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The use of self-administered questionnaires about food habits.

Relationships with risk factors for coronary heart disease and associations between coffee drinking and mortality and cancer incidence

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THE USE OF SELF-ADMINISTERED QUESTIONNAIRES ABOUT FOOD HABITS. RELATIONSHIPS WITH RISK FACTORS FOR CORONARY HEART DISEASE AND ASSOCIATIONS BETWEEN COFFEE DRINKING AND MORTALITY AND CANCER INCIDENCE.

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PREFACE

The work presented in this thesis was carried out during 1981-1983 at the Institute of Hygiene and Social Medicine, University of Bergen and during 1984-87 at the Institute of Community Medicine, University of Tromsø.

I want to express my thanks to the institutes for providing working facilities.

Professor Erik Bjelke introduced me to epidemiology and gave me the possibility to work with a prospective study, and I owe him my gratitude for this. Professor Dag S. Thelle has been my advicer in Tromsø, and I want to express my sincere thankfullness for his help, encouragement and criticism throughout the last 4 years.

Ivar Heuch and Gunnar Kvåle are gratefully acknowledged for their support and contributions during the years in Bergen, and all my colleagues at the Institute of Community Medicine are thanked for all help and advice. I also want to thank the steering committee of the Tromsø Heart Study, comprising representatives from the University of Tromsø, the community health service and the National Health Screening Service, for giving access to the data. Without their liberal attitude toward my use of the data, this work would not have been possible.

Financial support of the present work has been obtained from the National Cancer Institute, USA, the Norwegian Council for Science and Humanities, the Norwegian Society for Fighting Cancer, the University of Tromsø and the Norwegian Council on Cardiovascular Diseases. All these foundations and institutions are gratefully acknowledged.

I also want to thank my best friend, Lillian, for all encouragement and for never stop telling me that life is more than published papers and self-administered questionnaires.

LIST OF PAPERS INCLUDED.

I. The Tromsø Heart Study: Responders and non-responders to a health questionnaire, do they differ?
Jacobsen BK, Thelle DS.
To be published in revised version in Scand J Soc Med.

II. The Tromsø Heart Study: Comparison of information from a short food frequency questionnaire with a dietary history survey.
Jacobsen BK, Knutsen SF, Knutsen R.
Scand J Soc Med 1987; 15: 41-47.

III. The Tromsø Heart Study: food habits, serum total cholesterol, HDL cholesterol, and triglycerides.
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IV. The Tromsø Heart Study: The relationship between food habits and the body mass index.
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J Chron Dis 1987; 40: 795-800.

V. The Tromsø Heart Study: Is coffee consumption an indicator of a life style with high risk for ischemic heart disease?
Jacobsen BK, Thelle DS.
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VI. The Tromsø Heart Study: Risk factors for coronary heart disease and length of education.
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VII. Coffee drinking, mortality, and cancer incidence: Results from a Norwegian prospective study.
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J Natl Cancer Inst 1986; 76: 823-831.

INTRODUCTION

Nutritional habits are among the factors affecting the risk for several chronic disorders, of which coronary heart disease (CHD) and cancer are the most important in terms of number of deaths in the industrialized countries (1-4). Much of the present knowledge about the relationships between food habits and risk factors for disease stems from metabolic studies with strict control of diet and other variables. Due to technical and economical constraints, however, metabolic studies can only be conducted in relatively small groups of persons which makes it impossible to show relationships between diet and incidence of disease. An example is the relationship between the ratio between the intake of polyunsaturated and saturated fats (P/S-ratio) of the diet and total serum cholesterol. This association was first demonstrated in 1957 (5-7), whereas a direct relationship between the intake of saturated and polyunsaturated fats in individuals and risk for CHD was first convincingly demonstrated in a prospective study published in 1981 (8), more than 20 years after the first report by Keys et al. (5).

This illustrates one of the reasons for investigating food habits in large samples of the population, namely to demonstrate relationships between food habits and incidence or prevalence of disease. Other objectives may be to study associations between food habits and known risk factors of disease, or to obtain information about food habits in population in order to monitor changes as part of nutritional political measures.

Studies of the relationships between food habits and established or suspected risk factors of disease or disease incidence may support a hypothesis suggested by metabolic or animal studies. One of the first papers showing strong evidence for the cancer preventing properties of vitamin A in man (9) was the study by Bjelke in 1975 which demonstrated an inverse association between the intake of vitamin A (operationalized as an index mainly based on frequency of intake of beta-carotene containing food items) and the risk of lung cancer (10).

Epidemiological studies of associations between food habits and risk factors or disease occurrence may also reveal relationships which are not expected from current knowledge. An example is the positive association between coffee drinking and total serum cholesterol observed in some studies (11,12). Such unexpected observations may stimulate the search for mechanisms (13).

The relationship between food habits and health.

It may often be difficult to establish a direct relationship between food habits and the risk factors for disease (14-16), and, even more so, with disease occurrence. Most non-communicable chronic diseases are multifactorial and the relative risk estimate for exposure to one of the risk factors may be low with wide confidence intervals. Partly, these wide confidence intervals may be due to imprecise measurements both of the dependent and the explanatory variables.

When diagnostic categories are the endpoints, inaccurate death certificates may represent a source of error (17), particularly if the recorded cause of death is not based on autopsy or clinical evidence supporting the diagnosis (18). For instance, in analyses of risk factors for cancer, the relative risk estimates may for some cancer sites depend on whether the analyses are restricted to histologically confirmed cases (19). The determination of biological variables, like the serum lipids, may also be associated with error, e.g., there are intra-individual differences in serum cholesterol measured within hours during the same day (20).

However, in analyses of relationships between food habits and disease occurrence or risk factors for disease, the major problem is usually to describe the food habits of the individuals with sufficient accuracy. This problem contains two questions: The first is related to the present: How stable is each individual in the ranking of the individuals for some food habit? (i.e: intra- vs. interindividual variability). The second question points into the future and the past: How stable are the long-time dietary habits?

Both questions are important when evaluating relationships between food habits and disease occurrence. When concerned with chronic diseases, information about the current food habits is of little value if they do not reflect the long-time habits. The second question may be less important when relationships with biological variables are the focus of the study as both the dependent and the independent variables are measured at the same time.

The question of intra- vs. interindividual variation for food habits examined by self-administered questionnaires has been elaborated in the general discussion. Several studies show that information on food habits in adults at two occasions separated by years is statistically significantly correlated (21-23). It is, however, obvious that the probability of important changes in the habits increases with the length of follow-up, a problem which may be particularly important for food items (e.g. coffee drinking or egg consumption) influenced by symptoms or disease (VII).

Dietary survey methods.

The different dietary survey methods have been reviewed by other authors (24-27), and the purpose of the following brief synopsis is only to give a short introduction.

Dietary survey methods may be divided into three types: Chemical analysis of food samples, methods where the nutrient intake is calculated from food composition tables, and methods where only the intake of food items is recorded. When the nutrient intake is computed from tables, it is also possible to report the intake of food items.

Chemical analyses of the food can be perfomed from a duplicate portion or an aliquot of the food eaten (e.g. 10 per cent). It is also possible to use the equivalent composition method which consists of two parts. The weight of everything consumed during a period is recorded. Afterwards, a sample of raw foods, equal to the mean daily amount of food, is brought to chemical analysis. The main advantage

of the methods which include chemical analyses is that they make it possible to obtain informations about intake of nutrients without the use of food composition tables. This is particularly relevant for some trace elements.

The other survey methods (which are independent of chemical analyses) are record methods, interview methods and short-cut methods. The record methods implies the study subjects weigh and record the food consumed during a time period, or that everything eaten is recorded in household measures. The most common interview methods are the 24-hour recall and the dietary history. In the former, each subject is asked to recall everything consumed the last 24 hours, but the recall period may also be extended to several days or even weeks. In a dietary history interview, the subject is asked to report the usual diet.

The short-cut methods are dietary survey methods which intend to obtain information about the food habits with less time and efforts than the other methods, usually by asking the subjects about the frequency of consumption of the food items. Such information can be gathered by an interview or by a self-administered questionnaire.

Data about dietary habits can be obtained at four different levels: A) Mean consumption of a group, B) mean consumption and distribution of consumption in a group, C) the relative magnitude of the consumption of an individual (often summarized as rank order), D) the absolute magnitude of the consumption of an individual (27). In epidemiological studies evaluating relationships between dietary

habits and risk factors for disease or incidence of disease at the individual level, the objective will often be to assess the association between the level of consumption of a certain food item (usually categorized in relatively few groups) and a risk factor, e.g. higher serum cholesterol, or the incidence of CHD. This implies information at level C or D.

One method of obtaining information about the food habits is to take repeated 24-hour recalls. Balogh et al. (28) found that the correlation coefficient between information about the usual intake and the average of eight or more 24-hour recalls ranged between 0.56 for starch to 0.83 for oleic acid. The number of 24-hr. recalls required for a 95 % probability that the sample average was within ± 20 % of the true individual mean for 90 % of the population ranged from 9 for energy intake to 45 for cholesterol intake. Also other methods, like dietary history interview and different forms of recording methods can be used to rank the intake of the individuals (24,26).

Dietary surveys in large samples.

The 24-hour recall interview has been used to assess the dietary habits of thousands of subjects in numerous studies. Some examples are the US Health and Nutrition Examination Surveys (HANES I & HANES II) (29-33), the Jerusalem Lipid Research Clinic Study (34,35), in Japan, Hawaii and California (36,37), the Puerto Rico Heart Health Program (38) and in Rancho Bernardo, California (39). However, in big samples, financial constraints will usually make it impossible to use

dietary survey methods which involve an interview of the individual, which therefore leaves us with the self-administered questionnaire. Self-administered questionnaires about food habits have been used in several studies, both in Norway (10,11,19,40-46) and in other countries (e.g. 47-54).

