan låna verktyg eller köksredskap?

Antal personer: .....

STORT TACK FÖR DIN MEDVERKAN

Stoppa enkäten i det frankerade svarskuvertet och posta det, helst idag!

Appendix III



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KVINNER OG KREFT

Orientering om undersøkelsen

Du samtykket i 1991/92 til å fylle ut et fire siders spørreskjema som du mottok i posten – «Kvinner, livsstil og helse»/«Kvinner og kreft». Spørreskjemaet tok opp en rekke forhold knyttet til ditt liv som barnefødsler, p-pille bruk, kosthold, røking og sosiale forhold. Formålet med undersøkelsen var å se om disse forhold har betydning for utvikling av kreft hos kvinner. Resultatene vil bli publisert i dagspressen og i internasjonale fagtidsskrifter. Ansvarlig for undersøkelsen er professor Eiliv Lund.

Vi retter nå en ny forespørsel til deg om du nok en gang vil besvare det vedlagte spørreskjema. Begrunnelsen for å kontakte deg på ny er at mange av de spørsmålene du besvarte sist gjaldt levevaner som vi vet endrer seg med alderen. De fleste spørsmålene vil dreie seg om årene siden siste utfylling.

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

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

Det er frivillig om du vil være med i undersøkelsen. Du kan senere trekke deg uten begrunnelse og uten at det vil få noen konsekvenser for deg. Opplysninger du har gitt kan du be om å få slettet.

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

I tillegg vil vi senere kontakte en del av deltakerne for å få tatt en blodprøve. Det vil skje hos nærmeste lege og være gratis. Enkelte kvinner vil også bli forespurt om å delta i et kostholdsintervju over telefon.

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

Med hilsen

Eiliv Lund
professor dr.med.

KVINNER OG KREFT

I øst 1888

KONFIDENSIELT

Hvis du samtykker i å være med, sett kryss for JA i ruten ved siden av. Dersom du ikke ønsker å delta kan du unngå purring ved å sette kryss for NEI og returnere skjemaet i vedlagte svarkonvolutt.

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

Med vennlig hilsen

Elliv Lund
Professor dr. med

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

I hvilken kommune har du bodd lengre enn ett år?

Kommune:	Alder	
1. Fødested:	Fra 0 år	til ☐ år
2.	Fra ☐ år	til ☐ år
3.	Fra ☐ år	til ☐ år
4.	Fra ☐ år	til ☐ år
5.	Fra ☐ år	til ☐ år
6.	Fra ☐ år	til ☐ år
7.	Fra ☐ år	til ☐ år

Menstruasjonsforhold

Er menstruasjonen din;

☐ Regelmessig (naturlig)
☐ Uregelmessig
☐ Uteblitt pga. legemiddelbruk, sykdom, trening, annet
☐ Sluttet/stoppet

Hvis du ikke har menstruasjon;

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

Alder da menstruasjonen opphørte? ..... år

Graviditeter etter 1991

Fyll ut for hvert barn du har født etter 1991 fødselsår og antall måneder du ammet (fylles også ut for dødfødte eller for barn som er døde senere i livet). Dersom du ikke har født barn, fortsetter du ved neste spørsmål.

Barn Nr.:	Fødselsår	Antall måneder med amming

P-Pillebruk etter 1991

Har du noen gang brukt p-piller, minipiller inkludert, etter 1991? ☐ Ja ☐ Nei

Bruker du p-piller nå? ☐ Ja ☐ Nei

Vi vil be deg om å besvare spørsmålene om p-pillebruk etter 1991 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-pillemerket 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-pillen, sett usikker. For å hjelpe deg til å huske navnet på p-pille merkene ber vi deg bruke den vedlagte brosjyren som viser bilder av p-pille- merker som har vært solgt i Norge. Vennligst oppgi også nummeret på p-pillen som står i brosjyren.