There are three main studies on food habits using self-administered questionnaires in Norway. In 1967, Bjelke (55) sent a questionnaire on dietary habits to the surviving respondents of a cohort who in 1964 had filled in a questionnaire concerning smoking and cardio-respiratory symptoms. This was partly a random sample of Norwegian males, partly brothers of migrants to the United States. During 1967-69, spouses and siblings of individuals interviewed in a case-control study of gastro-intestinal cancer completed a similar questionnaire. In this way, he obtained information about food habits in 16 713 individuals. They have been followed up with special emphasis on cancer incidence. One of the very important findings of this study is the protecting effect of vitamin A on lung cancer risk (10). The last part of this thesis (Paper VII) is based on this material.

As a part of the second Tromsø Heart Study in 1979-80, a questionnaire was handed out to the 16 621 subjects who attended the screening. 14 667 returned the questionnaire. The questionnaire and response rate are described in detail below (Paper I,II), and some results from the survey are presented in Paper III-VI. Most of the questions concerning food habits were formulated by the Section for Dietary Research, University of Oslo and similar questions have been

used in the cardiovascular county studies. The most well known finding from the second Tromsø Heart Study is the positive relationship between coffee drinking and serum cholesterol (11).

The largest material on food habits in Norway is by far the dietary part of the cardiovascular county studies under the auspices of National Health Screening Service and the Section for Dietary Research, University of Oslo. Information about dietary habits have been collected for about 50 000 Norwegian adults (56), many of them have given information more than once. Results from these studies have mainly been published in reports from the Section for Dietary Research, University of Oslo (41-46).

The aims of this study.

The aims of the papers presented in this thesis are to demonstrate how information about food habits from a self-administered questionnaire can be used in epidemiological studies. The first four papers compare responders and non-responders to a self-administered questionnaire, assess the concordance between information from the questionnaire and a dietary history interview and relate the food habits to blood lipids and body mass index. In the next two papers, food-, smoking- and physical activity habits are related to coffee consumption and to length of education, respectively. In the last part of the thesis, information about coffee drinking obtained from a self-administered questionnaire is related to cause-specific mortality and cancer incidence in a prospective study.

SUMMARY AND MAIN CONCLUSIONS OF THE PAPERS

The present work is based on two population surveys. The first six articles are using information collected in the second Tromsø Heart Study (1979-80), whereas the last paper is based on the prospective study started in 1967 by professor Erik Bjelke.

The papers deal with five topics:

1. Who respond to self-administered questionnnaires and how well does information about dietary habits obtained from such questionnaires correspond with information obtained from a dietary history survey? (Papers I, II).

2. Relationships between food habits stated in a self-administered questionnaire and blood lipids and the body mass index. (Papers III and IV).

3. Relationships between information about coffee intake given in the questionnaire and some food habits related to risk of coronary heart disease. (Paper V).

4. Associations between length of education and blood lipids and blood pressure and the extent to which these can be explained by life style (including food habits) stated in the self-administered questionnaire (Paper VI).

5. Associations between information about coffee drinking given in a self-administered questionnaire and cancer incidence as well as mortality from major causes of death in a 11 1/2 years follow-up of more than 16 000 subjects (Paper VII).

1. Who respond to self-administered questionnaires and how well does information about dietary habits obtained from such questionnaires correspond with information obtained from a dietary history survey?

The first paper evaluates whether the 14 667 men and women who returned the questionnaire used in the second Tromsø Heart Study (1979-80) differed from the 1954 subjects who did not return the questionnaire. These two groups of subjects were similar with regard to age, blood lipids and blood pressure, but the proportions of individuals who were single and smokers were higher in the non-responders.

In paper II, answers to questions about dietary habits given in the questionnaire were compared with corresponding information given in a dietary history interview one to two years later in a group of 528 men. These men were 30-54 years old at screening and assumed to be at high risk for coronary heart disease because of high total serum cholesterol and/or low proportion of the total serum cholesterol in the high density lipoprotein fraction. (In this paper, it is erroneously stated that 14 667 subjects were examined in the second Tromsø Heart Study. As evident from the context, this is the number of subjects who returned the questionnaire). High concordance was found between the two methods for questions concerning types of foods most

commonly used. For most food items, the mean intake according to the dietary history corresponded well with intake reported in the questionnaire. For food items used every day in easily recorded units (slices of bread, cups of coffee, glasses of milk), the concordance at the individual level was better than for food items used less frequently.

2. Relationships between food habits stated in a self-administered questionnaire and blood lipids and body mass index.

Associations between food habits and total serum cholesterol, high density lipoprotein cholesterol (HDL-cholesterol) and serum triglycerides were examined. High body mass index was associated with high serum cholesterol, high triglycerides and low HDL-cholesterol. Positive associations were observed between high serum cholesterol and high coffee consumption, use of butter or hard margarine and low bread consumption. In women, negative associations were also noted for selecting low-fat milk and frequency of use of fruits and vegetables. The HDL-cholesterol level was 0.03-0.04 mmol/l higher in individuals who select butter or hard margarine as table fat than in subjects who select soft margarine. Use of low-fat milk and frequent use of fish dishes for dinner seemed to be related to low serum triglyceride levels.

In the second paper (Paper IV) relationships between food habits and body mass index (BMI) (kg/m^2) were explored in the same population as described in paper III. High BMI was most strongly associated with low bread consumption and use of low-fat milk. Weaker positive

associations were seen for coffee, fish and ground meat consumption, and with use of table fat with low P/S-ratio. Negative associations were seen for use of fruits and vegetables and amount of table fat at each slice of bread. Inconsistent relationships were noted for use of alcohol. The results suggest that individuals to some extent have changed their food habits in order to keep the BMI within limits they consider to be desirable, and underline the need for adjustment for BMI when e.g. relationships between the diet and blood lipids are studied.

3. Relationships between information about coffee intake given in the questionnaire and some food habits related to risk of coronary heart disease.

This paper describes associations between coffee consumption and smoking-, physical activity-, and food habits. Coffee drinking was related to presumably atherogenic food habits (use of butter or hard margarine, not selecting low fat milk and infrequent use of fruits and vegetables), smoking (75 % of subjects with high coffee consumption smoked, in contrast to 20-25 % of the subjects with low coffee consumption) and, in women and young men, to low physical activity. It is rather uncommon in this population to find a subject who drinks more than 8 cups of coffee per day and at the same time both is a non-smoker and have serum total cholesterol $\leq$ 5.2 mmol/l. The results suggest that high coffee consumption may be an indicator of a life style with high risk for coronary heart disease.

4. Associations between length of education and blood lipids and blood pressure, and the extent to which these can be explained by life style (including food habits) stated in the self-administered questionnaire.

Subjects with the longest education had lowest body mass index, smoked less, were more physically active in leisure time and had food habits assumed to be less atherogenic (i.e. drink little coffee, use soft margarine and low-fat milk and eat fruits and vegetables daily) than individuals with low education. Mean total serum cholesterol and systolic blood pressure were negatively associated with educational level. In women, a positive association was found for HDL-cholesterol. Adjustment of these relationship for several life style variables (including food habits) reduced the strength of the associations, which, however, remained statistically significant for total serum cholesterol and systolic blood pressure in men and women. After adjustments, a positive association emerged for HDL-cholesterol in men.

5. Associations between information about coffee drinking given in a self-administered questionnaire and cancer incidence as well as mortality in a 11 1/2 years follow-up of more than 16 000 subjects.

Paper VII describes associations in 13 664 men and 2891 women between coffee drinking, total mortality, mortality from all major causes of death and cancer incidence. No statistically significant positive associations were found between coffee consumption and disease. We

found strong effects of disease on coffee drinking habits with a seemingly negative association between coffee consumption and mortality in the first years of follow-up. A weak negative association was found between coffee consumption and total cancer incidence after stratification for cigarette smoking, and we observed negative associations between coffee drinking and risk of cancer of the kidney, non-melanoma skin cancer and colon cancer in subjects < 65 years old at start of follow-up.

GENERAL DISCUSSION

The papers included in this thesis focus on how data about food habits and other life style variables collected by self-administered questionnaires can be used in order to assess relationships between life style, particularily food habits, and risk factors for disease (Paper III & IV), variables connected to life style, i.e. coffee drinking and years of education (Paper V & VI), and disease occurrence (Paper VII).

The first two papers are mainly methodological. Paper I discusses briefly in what way attenders and non-attenders to a screening for cardiovascular risk factors (the second Tromsø Heart Study) differ, and in some detail whether responders and non-responders to the questionnaire used in the second Tromsø Heart Study have the same age-, sex-, and marital status distribution and the same level of risk factors for CHD. The results described in Paper I are likely to be applicable also for the cardiovascular county studies as the way of administrating the questionnaire, i.e. giving it to the subjects who attend a screening, was the same in the Tromsø Heart Study and the county studies.

In the second paper, we have compared information from the questionnaire with data from a dietary history survey. As there were up to two years between the two surveys, the results reflect the combination of the short-term (1-2 years) stability of food habits and the concordance between information from the two types of dietary surveys. From a methodological point of view, it would have been

desirable to separate the subject of short-term stability from that of concordance between the two dietary survey methods. However, this weakness in the design of the study does most probably result in a underestimation of the real correspondance between these two survey methods.

Paper III describes relationships between food habits and blood lipids. The associations are adjusted for age, physical activity, the number of cigarettes per day and the body mass index (BMI) (kg/m^2). BMI is, of course, closely associated with the food habits, and it may be debatable whether it is correct to adjust for the body mass index when assessing relationships between food habits and blood lipids. However, the associations between food habits and BMI are complex. As discussed in Paper IV, people do not only gain weight because they eat too much, they may also select particular food habits because they want to reduce the weight. Therefore, we have recommended to adjust relationships between food habits and blood lipids as well as morbidity for the BMI.

One of the main findings presented in Paper III was the confirmation of the association between total serum cholesterol and coffee drinking previously described in the Tromsø population (11), even when adjusted for other food habits recorded in this study. In Paper IV, a positive relationship was found between coffee drinking and the BMI. The former association has been highly publicized and several reports have discussed the relationship between coffee and serum cholesterol (12). Thus, in Paper V, we discussed the correlations between coffee drinking and other habits and concluded that coffee

drinking may be one indicator of a life style associated with increased risk of contracting CHD.

It should be emphasized that although we propose that coffee drinking may be regarded as one possible indicator of a life style with high risk for CHD, this does not imply that other variables can not be equally successful as marker of a high risk.

Another marker of high risk for CHD is short education. It is of considerable interest to evaluate whether this higher risk is due to amendable habits in the subjects with short education, given that these subjects have other habits than the individuals with the longest education. This was the topic for the sixth paper included in this thesis. Using the information about the habits (including food habits) from the self-administered questionnaire, it was possible to demonstrate that approximately 50 % of the difference in serum cholesterol between subjects with > 16 years of education compared to individuals with < 8 years could be attributed to cholesterol-elevating habits in the less educated. Taking into consideration that most of the habits are measured with considerable random error and that information about several relevant habits is lacking, the results indicate that most of the difference in blood lipids and blood pressure between subjects with short and long education is due to different habits in these different segments of the population.

Paper III-VI describe cross-sectional analyses evaluating the relationships between habits stated in a self-administered question-

naire and factors that may be associated with risk of CHD. Paper VII demonstrates another aspect of the use of self-administered questionnaires, i.e. in a prospective study. In some of the previous papers, different associations between coffee drinking and risk factors for CHD, life style and one marker of socio-economic status have been discussed. In the prospective study, coffee consumption is related to cancer incidence and mortality from a number of diseases, including CHD, in a 11 1/2 years follow-up. Coffee drinking is, however, but one example of how information from self-administered questionnaires can be related to morbidity.

In this general discussion, I do not intend to elaborate the findings of the different papers, but rather to concentrate on selected aspects of the use of self-administered questionnaires as a source of information about food habits. The reason for this is that the leitmotif of this thesis is the use of self-administered questionnaires.

Thus, in the following, I will first focus on whether responders to postal questionnaires about food habits tend to differ from non-responders, thereafter on the concordance between the information from questionnaire and other dietary survey methods. A discussion of the reproducibility of data from such questionnaires constitutes the last part of the general discussion.

The use of self-administered questionnaires requires an awareness of the inherently implicated assumptions. It is assumed that the responders are willing and able to provide the desired information, that the questions are interpreted in the same way by the responder

and the researcher, and, thirdly, that the questions are answered honestly. These assumptions can be summarized into one: That the results are unbiased, which is one of the most important questions in all epidemiological studies.

Bias can be defined as "Any process at any stage of inference which tends to produce results or conclusions that differ systematically from the truth" (57). It is in this context important to examine whether the subjects who fill in the questionnaire differ in important ways from those who do not (non-response bias), and to assess whether we measure what we want to measure, i.e. rank the consumption of the individuals sufficiently well.

Non-response bias

In the present context, non-response bias refers to misrepresentation of the target population by the sample constituted by the responders.

Non-response bias may increase, decrease or not influence the associations derived from screening surveys (57-61). The strength of the relationship between two variables may be affected only if response is related to both the independent (e.g. food habits) and the dependent variable (e.g. blood lipids or risk of cancer). For example, the possible inverse association between serum cholesterol and use of vegetables may be biased if the subjects who provide information are those with both low serum cholesterol and frequent use of vegetables. However, if there is no difference between subjects who participate and those who do not with respect to serum

cholesterol or frequency of use of vegetables, the strenght of the association will not be affected.

The most effective way to avoid non-response bias is to increase the response rate. As self-administered questionnaires require less time and efforts for each individual than any other dietary survey method, it may be assumed that the response rate in questionnaire surveys is higher and therefore the risk of non-response bias lower. However, most people in Norway are willing to co-operate even in complicated and cumbersome weighing surveys. Trygg managed, for example, to have more than 80 % of two groups of men (38 and 76 men, respectively) to take part in the weighing surveys among forest workers in Hurdal and men in the Oslo Study (62,63). However, information from relatively few subjects is obtained in this way, and the main asset of a self-administered questionnaire in this context may be the much larger number of subjects which can be included in the survey.

In the Norwegian county surveys and the Tromsø Heart Study, non-response bias may result both from the non-attenders to the screening and from non-responders to the questionnaire about food habits. The rate of attendance (not adjusting for legitimate reasons for absence) in the county surveys has been high (80-90 %) (64), in the Tromsø Heart Study somewhat lower (74 & 77 %) (65,I). The response rate to the questionnaire in the county surveys (per cent of the attenders who actually returned the questionnaire) was 85-95 % after one reminder (56). This figure is comparable to the results from Tromsø (88 %) where there was no reminder (I). Collumn 3 of table 1 displays the proportion of invited subjects in five population surveys who

Table 1. The number of subjects invited to the county surveys in Finnmark-II (1977/78), Oppland-I (1976/78), Oppland-II (1981/83) and Sogn og Fjordane-II (1980), Tromsø-II (1979/80) and Tromsø-III (1986/87), the number of subjects who attended and gave information about food habits (per cent of invited).

	Invited	Attended	Gave information about food habits
Finnmark-II	20 647	17 145 (85 %)	14 905 (72 %)
Oppland-I	31 620	28 399 (90 %)	26 897 (85 %)
Oppland-II	31 581	28 437 (90 %)	26 372 (84 %)
Sogn og Fjordane-II [1]	13 103	11 819 (90 %)	10 953 (84 %)
Tromsø-II	21 329	16 621 (77 %) [2]	14 667 (68 %)
Tromsø-III	28 885	21 839 (76 %)	20 029 (69 %)

1 In 21 municipalities where the questionnaire about food habits were handed out.

2 In several papers from the Tromsø Heart Study, included Paper III-VI, it is stated that 78 % (16 621 out of 21 329) attended the screening. However, 112 subjects were examined without being invited and 77.4 % of those invited attended the screening.

Refs: 41,43,44,64,I and personal communications.

actually gave information about food habits. The percentages are similar to, or somewhat lower than, the response rate (i.e. 84 %) to the mail survey (without any screening, but with 1-2 reminders) conducted by Bjelke in the 1960's (VII). The screening may constitute an obstacle due to the collection of blood samples and other measurements considered unpleasant by the participants. It is on the other hand possible that some people find it in their interest to take part in a screening, thereby increasing the participation of the "worried well" (66).

Any response rate below 100 % is a cause for some concern. Still, the response rate to the questionnaire used in the county studies and in Tromsø (85-95 %) may be considered adequate, particularly as the responders do not differ much from the non-responders with regard to age and risk factors for CHD except for smoking (I). Therefore, the major non-response bias associated with the Tromsø Heart Study and the county studies must be considered a result of the non-attendance to the screening, and not the questionnaire.

In what way may non-response bias influence the results presented in this thesis? We know that the subjects who did not attend the screening tended to be young and single (I). Based on other studies of non-participants, there are reasons to believe that they had more socio-psychological problems and used more alcohol than those who attended the screening. A small survey in non-attenders to the first Tromsø Heart Study in 1974 indicates that there were more non-attenders than expected among men with particularily high and low socio-economic status. However, in general, the non-attenders tended

to be cigarette smokers, have low physical activity and receive social benefits (Thelle, personal communication). It is therefore likely that the non-attenders as a group have some similarity with subjects with low education with regard to e.g. body mass index.

If the non-attenders differ from the attending subjects with regard to e.g. mean serum cholesterol and body mass index, and there are differences between attenders and non-attenders with regard to the independent variables, the strength of the association between these may be influenced. Often the observed regression coefficients are underestimated because of the non-attenders. This is usually considered a less serious mistake than the opposite. However, it is possible that some of the regression coefficients presented in this thesis are overestimated because of non-attenders. For example, if non-attenders tend to have high BMI and select whole fat milk, the positive association between BMI and use of low fat milk observed in Paper IV may have been overestimated.

Who are the non-responders to postal questionnaires?

The question of non-response bias associated with the use of postal questionnaires is not a new topic, and after some less encouraging experiences, it was in 1946 concluded that "Mailed schedules or the telephone may satisfy the less scrupulous but such methods should be taboo" as a source of attitude data (cited by Clausen & Ford (67)).

In spite of this, postal questionnaires have been used extensively during the last 40 years. Response bias and other aspects of the use

of postal questionnaires have been reviewed in several publications (e.g. 68-70), and only selected aspects are included in this brief summary.

There is no clear evidence of a marked effect of sex and age on response rate, some studies report higher response rate in young people, and other studies the opposite (68,71-73).

Non-responders tend to have low socio-economic status and level of education (68,71,74,75). This has, however, not been found in all studies (72) and may be less important in relatively egalitarian societies like the Scandinavian countries.

A third important conclusion that may be drawn is that although common sense might suggest that the response rate to a long questionnaire is lower than to a short one, the effect of length of questionnaire is not obvious from the literature (68-71,76). The response rate to the 20 pages postal questionnaire used by Smith et al. was 73 % (73), and Shapiro et al. (54) reported that 74 % of the 4209 subjects included in their study filled in and returned the 28 pages self-administered questionnaire.

Smokers tend to be non-responders (77,I), but Oakes et al. found that smokers with symptoms responded better than smokers who feel well (78). This may influence relationships between smoking and diseases related to smoking, and may also have implications for associations where food habits associated with smoking are included as independent variables.