Årstall	Alder ved start	Brukt samme p-pille sammenhengende år	måneder	P-pillene (se brosjyren) Nr.	Navn

Hormonspiral

Har du noengang brukt hormonspiral (Levonova)? ☐ Ja ☐ Nei

Hvis Ja; hvor lenge har du brukt hormonspiral i alt? ..... år

Hvor gammel var du første gang du du fikk innsatt hormonspiral? ..... år

Bruker du hormonspiral nå? ☐ Ja ☐ Nei

Holdning til bruk av østrogen

Hvilket av følgende alternativer dekker best ditt syn på østrogenbehandling i forbindelse med overgangsalderen (sett ett kryss)

Positivt - en hjelp som bør tilbys alle kvinner ☐
Et nødvendig onde- bør bare brukes av de med store plager ☐
Negativt- bør ikke «klusse med naturen» ☐

Bruk av hormonpreparater med østrogen i overgangsalderen

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

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

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

- Har nettopp startet behandlingen ☐
- Er kvitt plagene ☐
- Redd for skadevirkninger ☐
- Fikk plagsomme bivirkninger ☐
- Annet ☐

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

Hvorfor begynte du å bruke østrogentabletter/plaster?

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

Bruker du tabletter/plaster nå? ☐ Ja ☐ Nei

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

For hver periode med sammenhengende bruk av samme østrogenpreparat håper vi du kan si oss hvor gammel du var da du startet, hvor lenge du brukte det samme østrogenpreparatet, 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 østrogenpreparatet sett «usikker». For å hjelpe deg til å huske navnet på østrogenpreparatene ber vi deg bruke den vedlagte brosjyren som viser bilder av østrogenpreparater som har vært solgt i Norge. Vennligst oppgi også nummer på østrogentabletten/plasteret som står i brosjyren.

Periode	Alder ved start	Brukt samme østrogen-tablett/plaster Sammenhengende år	måned	Østrogentablett/ plaster (se brosjyre) Nr.	Navn
Første					
Andre					
Tredje					
Fjerde					
Femte					

Har østrogenpreparatene gitt deg bivirkninger? ☐ Ja ☐ Nei

Hvis Ja; kryss av for hvilke bivirkninger:

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

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

Hvis ja;

- Skiftet østrogenpreparat ☐
- Sluttet ☐
- Annet, angi ☐

Østrogenpreparat til lokal bruk i skjeden

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

Bruker du krem/stikkpille nå? ☐ Ja ☐ Nei

Selvopplevd helse

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

☐ meget god ☐ god ☐ dårlig ☐ meget dårlig

Sykdom

Har du eller har du hatt noen av følgende sykdommer?

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

For følgende tilstander kryss av for hvilket år tilstanden oppsto eller angi årstall for perioden før 1991.

	før 91	91	92	93	94	95	96	97	98
Muskelsmerter (myalgi)	☐	☐	☐	☐	☐	☐	☐	☐	☐
Fibromyalgi/Fibrositt	☐	☐	☐	☐	☐	☐	☐	☐	☐
Kronisk tretthetssyndrom	☐	☐	☐	☐	☐	☐	☐	☐	☐
Ryggsmerter ukjent årsak	☐	☐	☐	☐	☐	☐	☐	☐	☐
Nakkeslengskade	☐	☐	☐	☐	☐	☐	☐	☐	☐
Osteoporose/(b.skjørhet)	☐	☐	☐	☐	☐	☐	☐	☐	☐
Brudd									
Underarmen (håndledd)	☐	☐	☐	☐	☐	☐	☐	☐	☐
Ryggvirvel (kompresjon)	☐	☐	☐	☐	☐	☐	☐	☐	☐
Andre brudd angi :.....	☐	☐	☐	☐	☐	☐	☐	☐	☐

Sosiale forhold

Er du: (Sett ett kryss) ☐ gift ☐ samboer ☐ annet

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

Yrke? .....

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

Røykevaner

	Ja	Nei
Har du noen gang røkt?	☐	☐

Hvis Ja, ber vi deg om å fylle ut hvor mange sigaretter du i gjennomsnitt røkte pr. dag i perioden 1991-1998.

	Antall sigaretter hver dag						
Årstall	0	1-4	5-9	10-14	15-19	20-24	25+
1991-94							
1995-98							

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

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

Brystkreft i nærmeste familie

Har noen nære slektninger hatt brystkreft;

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

Hvor mange helsøsken har du? ☐ **Søstre** ☐ **Brødre**
(oppgi antall)

Hvilket nummer i søskenflokken er du? Nummer ☐

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

Fysisk aktivitet

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

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

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

	mindre enn ½ time	½-1 time	1-2 timer	mer enn 2 timer
Vinter				
Vår				
Sommer				
Høst				