Finally, it is likely that the response rate depends upon the design of the questionnaire (69,70) and that the subjects find the questions sensible and relevant for the stated purpose. Clausen and Ford (67) actually observed an increase in response rate when additional questions of general interest were added to an uninteresting questionnaire.

The validity of a self-administered questionnaire about food habits

Assessing non-response bias is one important part of evaluating the validity of self-administered questionnaires. In the following, however, the validity of self-administered questionnaires about food habits is understood as the concordance with information from other, presumingly more valid, sources of information. This comparison must, of course, be accomplished in subjects who are willing to complete the questionnaire.

The validity of self-administered questionnaires about food habits is difficult to establish. One problem, which is common to all surveys using self-administered questionnaires, is that one never knows whether it is the person intended who actually answers the questions. Scott (68) found that about 10 % of the questionnaires had been passed on, most often to the spouse. In the comparison of data from a questionnaire and dietary history survey included in this thesis (II), the data from the questionnaire may have been given by e.g. the wives, and not the men included in the study. Another problem which makes it difficult to establish the validity is common for all

dietary survey methods: It is difficult to assess the usual food intake of a free living individual.

Block et al. (79) suggest that self-administered questionnaires should be used not only to rank individuals by relative levels of nutrient intake, but also to estimate absolute levels of nutrient intake. However, the most relevant point for the discussion here is whether the questionnaire ranks the individual intake sufficiently well.

The attempt to record the food habits may itself influence the habits. If the individual is asked to record or weigh every food item eaten during a day or a week, the computed energy intake may be lower than the true intake as food items which the subject considers to be unhealthy may not be consumed or recorded. Another possibility is that the energy intake is reduced because of the inconvenience of measuring everything. It is therefore not surprising that the dietary history interview tends to give higher energy intake than survey methods which include recording or weighing of the food (26,80). This result might also emerge if the dietary history method overestimates the intake. It is likely that the change in diet because of the survey is related to the extent the survey influences the daily life of the study subjects. In this respect, the self-administered questionnaire is the dietary survey method least susceptible to this type of bias.

There is, however, no reason to believe that informations about food habits collected by self-administered questionnaires are devoid of,

conscious or subconscious, biased reporting of habits. A phenomenon encountered in questionnaire surveys is response styles or response sets, which is defined as a reliable, systematic, non-authentic source of variance in responders answers to items comprising attitude (81). Answers to questions about food habits may to some extent reflect e.g. attitudes concerning health. One problem is lack of motivation. If responders are not motivated, they may skip some questions, answer several questions the same way or give answers which are difficult to interpret.

A second component of response sets is social desirability or the tendency for responders to give the socially most acceptable answer. The reason for this behavior may be need for approval and/or denial (81). Some people may, in spite of the anonymity related to the questionnaire, find it unacceptable to report in the questionnaire the true food habits if they think that they are far from what nutritionists and physicians advocate. For food habits, however, this problem may be less important for self-administered questionnaires than for interview surveys. Callmer and Hedberg (82) found that the food frequency questionnaire tends to give lower estimates of frequency of intake than a dietary history interview, except for the frequency of use of sweets and liquor. For these items, higher intakes were indicated in the questionnaire than in the interview. The findings of the questionnaire survey may therefore reflect the true state of affairs.

Some individuals have a tendency to agree with positively worded questionnaire items ("yeasayers"). This problem is perhaps of minor

importance for information about food habits as these questions usually are formulated: "That type ..." and "How often...", not: "Do you usually select.....". A problem of greater importance is that some subjects tend to select extreme categories, or select the middle response. The former phenomenon is well known in dietary research and one example is given in table II of Paper II.

One way to obtain information about the validity of self-administered questionnaires is to compare the results with blood samples or urine excretion of e.g. nitrogen as an indicator for nitrogen intake (83) and sodium as an indicator of salt intake (84). An example is the association between sodium excretion and answers to some questions about food habits in a self-administered questionnaire used in Finland (85).

Correlations between information from questionnaires and blood samples have been evaluated in a study concerning intake of vitamins. Willett et al. (86) found that the intake of carotene and vitamin E estimated from the self-administered questionnaire was positively correlated to plasma carotenoid and alfa-tocopherol, respectively. Intake of preformed vitamin A was not correlated with plasma retinol. This was expected as it is known that plasma retinol is not sensitive to dietary retinol supplementation, whereas serum carotenoids and alfa-tocopherol are (87,88).

Except for one study limited to salt added to the meals (89), only one study has, to my knowledge, tried to compare the intake of food items stated in a questionnaire with the actual consumption without

the knowledge of the persons studied (90). In this study with 31 college students who obtained most of their food in a cafeteria, the authors conclude that the food frequency method was successful for estimating the intake of groups, but could not be used as a precise tool to estimate the usual intake of each individual. The Pearson's correlation coefficient between the observed frequency of intake and that estimated from the questionnaires for 169 foods was in 30 of 31 subjects $\geq$ 0.47, and the degree of gross over- or underestimation relatively low. The authors found that the method seems to work best for food groups which are a major component of the diet, while food groups used in small quantities were estimated with lower validity. In general, there were indications of a higher intake stated in the questionnaire than observed by the research team, but part of the difference could be explained by food purchased outside the dining commons.

With regard to nutrients, several studies have compared the results from self-administered food frequency questionnaires with dietary survey methods considered to be more valid (interview and weighing methods) (e.g. 47,91-98). The probably most comprehensive study has been conducted by Willett et al. (98) as a part of a survey of 95 000 American nurses. They compared information from questionnaires with four one-week diet records with approximately three-months intervals in 173 nurses, and found that the informations from the questionnaire and mean intake according to the diet records was highly correlated. The degree of gross misclassification was low, and the authors conclude that the questionnaire can usefully measure individual intake of a number of nutrients. May be a little

enthusiastic, Russel-Briefel et al. (94) concluded from their study of 82 adult men that compared to the 24-hour recall or food records, the questionnaire is the preferable method for estimation of vitamin A intake of individuals. The importance of information about the use of supplements when assessing intake of vitamin A and C is evident from three recent studies which have evaluated this subject (47,94, 98).

A summary of studies on the concordance between information from a self-administered questionnaire and other dietary research methods concerning intake of food items is given in table 2.

Table 2. Studies which have evaluated the concordance of information from self-administered questionnaires and other dietary survey methods concerning intake of food items.

Authors	Year of study	Number of subjects	Reference method
Solvoll (45)	1983	1609	24-hr. recall
Karinpää & Seppänen (99)	1983	75	24-hr. recall
Callmer & Hedberg (82)	1983	58	Dietary history
Jacobsen et al. (II)	1987	528	Dietary history
Bjelke (55)	1973	122	Interview

Arab-Kohlmaier has in a yet unpublished report compared data from 7-day dietary records and food frequency in a German study. Her results are disturbing and call for some caution. For many food items, she found gross misclassification of the intake by the food frequency questionnaire, e.g. 15 % of the subjects in her study was grossly misclassified with regard to milk consumption. She is therefore rather sceptical about the use of food frequency questionnaires. However, for some food items, the concordance was good, and less than three percent of the responders were grossly misclassified with regard to coffee consumption (Arab-Kohlmaier, personal communication).

Kari Solvoll's comparison of information about food habits from a self-administered questionnaire in 1609 men and women with information from a 24-hour recall (45) is to my knowledge the largest study conducted to evaluate this topic. She used a 24-hour recall as the "gold standard". This may have some drawbacks as the questions describing frequency of consumption of food not used daily are not directly comparable. The main finding of this study was the high concordance for questions about types of foods most commonly used. The concordance for questions about the amount of food items used daily (bread, milk, coffee, tea) was also good.

Karinpää and Seppänen (99) compared a self-administered 24-hour recall with an interview in 75 men and women. They used the same questionnaire and conducted the interview 1/2-2 hours after the subjects had filled in the questionnaire, and found that for most

food items the mean intake according to interview and self-administered questionnaire was similar or identical. However, the questionnaire gave higher frequencies for food items eaten at meals (cheese, white bread, fish, processed meat and fish products, peas and beans, vegetables and fruits and berries), whereas the opposite was true for food items associated with snacks (coffee, cakes and buns). The kappa-coefficients (indicating the extent to which the observed aggreement between the interview and self-administered questionnaire is in excess of the agreement expected by chance (100)) were in general high, particularly for frequently used food items, an interesting exception being coffee consumption. The low concordance for information about coffee drinking is in contrast to the Norwegian observations (45,II).

Callmer and Hedberg (82) compared information from a food frequency questionnaire in 58 subjects with data from a dietary history interview. The concordance was best for questions concerning types of food and serving size, but even for questions about frequency of use of food items, more than 70 % of the respondents gave identical answers to two thirds of the questions. There was a tendency toward a lower intake stated in the questionnaire. The opposite was true for consumption of sweets and liquor.

Paper II gives the results from our own study. We compared information from a questionnaire with a dietary history interview in 528 men conducted 1-2 years later. The aim of the dietary history interview was to describe the usual diet of the individual. However, as the dietary history interview methodology is not standardized and

usually is modifications of the method described by Burk in 1947 (101), the dietary history interview will be described here in some more detail than it was possible to do in Paper II. The dietary history interview was performed by a dietician and supervised by Dr. Synnøve F. Knutsen.

The dietary history interview was done by three dieticians. In order to reduce the observer bias, previous to the collection of the dietary histories, standardization of the three dieticians was done using food models, weighing foods of different sizes and coming to agreement on standard weights for the most common foods when measured in conventional household units (teaspoons, tablespoons, cups etc). Food models were developed for both different dinner entrees, vegetables and different sizes of cakes and agreement on the weight of the different models was achieved. The men who were interviewed were asked to cut one slice of bread and then spread it with the usual amount of fat. The slice was weighed before and after putting on fat, thus achieving correct weight of both the slice of bread and the amount of spreadfat. For beverages, the man was asked to show his usual glass and coffee cup size and how much he filled. Thus, the dietician was able to estimate the amount. Real plates were used to put the food models on when interviewing the man. For soups, stews, porridge etc., the plate was filled with puffed rice to the extent the man indicated filling his bowl with the soup etc. The amount was then estimated according to preset standardization criteria for the different kinds of foods.