	Ja	Nei
Arbeider du utendørs i yrkessammenheng?	☐	☐

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

Høyde og vekt

Hvor høy er du? ..... cm

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

Kosthold

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

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

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

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

	aldri/ sjelden	1-6 pr. uke	1 pr. dag	2-3 pr. dag	4-5 pr. dag	6-7 pr. dag	8+ pr. dag
Kokekaffe	☐	☐	☐	☐	☐	☐	☐
Traktekaffe	☐	☐	☐	☐	☐	☐	☐
Pulverkaffe	☐	☐	☐	☐	☐	☐	☐

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

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

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

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

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

☐ aldri/nesten aldri ☐ 1-3 pr. uke ☐ 4-6 pr. uke ☐ 1 pr. dag

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

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

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

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

	0 pr. uke	1-3 pr. uke	4-6 pr. uke	1 pr. dag	2-3 pr. dag	4+ pr. dag
Syltetøy og annet sott pålegg						
Brun ost, helfet						
Brun ost, halvfet/mager						
Hvit ost, helfet						
Hvit ost, halvfet/mager						
Kjøttpålegg, leverpostei						

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

	0 pr. uke	1 pr. uke	2-3 pr. uke	4-6 pr. uke	7-9 pr. uke	10+ pr. uke
Makrell i tomat, røkt makrell						
Kaviar						
Annet fiskepålegg						

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

☐ bruker ikke fett på brødet
☐ smør
☐ hard margarin (f. eks. Per, Melange)
☐ myk margarin (f. eks. Soft)
☐ smørblandet margarin (f. eks. Bremykt)
☐ Brelett
☐ lettmargarin (f. eks. Soft light, Letta)

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

☐ skrapet (3 g) ☐ tynt lag (5 g) ☐ godt dekket (8 g) ☐ tykt lag (12 g)

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

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-4 pr. uke	5-6 pr. uke	1 pr. dag	2+ pr. dag
Epler/pærer							
Appelsiner o.l.							
Bananer							
Annen frukt (f.eks. druer, fersken)							

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

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

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

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

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

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

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

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

Hvor ofte spiser du risengrynsgrøt? (Sett ett kryss)

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

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

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

Fisk

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

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

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

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

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

- kokt fisk (skive) ☐ 1 ☐ 1,5 ☐ 2 ☐ 3+
- stekt fisk (stykke) ☐ 1 ☐ 1,5 ☐ 2 ☐ 3+

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

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

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

☐ 1 ☐ 2 ☐ 3-4 ☐ 5-6 ☐ 7+

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

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

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

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

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

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

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

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

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

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

Andre matvarer

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

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

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

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

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

☐ 0 ☐ 1 ☐ 2 ☐ 3-4 ☐ 5-6 ☐ 7+

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

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

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

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

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

☐ 1 dl ☐ 2 dl ☐ 3 dl ☐ 4+ dl

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

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-3 pr. uke	4-6 pr. uke	7+ pr. uke
Gjærbakst(boller)						
Kaker						
Pannekaker						
Vafler						
Småkaker						

Hvor ofte spiser du dessert? (Sett ett kryss)

	aldri/ sjelden	1-3 pr. mnd	1 pr. uke	2-3 pr. uke	4-6 pr. uke	7+ pr. uke
Pudding Sjokolade/karamell						
Riskrem, fromas						
Kompott, fruktgrøt hermetisk frukt						

Hvor ofte spiser du sjokolade? (Sett ett kryss)

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

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

☐ 1/4 ☐ 1/2 ☐ 3/4 ☐ 1 ☐ 1,5 ☐ 2+

Hvor ofte spiser du salt snacks? (Sett ett kryss)

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

Tilberedningsmåte

Har du mikrobølgeovn? ☐ Ja ☐ Nei

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

middagslaging? .....
annet? .....

Hvilken farve foretrekker du på stekeskorpen?

☐ Lys brun ☐ Middels ☐ Mørk brun

Hvor ofte spiser du stekt eller grillet mat?

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

Bruker du stekefettet eller sjyen etter steking?

☐ nei, aldri ☐ av og til
☐ som oftest ☐ ja, alltid

Tran og fiskeoljekapsler

Bruker du tran (flytende)? ☐ Ja ☐ Nei

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

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

Hvor mye tran pleier du å ta hver gang?

☐ 1 ts ☐ 1/2ss ☐ 1+ss

Bruker du tranpiller/kapsler? ☐ Ja ☐ Nei

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

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

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

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

Bruker du fiskeoljekapsler? ☐ Ja ☐ Nei

Hvis ja; hvor ofte tar du fiskeoljekapsler?

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

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

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

Kosttilskudd

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

Hvis ja; hvor ofte tar du slike kosttilskudd?

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

Navn .....

Alkohol

Er du total avholdskvinne? ☐ Ja ☐ Nei

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

	aldri/ sjelden	1 pr. mnd	2-3 pr. mnd	1 pr. uke	2-4 pr. uke	5-6 pr. uke	1+ pr. dag
Øl (½ L)	☐	☐	☐	☐	☐	☐	☐
Vin (glass)	☐	☐	☐	☐	☐	☐	☐
Brennevin (drinker)	☐	☐	☐	☐	☐	☐	☐

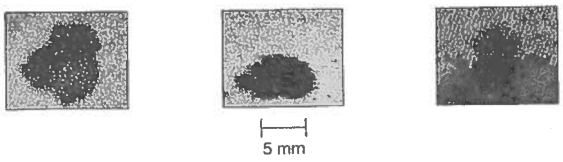
Solvaner

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

Hvor mange føflekker har du sammenlagt på begge armer (fra fingertuppene til skuldrene)?

☐ 0 ☐ 1-10 ☐ 11-50 ☐ 51+

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



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

Hvor mange små, regelmessige føflekker har du sammenlagt på begge armene (fra fingrene til armhulene)?

☐ 0 ☐ 1-10 ☐ 11-50 ☐ 51+

Hva er din opprinnelige hårfarge? (sett ett kryss)

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

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

Hvor ofte dusjer eller bader du?

	Mer enn 1 g dagl	1 g dagl	4-6 g pr. uke	2-3 g pr. uke	1 g pr. uke	2-3 g pr. mnd.	Sjelden aldri
Med såpe/shampo							
Uten såpe/shampo							

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

Årstall	Aldri	Høyst 1 gang pr. år	2-3 g. pr. år	4-5 g. pr. år	6 eller flere ganger
1991-94					
1995-98					

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

Årstall	Aldri	1 uke	2-3 uker	4-5 uker	7 uker eller mer
1991-94					
1995-98					

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

Årstall	Aldri	1 uke	2-3 uker	4-5 uker	7 uker eller mer
1991-94					
1995-98					

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

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

Hvilke solfaktorer bruker du i disse periodene?

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

Hvilke solkremmerker bruker du? Angi faktor hvis du husker.

	Ja	faktor		Ja	faktor
Piz Buin	☐	....	Cosmica	☐	....
Ambre Solairé	☐	....	Natusan	☐	....
HTH	☐	....	Delial	☐	....
Andre, angi navn.....		....			

Hvor ofte har du solt deg i solarium?

Alder	Aldri	Sjelden	1 gang pr. mnd.	2 ganger pr. mnd.	3-4 ganger pr. mnd	oftere enn1 gang pr. uke
1991-94						
1995-98						

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

☐ Ja ☐ Nei

Takk for at du ville delta i undersøkelsen

LUNDBLAD GRAFISK AS TROMSØ TLF 77 67 51 01

ISM SKRIFTSERIE - FØR UTGITT:

1. Bidrag til belysning av medisinske og sosiale forhold i Finnmark fylke, med særlig vekt på forholdene blant finskættede i Sør-Varanger kommune.
Av Anders Forsdahl, 1976. (nytt opplag 1990)

2. Sunnhetstilstanden, hygieniske og sosiale forhold i Sør-Varanger kommune 1869-1975 belyst ved medisinal-beretningene.
Av Anders Forsdahl, 1977.

3. Hjerte-karundersøkelsen i Finnmark - et eksempel på en populasjonsundersøkelse rettet mot cardiovasculære sykdommer. Beskrivelse og analyse av etterundersøkelsesgruppen.
Av Jan-Ivar Kvamme og Trond Haider, 1979.

4. D. The Tromsø Heart Study: Population studies of coronary risk factors with special emphasis on high density lipoprotein and the family occurrence of myocardial infarction.
Av Olav Helge Førde og Dag Steinar Thelle, 1979.

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Av Jan-Ivar Kvamme, 1980.

6. Til professor Knut Westlund på hans 60-års dag, 1983.

7.* Blodtrykksovervåkning og blodtrykksmåling.
Av Jan-Ivar Kvamme, Bernt Nesje og Anders Forsdahl, 1983.

8.* Merkesteiner i norsk medisin reist av allmennpraktikere - og enkelte utdrag av medisinalberetninger av kulturhistorisk verdi.
Av Anders Forsdahl, 1984.