The interview was done using a standard questionnaire where the

most commonly ingested foods had already been put down, but where the dietician filled in the frequency of intake and the amount eaten each time. The recording of several foods was done as multiplicatives of already standard sizes such as potatoes of 70 grams, cheese slices of 15 grams, cakes of 10 grams etc. This does, however, not indicate that the dietician put down 15 gram of cheese on each slice of bread when the man said he used cheese on bread; the man was asked how much cheese he used on his bread and the amount was then registered as a multiplicative of a standard slice of cheese. The same procedure was used for all food items where standard sizes had been estimated as for example for the food models. The questionnaire used in the interview is available on request.

In the interview, the man was first asked about the bread meals, which in this population are more or less the same each day. The dietician would ask questions of the following type: "How many slices of bread do you usually eat for breakfast?" Then the type of bread, type and amount of spreadfat, jam, cheese and other types of spreads was recorded. Milk, coffee and other additional foods usually ingested for breakfast were also recorded. Next the dietician did the same with the lunch and/or evening meal. Thereafter, the dinners were investigated in the same way, including desserts and beverages. Using food models, the men were asked to show the dietician how much potatoes, meat etc. he normally ate for dinner. Thereafter, the dietician noted the amounts. The method of preparation (baked, fried, boiled) was recorded and additions of extra sugar, cream or fat during preparation or serving was noted.

After the regular meals had been investigated, the dietician registered snacks, coffee-brake intakes, between-meal drinks and special week-end deviations from the usual. Also special seasonal foods were registered, as well as dietary supplements such as cod-liver oil. The alcohol intake was recorded as weekly intake. Before finishing the interview, the dietician made sure there were not recorded more dinners than 30 per month and not more types of bread spreads than the number of slices of bread recorded for each day.

For the present purpose, i.e. to compare the information from questionnaire and dietary interview concerning the daily consumption of some food items (e.g. slices of bread) and the frequency of use of some food groups, only parts of the dietary history survey are important. For example, whether the portion size is recorded precisely or not does not matter.

The results presented in Paper II are similar to those found in the study of Solvoll (45). We observed that high consumption stated in the questionnaire tended to be lower in the interview, and vice versa for low consumption stated in the questionnaire. This was particularly evident for food items used less often than every day. This phenomenon has also been observed in other studies (e.g. 45, 102). If we assume that the dietary history interview gives the correct information, the use of self-administered questionnaires may reduce the strength of any real associations between these food items and other variables.

Bjelke (55) compared information from the postal self-administered questionnaire with interview in 122 subjects. After recoding the results from the interview into the consumption categories in the questionnaire, he found correlation coefficients between 0.21 and 0.72. The highest correlation coefficients ($r > 0.60$) were in general found for food items where the answer alternatives were "per day" (cups of coffee and tea, number of potatoes and slices of bread) but were also observed for some other food items (the frequency of use of salted meat and apples per month) and for use of spirits. The mean frequency of use indicated on the postal questionnaire tended to be lower than reported at the interview.

An additional argument for the validity of self-administered questionnaires about food habits is the observation by Bjelke who found a strong negative association between a vitamin A-index and the risk of lung cancer. This shows that even a relatively crude index (mainly based on the frequency of intake of food items containing beta-carotene) was valid in the sense that it discriminates between individuals with high and low risk for lung cancer (10). Similar argument may be put forward using examples from studies in e.g. Seventh-Day Adventists (48,49) or American nurses (50).

Based on the presented results and the reviewed literature, I find it likely that information about food habits obtained from self-administered questionnaires rank the individuals most correctly for food items used every day, and with somewhat lower correlation for less frequently used food items. There is no reason to believe that

data from self-administered questionnaires are more susceptible to bias than other dietary survey methods. On the contrary, the use of a questionnaire may reduce the risk of certain biases as filling in a questionnaire is usually associated with an apparent anonymity and takes less effort than being interviewed or, even more, taking part in surveys which include weighing or recording everything eaten.

The stability of food habits

It is well known that the dietary habits change with season. The current consumption may influence the answers to the questionnaire (44,55), which are supposed to reflect the usual consumption. This may also obscure relationships between health variables and food habits recorded by self-administered questionnaires. In addition, the dietary habits in the Norwegian population are constantly changing. From the point of view of public health, some of these changes are beneficial. However, from a analytical point of view, the changes may represents at least two problems.

The first problem is related to the validity of the data about food habits when these are used in a prospective study. As the habits change, the data about exposure may become less valid. This information bias will usually be independent of any misclassification with regard to disease (nondifferential misclassification) and therefore result in a underestimation of any association between the recorded food habit and disease.

This is relevant for the discussion of the results presented in paper VII. The combined results from the Tromsø Heart Study and Paper VII indicate that the mean coffee consumption increases from the age of 20 to the age of 40, thereafter it is reduced (V,VII). If the consumption of each individual, relatively speaking, is the same; i.e., that a man with high coffee consumption 50 years old has a lower consumption 12 years later, but still higher than the mean consumption of men at the age of 62, the data would still reflect the coffee consumption of each individual relative to other subjects. Thus, it should be possible to reveal relationships between coffee consumption and disease. Unpublished results from the county study in Oppland indicate relatively high stability of the coffee consumption habits in this population with an age-distribution similar to that in Tromsø Heart Study (Løken, personal communication). In the older population, which constitutes the cohort examined in Paper VII, disease related changes in coffee consumption is evident, and the stability of the coffee drinking habits is likely to be lower, also relatively speaking. If there were an established relationship between coffee consumption and mortality or cancer incidence, the confirmation of this association in Paper VII might have been one possible way to validate the coffee consumption data. Unfortunatly, there are at present no such established relationships.

Even in cross-sectional studies, the changing habits may represent a problem. Associations between e.g. food habits and serum lipids found in one study may not be found in another study conducted some years later. This may indicate that the association was a coincidence. A second possibility is that the association is not a causal relation-

ship, but one reflecting an association between a variabel correlated with the food habit first incriminated and the serum lipid.

There is, however, a third possibility. There are many determinants for e.g. serum cholesterol, both dietary and non-dietary. As the food habits change, the relative importance of these determinants may change. It is not possible to demonstrate a relationship between a habit (e.g. use of soft margarine) and serum cholesterol if all subjects in the population have the habit.

The results from the cross-sectional studies presented in this thesis should be evaluated in this context. They reflect the relationships between the dependent and independent variables late in the 1970's in Tromsø. This, however, does not imply that the results have no value ten years later or in a different population. Whether they reflect causal relationships or not, is, however, a question that only can be answered by comparing the results with those found in similar studies and other types of studies. To what extent the results found in the papers included in this thesis are in accordance with other studies has been discussed in the relevant papers (III-VI).

With these facts in mind, it may be of some interest briefly to discuss the changes in the Norwegian diet which have taken place the last years (from 1975 to 1986). The consumption of vegetables, fruits and berries and sugar has increased, the consumption of potatoes (as such) decreased, whereas the use of potato products increased considerably during this time periode. One of the most interesting time trends is the shift from whole fat milk to low-fat milk. Based

on gross sale data, the mean annual per capita consumption of milk in Norway in 1975 was 195 kg, comprising 169 kg whole fat milk and 26 kg skimmed milk. In 1986, the mean consumption was 179 kg, 110 kg whole fat milk, 40 kg low-fat milk and 29 kg skimmed milk. The per capita consumption of butter has not changed much, but there has been a reduction in the consumption of hard (ordinary) margarine. The percentage of energy from fats has during the 11-year period decreased from 40 % to 37 %, whereas the P/S-ratio has not changed and is approximately 0.37 (103).

The reproducibility of a self-administered questionnaire about food habits.

Willett et al. (98) have evaluated the reproducibility of a self-administered questionnaire with respect to intake of nutrients. They found rather high correlation coefficients, ranging from 0.52 to 0.71. Pietinen et al. (96) concluded that the reproducibility of a short food frequency questionnaire was better than the reproducibility of a very long and time consuming self-administered dietary history questionnaire.

The largest study conducted so far which evaluates the reproducibility of self-administered questionnaire on food item rather than nutrient level is the study of Løken & Solvoll (56). They used data from 734 women who twice filled in the questionnaire used in the cardiovascular county study in Oppland, and found close agreement between the group results from the two occasions. 89 % of the women gave identical

answers on the two questionnaires concerning type of table fat most commonly used.

Bjelke (55) sent his questionnaire to 212 subject at two occasions. He found that the correlation coefficients between answers given were high, ranking from 0.83 for number of potatoes per day to 0.42 for frequency of use of beans. The mean consumption estimated from the first questionnaire differed only slightly from that derived from the second questionnaire. The concordance was highest (correlation coefficient $0.68 \leq r \leq 0.83$) for food items used daily (slices of bread, cups of coffee, cups of tea, potatoes, glasses of milk per day).

Callmer and Hedberg tested the reproducibility of their questionnaire in 65 men and women. 50-60 % of the responders gave identical answers at the two occasions (82).

Smith-Barbaro et al. (104) have compared the reproducibility of several types of questionnaires and found that the reproducibility was best for questionnaires containing broad categories of food items presented in order of the meals in which they are consumed. Their findings are, however, based on only 12 subjects.

As a conclusion, it may be stated that the reproducibility of a self-administered questionnaire about food habits seems to be good, at least when it comes to food items used daily.