9. "Balsfjordsystemet." EDB-basert journal, arkiv og statistikksystem for primærhelsetjenesten.
Av Toralf Hasvold, 1984.

10. D. Tvunget psykisk helsevern i Norge. Rettsikkerheten ved slikt helsevern med særlig vurdering av kontrollkommisjonsordningen.
Av Georg Høyer, 1986.

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Av Bjarne Koster Jacobsen, 1988.

12.* Helse og ulikhet. Vi trenger et handlingsprogram for Finnmark.
Av Anders Forsdahl, Atle Svendal, Aslak Syse og Dag Thelle, 1989.

13. D. Health education and self-care in dentistry - surveys and interventions.
Av Anne Johanne Søgaard, 1989.

14. Helsekontroller i praksis. Erfaringer fra prosjektet helsekontroller i Troms 1983-1985.
Av Harald Siem og Arild Johansen, 1989.

15. Til Anders Forsdahls 60-års dag, 1990.

16. D. Diagnosis of cancer in general practice. A study of delay problems and warning signals of cancer, with implications for public cancer information and for cancer diagnostic strategies in general practice.
Av Knut Holtedahl, 1991.

17. D. The Tromsø Survey. The family intervention study. Feasibility of using a family approach to intervention on coronary heart disease. The effect of lifestyle intervention of coronary risk factors.
Av Synnøve Fønnebø Knutsen, 1991.

18. Helhetsforståelse og kommunikasjon. Filosofi for klinikere.
Av Åge Wifstad, 1991.

19. D. Factors affecting self-evaluated general health status - and the use of professional health care services.
Av Knut Fylkesnes, 1991.

20. D. Serum gamma-glutamyltransferase: Population determinants and diagnostic characteristics in relation to intervention on risk drinkers.
Av Odd Nilssen, 1992.

21. D. The Healthy Faith. Pregnancy outcome, risk of disease, cancer morbidity and mortality in Norwegian Seventh-Day-Adventists.
Av Vinjar Fønnebø, 1992.

22. D. Aspects of breast and cervical cancer screening.
Av Inger Torhild Gram, 1992.

23. D. Population studies on dyspepsia and peptic ulcer disease: Occurrence, aetiology, and diagnosis. From The Tromsø Heart Study and The Sørreisa Gastrointestinal Disorder Studie.
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25. D. Relationship between hemodynamics and blood lipids in population surveys, and effects of n-3 fatty acids.
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27. Utdrag av medisinalberetninger fra Sulitjelma 1891-1990.
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28. Helse, livsstil og levekår i Finnmark. Resultater fra Hjerte-karundersøkelsen i 1987-88. Finnmark III.
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31. D. Arrhythmia, electrocardiographic signs, and physical activity in relation to coronary heart risk factors and disease. The Tromsø Study.
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41.* D. Physical activity and risk of cancer. A population based cohort study including prostate, testicular, colorectal, lung and breast cancer.
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Av Tone Smith-Sivertsen, Valeri Tchachtchine, Eiliv Lund, Tor Norseth, Vladimir Bykov, 1997.

43. D. Use of alternative medicine by Norwegian cancer patients
Av Terje Risberg, 1998.

44 D. Incidence of and risk factors for myocardial infarction, stroke, and diabetes mellitus in a general population. The Finnmark Study 1974-1989.
Av Inger Njølstad, 1998.

45. D. General practitioner hospitals: Use and usefulness. A study from Finnmark County in North Norway.
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46. D. No går det på helsa laus. Helse, sykdom og risiko for sykdom i to nord-norske kystsamfunn.
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Av **Henrik Schirmer, 2000.**

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Av Tormod Brenn, 2000.

52 D. Ultrasound assessed carotid atherosclerosis in a general population. The Tromsø Study.
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53. D. Risk factors for carotid intima-media thickness in a general population. The Tromsø Study 1979-1994.
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57. D. Individual fatty acids and cardiovascular risk factors.
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Av Anders Forsdahl, Fylkesnes K, Hermansen R, Lund E, Lupton B, Selmer R, Straume E, 2001.

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66. Helseundersøkelsen i Arkangelsk 2000.
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75. Kreftregisteret i Arkhangelsk oblast i nordvest Russland. Med en sammenligning av kreftforekomst i Arkhangelsk oblast og Norge 1993 - 2001.
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79. **Prosjekt egenmelding Kristiansand kommune.**
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