Conclusions

It has been common in nutritional research on risk factors for CHD to concentrate on intake of nutrients, particularly intake of saturated and polyunsaturated fat. There are obvious reasons and a long tradition for this approach which has the advantage of measuring fat intake more directly than it is possible if limiting the analysis to fat containing food items.

However, as there is no reason to believe that all nutritional factors affecting serum cholesterol and risk for CHD are known, relationships between food items and risk factors for disease or incidence of disease should still be investigated. It is known from other parts of the nutritional physiology that the intake of nutrients in very small amounts (e.g. vitamins and trace elements) is of tremendous importance for the health. It can not be excluded that there are food items containing substances in relatively small amounts which may influence the level of risk factors for CHD (or other chronic diseases) in ways which are unexplained by the present basic or biochemical knowledge.

An example is coffee drinking, a "food item" totally devoid of saturated fat or any other nutrient previously associated with blood lipids, and yet associated with total serum cholesterol in all Norwegian populations examined (11,105) and in several (but not all) other cross-sectional studies (12). It is likely that parts of this association can be explained by a high fat intake in individuals with

high coffee consumption, but the results from experiments suggest that at least use of boiled coffee has an effect on serum cholesterol (106-108).

It is by no means a new approach to explore relationships between food items and risk factors of disease or disease occurrence. For instance, Burkitts observation of the rarity of colorectal cancer and CHD in Africa and the high fiber diet common in the African population was the starting point for the reseach on fiber and disease (109).

The etiology of chronic diseases is often concealed by poor data, especially those describing exposure to external factors. This is also true for data about the food habits, and it is important to improve the quality of data. This will increase the possibility of disclosing true relationships between food habits and incidence of disease. However, often the epidemiologist must work with fallible data because they are the only data available, as is the case for data about food habits. The true extent of exposure to food items and nutrients is almost never known.

A well conducted interview or weighing survey will usually give a more comprehensive picture of the intake of macro- and micronutrients than what can be obtained from most self-administered questionnaires. Except for the dietary history interview, these dietary survey methods give information about the dietary intake for a limited time period. However, as interviews are expensive, the scientist may have no real choice but to rely on a self-administered questionnaire.

This review suggests that the use of a self-administered questionnaire provides an inexpensive method to obtain relatively unbiased, although not necessarily very precise, estimates of the usual food habits of a large number of subjects.

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ERRATA

Paper II, Table II: The Kendalls's tau for amount of table fat should read 0.33 (not 0.35).

Paper III, Table 4: The unstandardized B-value (-0.04) for the association between leisure physical activity and serum triglycedides in women has been placed on the line above the correct one.

Paper IV: p. 795: The study was supported by the Norwegian Council on Cardiovascular Diseases (not Cariovascular)".

APPENDIX PAPER I

THE TROMSØ HEART STUDY: RESPONDERS AND NON-RESPONDERS TO A HEALTH QUESTIONNAIRE, DO THEY DIFFER?

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Supported by the Norwegian Council on Cardiovascular Diseases.

Running headline: Non-responders to a health questionnaire.

SUMMARY

In 1979-80, 21,329 subjects, 20-54 years old, were invited to a screening for coronary heart disease risk factors in Tromsø. 16,621 (77 %) attended the screening, the response rate was higher women than in men, lower in single than married and lowest in young (20-29 years) men. At the screening, the men and women were given a second questionnaire which they were asked to fill in and return by mail. 14,667 (88.2 %) of the subjects did so. Based on information obtained at the screening, the differences between these 14,667 subjects and the 1954 men and women who failed to return the questionnaire are presented. 10.9 % of the women did not return the questionnaire, the corresponding figure for men was 12.6 %. The differences in age, body mass index (kg/m^2), blood lipids and blood pressure were minor or non-existent. The subjects who returned the questionnaire tended to be married, non-smokers and report respiratory symptoms less often than non-responders. Individuals who returned the questionnaire seem to have a somewhat more sedentary occupation with less sick leave.

Postal self-administered questionnaires are frequently used in order to obtain information about individual habits (1-3), and symptoms, as for example in the Tromsø Heart Study (4-6). It is well known that non-responders to health screenings differ from the responders in a number of respects (7-9). Less is known about about those who turn up to a screening, but not respond to questionnaires.

More than 60,000 subjects in the Tromsø Heart Study (3) and the cardiovascular county surveys in Norway (10) have given information about prodominately the diet on a questionnaire handed out to subjects who attended a screening for cardiovascular risk factors. It may be important to know whether the responders to the questionnaire differ from those who fail to return the questionnaire as it may reveal a bias. This question is particularly relevant for questions which may be regarded as sensitive by some individuals, e.g. questions about alcohol consumption or symptoms of mental problems.

In the second Tromsø Heart Study (1979-80), 16,621 men and women (out of 21,329 invited) attended the screening and were given a questionnaire to fill in and return. 14,667 returned the questionnaire. The present study gives first information about the response rate to the screening according to age, sex and marital status, and, second, using information obtained at the screening, compares the subjects who attended and returned the questionnaire with those who did not return the questionnaire.

MATERIAL AND METHODS

In 1979-80, all men 20-54 years old and all women 20-49 years old were invited to take part in a health survey in the municipality of Tromsø. The examination comprised the administration of a questionnaire concerning previous diseases, symptoms possibly caused by atherosclerotic diseases, physical activity in leisure time, smoking habits, type of work and family history of myocardial infarction and whether the grandparents were Finnish or Lappish. The blood pressure, weight and height were measured and a venous nonfasting blood sample was drawn for lipid and glucose analyses. This study was to a large extent a replication of the first Tromsø Heart Study in 1974 and the cardiovascular county surveys in Norway, and the methods and details have been described in previous papers (3,10,11).

A second questionnaire, which was four A-4 pages, concerning questions on food habits, previous diseases and social and psychological problems was given to those who attended the screening. The subjects were asked to fill it in at home and return it by mail. The nutritional part of the questionnaire covered questions about kind and quantity of bread normally used, type and quantity of table fat and milk, coffee drinking, alcohol habits and the use of fish and minced meat as well as fruits and vegetables. English translation of this part of the questionnaire is given elsewhere (12). In the second part of the questionnaire, there were a number of questions about present diseases and symptoms particularly in connection to gastro-intestinal problems and rheumatic diseases and about consumption of iron and over-the-counter analgetica. The last part of the questionnaire

contained questions about economical situation in the family during childhood, sleeping problems, mental depression and problems with coping with the problems of daily life.

No reminder was given to subjects who did not return the questionnaire. Subjects who were invited, but for some reason were not able to attend the screening were asked to state the reason and mail the note to the local health authority.

Differences between responders and non-responders to this questionnaire are evaluated with X^2-test for categorial variables and differences between means with Students t-test.

RESULTS

Table 1 shows the percentage of the invited subjects who attended the screening. 21,329 subjects (11,423 men and 9,906 women) were invited. 60 men and 52 women who had moved to Tromsø shortly before or during the screening met without being invited. They are not included in the computation of response rate. The response rate was highest in women (81.7 %) and in subjects in the highest age-groups (63.4 % in men and women 20-24 years old vs. 87.4 % in men and women in the 45-49 years bracket). However, some of the invited subjects had reasons for not attending (e.g. temporary living outside Tromsø, military service), had moved or were dead. After adjustment for these factors, the mean respons rate in men was 81.7 % and in women 88.4 %. The effect of taking into consideration legitimate reasons for not attending is particulary evident for subjects in the 20-24 year bracket where 36.6

% did not attend the screening. The per cent of non-attenders fell to 23.4 when those who gave reasons for not attending were excluded. The non-attenders tended to be single. In attenders, 62 % of the men and 66 % of the women were married, the corresponding figures for non-attenders were 45 and 50 %. These figures are adjusted for age but not for legitimate reasons for absence.

Out of the 8,478 men and 8,143 women who attended the screening (inclusive the 112 subjects who met without invitation), 1,068 men (12.6 %) and 886 women (10.9 %) did not return the questionnaire. This difference is statistically significant ($P < 0.001$).

The age-distribution (not shown), mean age, body mass index, blood lipids and blood pressure in women who returned the questionnaire did not differ from the rest of the women who attended the screening, whereas the men who failed to return the questionnaire were about one year younger (because of a relatively low proportion, 82.8 %, of the men aged 20-24 years who returned the questionnaire), had 0.07 mmol/l higher serum triglycerides and 0.7 mmHg higher diastolic blood pressure than other men (Table 2).

There were no differences between the subjects who returned the questionnaire and those who did not with regard to previous or present ischemic heart disease, atherosclerosis of legs, stroke, diabetes, use of nitroglycerine, treatment for hypertension or symptoms of angina pectoris or intermittant claudication.

Table 3 shows that non-responders tended to be single (40.5 % vs. 34.4 and 36.2 % vs. 31.5 % for men and women, respectively), smokers (approx. 11 % higher than in responders) and report morning coughing. Non-responding, non-smoking females tended to be ex-smokers. There were no differences with regard to pipe or cigar smoking, and non-responding smokers did not smoke more cigarettes per day than responding smokers. Responding men tended to have sedentary work (41.5 % vs. 34.9 %). This was not true for women. There were no associations in men or women between returning the questionnaire and physical activity in leisure. A greater part of the women who returned the questionnaire had domestic work as their main occupation (41.2 vs. 37.7 %, $p < 0.05$). Subjects with shift or night work tended to be non-responders. Inconsistent associations were observed between the probability of returning the questionnaire and whether the subject is on sick leave or receive rehabilitation wages (Table 3). We did not find any indications of a lower response rate in commuters, in subjects who receive or have received unemployment benefits the last year or in individuals who receive disability pension.

DISCUSSION

The response rate both to the first screening (77.4 % not adjusting for legitimate reasons for absence) and to the postal questionnaire (88.2 %) was high. Our findings with respect to the age, sex and marital status of the non-attenders are in accordance with most other Scandinavian studies (7,8,10). Rinder et al. found, however, few differences between attenders and non-attenders (13). The response rate

was somewhat lower than in the cardiovascular county studies in Norway (10).

A high response rate to the questionnaire was expected as the subjects had already demonstrated their motivation by attending the screening. The subjects who were invited, but did not attend the screening, differ more in terms of age (table 1 & 2) and marital status from the 16,621 who attended, than the subjects who did not return the questionnaire differ from those who did so. There were few differences between responders and non-responders to the questionnaire, the most important seems to be that the non-responders tended to be single, smoker and (in men) have somewhat higher serum triglycerides and blood pressure. Our finding of a lower response rate in smokers is in accordance with the data of Seltzer et al. (14).

There are at least two reasons why individuals who attended the screening did not return the second questionnaire. Firstly, the subject may have decided not to fill in the questionnaire due to the nature of the questions. Secondly, he or she may simply have forgotten to mail the prepaid envelope. We have no data to evaluate the relative importance of these reasons. The first reason is the most important one with regard to possible bias.

The reasons for not being willing to fill in the questionnaire may be many, including general lack of confidence to giving information on questionnaires ("Who will read it?"). Some questions may have been considered too sensitive as reflected by uncomplete questionnaires.

For instance, 96.6 % of those who returned the questionnaire did answer the questions about mental depression, 97.8 % answered the question about the frequency of use of beer, whereas 99.4 % answered the question about coffee drinking.

It might cause a problem if those who attended the screening but did not return the questionnaire had higher than average alcohol consumption. This would bias the results from the cross-sectional analyses (15). However, gamma-glutamyltransferase (GGT) was measured in 1579 men and 1654 women who attended the screening (16), and GGT in subjects who did not return the questionnaire was not higher than in subjects who did so. Furthermore, as HDL cholesterol did not differ between the responders and non-responders, we assume that the alcohol consumption is similar in the two groups.

If the object of a study is to give valid picture of some factor, e.g. serum cholesterol or food habits, in a population, any response under 100 % is a cause for some concern. It is a inherent problem in all studies of this type that little is usually known about the non-attenders. We believe that with a response rate to the screening of 73.7 % in men and 81.7 % in women, the data give some indications of the blood lipid levels and smoking habits of this population. It may, however, be true to say that in this study we have predominantly measured the attributes and habits of middle-aged, married subjects.

Only 68 % of those originally invited to the screening returned the questionnaire about symptoms and food habits, and one may question whether the information about food habits from this survey reflects

the habits of the Tromsø population. As the differences between responders and non-responders to the questionnaire are relatively minor, we believe that the data may be used to examine relationships between factors measured at the screening and information given in the questionnaire, and that strong associations found in the part of the population constituted by the responders to both surveys are likely to be generalizable at least to those who attended the screening.

Because of the strong association between cigarette smoking and coffee drinking seen in this (17) and other (18,19) studies, it may be that coffee drinking in the Tromsø population is somewhat underestimated by the information from the questionnaire. Total serum cholesterol does, however, not differ in responders and non-responders to the postal questionnaire. If the age-adjusted serum cholesterol is different in attenders and non-attenders, it is likely to be higher in the latter. It is therefore not likely that selection bias is the reason for the association between coffee drinking and total serum cholesterol found in this population (3).

The main finding of this study is that the subjects who did return the questionnaire were remarkably similar with regard to age, body mass index, blood lipids and blood pressure to the non-responders, and we believe that the results from analyses using such questionnaires in general seem to be trustworthy.

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Table 1. Population invited and examined in the second Tromsø Heart Study (1979-80) according to age and sex.

Age-group	Subjects invited		Response rate +		Adjusted response rate ++	
	Men	Women	Men	Women	Men	Women
20-24	1776	1979	57.4	68.8	71.1	81.6
25-29	2241	2269	65.0	75.7	73.6	83.8
30-34	2266	2080	75.1	85.4	82.8	90.0
35-39	1778	1537	79.5	89.4	84.9	92.7
40-44	1206	1085	82.6	91.7	88.5	94.5
45-49	1072	956	84.6	90.6	89.4	93.5
50-54	1084	-	85.1	-	89.4	-
20-49	10339	9906	72.5	81.7	80.8	88.4
20-54	11423	-	73.7	-	81.7	-

+ Excluding 112 persons who met without invitation.

++ Excluding those who gave reasons for not attending the screening, subjects who had moved out of the municipality and dead persons.

Table 2. Responders and non-responders to the postal questionnaire according to mean age (years), body mass index (BMI) (kg/m^2), total serum cholesterol (mmol/l) (T-CHOL), HDL-cholesterol (mmol/l) (HDL), triglycerides (mmol/l) (TG), systolic blood pressure (mmHg) (SYSBP) and diastolic blood pressure (mmHg) (DIABP). Tromsø Heart Study, 1979-80.

	Responders		Non-responders	
	Men	Women	Men	Women
Number of subjects	7410	7257	1068	886
Age	35.8 (9.3)+	32.9 (7.9)	34.9 (9.6)**	33.0 (7.9)
BMI	24.3 (2.8)	22.6 (3.2)	24.3 (3.0)	22.5 (3.2)
T-CHOL	6.01 (1.29)	5.67 (1.17)	5.97 (1.31)	5.68 (1.23)
HDL	1.45 (0.45)	1.74 (0.42)	1.45 (0.46)	1.76 (0.42)
TG	1.64 (0.97)	1.10 (0.59)	1.71 (1.04)*	1.09 (0.62)
SYSBP	130.5 (13.6)	120.9 (13.4)	131.3 (14.8)	120.4 (13.5)
DIABP	82.3 (10.6)	77.9 (9.7)	83.0 (11.2)*	78.0 (9.9)

+ Mean (Standard deviation)

The difference between responders and non-responders is statistically significant * $p = 0.05$, ** $p = 0.002$.

Table 3. Per cent of responders and non-responders to the postal questionnaire who are married, daily smokers, ex-smokers, report respiratory symptoms, different types of work and being on sick leave. Tromsø Heart Study, 1979-80.

	Responders		Non-responders	
	Men	Women	Men	Women
Number of subjects	7410	7257	1068	886
Married	65.6	68.5	59.5 ***	63.8 **
Daily smoker	49.1	46.2	59.8 ***	57.2 ***
Ex-smoker +	50.7	35.3	48.8	41.7 **
Morning coughing	12.6	7.0	14.9 *	10.3 ***
Morning phlegm	9.3	4.8	9.6	6.4 *
Domestic work as main occupation	-	41.2	-	37.7 *
Mainly sedentary occupation	41.5	29.4	34.9 ***	29.0
Shift or night work	16.8	12.2	17.5	14.6 *
On sick leave	3.8	2.5	2.7	4.4 ***

Statistical significance for the difference for responders and non-responders: ***: $p \leq 0.001$, ** : $p \leq 0.01$, * : $p \leq 0.05$.

+ % of current non-smokers.

APPENDIX PAPER II

Scand J Soc Med 15:41–47, 1987

The Tromsø Heart Study: Comparison of Information from a Short Food Frequency Questionnaire with a Dietary History Survey

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The Tromsø Heart Study: Comparison of information from a short food frequency questionnaire with a dietary history survey. Jacobsen, B. K., Knutsen, S. F. and Knutsen, R. (Institute of Community Medicine, University of Tromsø, Box 417, N-9001 Tromsø, Norway).

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In a group of 528 men, 30–54 years old, answers to various questions about dietary habits given in a questionnaire were compared to corresponding information given in a dietary history interview two years later. High concordance was found between the two methods for questions concerning types of foods most commonly used. For most food items, the mean intake according to the dietary recall corresponds well with intake reported in the questionnaire. For food items used every day in easily recorded units (slices of bread, cups of coffee, glasses of milk), the frequency questionnaire can be used to rank individuals according to consumption. For other food items, the concordance is less satisfactory.

Key words: diet, dietary history, food habits, frequency questionnaire.

Increasing awareness of the relationship between diet and some diseases has increased the demand for simple survey methods for assessing the dietary habits in epidemiological studies. The usual dietary history or registration (or even weighing) of the diet in 1–7 days is impractical for large population studies. Self-administered food frequency questionnaires have been used in several epidemiological studies (e.g. 1, 2). However, the validity of recording food frequency has been disputed (3–5) and is difficult to show due to lack of a "gold standard".

The aim of the present study was to compare the results of a self-administered dietary questionnaire with dietary history interview data from the same population sample. Acknowledging the limitations of such a dietary history interview, we nevertheless regarded it as the standard, and the usefulness of the questionnaire was assessed in that context. The questionnaire covers only a few dietary items, and therefore concordance between the two dietary surveys can only be evaluated for food items, not for nutrients.

MATERIAL AND METHODS

Population

7 410 men, 20–54 years, and 7 257 women, 20–49 years, were examined in a survey for coronary risk factors in Tromsø in 1979–80 (the second Tromsø Heart Study). The screening included a questionnaire on dietary habits, alcohol and coffee consumption and previous diseases (6).

Following the survey, a high risk group of men was identified, 30–54 years old, with relative HDL (HDL-cholesterol/total cholesterol) in the lowest quintile and/or total cholesterol in the highest decile. After random allocation to control or intervention, men in the intervention group were interviewed by trained dieticians using the dietary history method (7).

The interview was done one to two years after the initial screening. Complete dietary questionnaires were not available for all men, leaving a maximum of 528 men for the present analysis.

Frequency questionnaire

The dietary questionnaire was administered to the men at the screening, completed at home, and returned by mail. The respondents did not know that they later would be subject to dietary history interview. In the questionnaire the men gave information about both type and quantity of bread, table fat and milk normally used (slices of bread per day, amount of table fat on each slice of bread, glasses of milk per day), cups of coffee per day, and information about the frequency of use of alcohol, fish or fish dishes for dinner, minced meat as well as fruits and vegetables (Appendix).

Dietary history

The objective of the dietary history interview was to describe quantitatively and qualitatively the usual diet of the respondent. Three dieticians had been standardized using food models that later were used in the interview and by standardizing the weight of different foods when

Table I. *Type of table fat and milk normally used. Agreement between information from questionnaire (1979/80) and dietary history (1980/81)*

	No. of men	Kappa
Type of table fat		
Butter	49	0.76
Ordinary margarine	97	0.72
Soft margarine	299	0.71
Overall	445	0.72
Type of milk		
Non-drinkers	34	0.46
Whole fat milk	347	0.69
Skimmed milk	93	0.70
Mixtures	52	0.42
Overall	526	0.61

measured in conventional household units (teaspoons, tablespoons, etc.). During the interview, information about frequency of use of different foods (per day, week or month) and the amount consumed each time was recorded. The cooking method (baked, boiled, fried) for selected foods and addition of butter, margarine or sugar to the meal was noted. Food models, as well as real plates, cups, and glasses were used to help the respondent estimate portion size. In addition, the respondent was asked to cut a slice of bread and spread it with fat. The slice was weighed with and without fat to estimate weight of bread and amount of fat. Consumption of beverages (milk, soft drinks, coffee and alcohol) was coded as grams per day. In the analysis one cup of coffee is set to 150 g and a glass of milk to 200 g. Supervision of coding and control was done by one of the authors (S. F. K.).

Statistical methods

Concordance of information concerning type of table fat and milk normally used is evaluated with the kappa-statistic. Kappa indicates the extent to which the observed agreement between the two dietary survey methods is in excess of the agreement expected by chance (8). Although kappa values depend on the frequency of use of the different food items, Landis and Koch (9) have given the following guidelines for interpretation of the kappa values: Below 0.20 indicate poor agreement, 0.21 to 0.60 fair to moderate and 0.60 to 1.0 (the highest possible value), substantial agreement.

It was not possible to evaluate the concordance between information on type of bread normally used because the answers are not comparable in the two surveys. Furthermore, the answer alternatives "vegetable margarine" and "soft margarine" in the questionnaire are pooled into one category, "soft margarine".

Concordance at group level for questions concerning quantity is presented as the mean intake recorded in the dietary history (gram, glasses of milk etc.) for each consumption category in the questionnaire. Occasionally, two or more categories have been pooled due to few cases.

Kendall's tau was used to assess the correlation between answers in the two surveys at the individual level. This rank correlation coefficient was used because there are few categories in the questionnaire, each with many respondents. The absolute value is lower than for the Spearman's rank correlation coefficient. Data from the dietary history survey are used without grouping and correlated with data from the questionnaire, grouped as shown in Table II.

RESULTS

High agreement between the two dietary surveys was found for questions concerning type of food (Table I). The kappa values were high for all types of spread fats and for type of milk usually consumed. The concordance for non-milk-users (<100 g milk per day at interview) and those using mixtures of milk was somewhat lower.

Table II displays the concordance between the methods for questions on quantity or frequency rather than type of food. For table fats, the concordance was less satisfactory for quantity than for type of fat used. One should, however, note that for the three lowest consumption categories (comprising 83% of the subjects), the mean intake levels found in the dietary history interview are well separated, indicating that the questionnaire, for most respondents, has picked up some information at group level. Of the 40 men reporting no use of spread fat in the questionnaire, 29 (73%) confirmed this in the dietary history interview.

For bread, milk and coffee consumption, the answers agreed well, both for groups of men and for each individual. For fish, mean frequency of intake according to the dietary history differed significantly for each frequency category in the questionnaire. The same was true for the use of fruits and vegetables when combining the different categories of low consumption (≤ once a week) into one category. The lowest concordance was found for minced meat.

For the highest and lowest consumption categories of foods listed in Table II, a lower, respectively higher, intake was later recorded in the interview.

DISCUSSION

This study describes the consistency of information about own dietary habits given by adult men at two different points in time using two different dietary survey methods where there is reason to believe

Table II. *Agreement between information from questionnaire (1979/80) and dietary history (1980/81). Consumption category in the questionnaire and mean intake according to the dietary history survey*

	No. of men	Consumption category	Mean intake	Kendall's tau
Amount of table fat on each slice of bread (g)	40	0	1.7 (0.7–2.7)[a]	0.35
	231	3	4.8 (4.5–5.1)	
	163	6	6.0 (5.7–6.4)	
	69	9	6.6 (5.9–7.3)	
	22	12	8.1 (6.9–9.4)	
No. of slices of bread per day	16	<2	2.6 (1.7–3.4)	0.52
	350	2–6	5.5 (5.3–5.6)	
	160	>6	8.3 (7.9–8.6)	
No. of glasses of milk per day (1 glass=200 g)	117	<1	1.0 (0.8–1.2)	0.60
	215	1–2	1.9 (1.8–2.0)	
	164	3–4	4.0 (3.7–4.3)	
	29	>4	4.7 (3.9–5.6)	
No. of cups of coffee per day (1 cup=150 g)	17	<1	0.4 (0.0–0.9)	0.53
	147	1–4	4.5 (4.1–4.8)	
	268	5–8	7.5 (7.1–7.9)	
	96	>8	10.3 (9.5–11.1)	
Use of fish and fish dishes for dinner (times per week)	21	<1	1.5 (1.0–2.0)	0.37
	204	1–2	3.0 (2.8–3.1)	
	283	3–4	3.6 (3.5–3.7)	
	20	5–6	4.4 (4.1–4.7)	
Use of fruits and vegetables (times per week[b])	139	<2	3.1 (2.7–3.4)	0.43
	176	2–3	4.3 (4.0–4.6)	
	213	6–7	6.2 (5.9–6.5)	
Use of minced meat (times per month)	15	<1	1.9 (1.0–2.8)	0.25
	92	1–2	3.8 (3.4–4.2)	
	203	3–4	5.1 (4.7–5.4)	
	166	5–8	5.6 (5.2–6.1)	
	52	>8	6.5 (5.4–7.6)	

[a] 95% confidence interval for the mean.
[b] Categories used in the questionnaire: ≤ once a week, 2–3 times a week, about every day.

that the dietary history interview gives the more comprehensive picture of the food habits.

The questionnaire was completed with the subjects unaware of their increased risk, whereas the interview took place one to three weeks after a letter had notified them of their need for life-style changes and they had been subject to new blood tests, blood pressure measurement and information about CHD risk factors by a physician. The dieticians were, however, instructed to obtain the dietary history for the period preceding any changes made due to receiving this letter or talking to the physician.

Except for the possible effects of awareness of own high risk on the interview data, the answers should only be affected by differences in the dietary survey methods and by changes in food habits due to the general nutrition information since the screening. The systematic biases thus implied would diminish the degree of correspondence between the two surveys. The use of more than one observer in the interviews increases the amount of random error in the material, but because this study was not contemplated at the time of the dietary survey and the dieticians did not know what the men had stated in the questionnaire (and the men themselves probably did not remember), there is no reason to believe that there should be a systematic observer bias tending to increase the correspondence between the two methods.

The very high concordance observed for information about type of milk and spread fats in the two surveys shows that questionnaires are suitable for obtaining such information. Also for the question whether spread fat was used or not, the agreement was quite good (kappa=0.57).

The difficulties of assessing amount of spread fat used on each slice of bread through a self-administered questionnaire is reflected in the low rank correlation coefficient. But some information at

group level was picked up by having the respondents indicate the usual amount on pre-drawn cubes. Our results are in this respect similar to the findings in another Norwegian study (10), and we must conclude that a reliable method for obtaining information on the amount of table fat used by each individual using a self-administered questionnaire is still lacking.

The good correlations found both at the individual and group level for questions concerning slices of bread, glasses of milk and cups of coffee per day suggest that self-administered questionnaires can be used at the individual level for estimating consumption of food items used daily in easily recalled units. This is not true to the same extent for questions asking about frequency of food intake. Here the tau-values were lower, although statistically highly significant. Thus, these types of questions are more suitable for information at the group level. However, Marshall and co-workers found that if subjects are classified in the category next to the correct one (which is the most common misclassification in this study) in a random manner, a rather high misclassification rate can be tolerated without dramatically reducing the relative risk estimate found in a case-control or cohort study (11).

Although a number of recent studies have explored the validity of different food frequency survey methods concerning nutrients (e.g. 12–16), studies which give information about concordance at food item level are scarce. Using a different approach than in the present study, but looking at food items, Chu and co-workers (17) found a relatively good correlation between frequency and quantity at group level, but less satisfying concordance at the individual level. Our findings are, with some exceptions, in line with those reported from other surveys which have evaluated the concordance of information about intake of food items collected by a self-administered questionnaire and 24-hour recall (10, 18), dietary history (19) or the actual eating habits (20).

In summary, this study indicates that food frequency questions can be used to obtain information on food consumption at group level. Reliable information on food consumption can also be obtained at the individual level for foods that are used daily in easily recalled units. The frequency questionnaire seems to be highly suitable for collecting information about types of foods commonly used. The men in this study constitute a highly selected group, but there is no obvious reason for a higher concordance in this study than in a population with similar dietary habits.

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APPENDIX

English translation of the parts of the postal questionnaire used in this study.

Your own diet

1. What type of bread do you eat most frequently? Make a cross in the box where "Yes" fits best.

	YES
White bread	☐
Normal bread	☐
Dark bread	☐
Home-made bread	☐

2. What type of butter or margarine do you use most frequently? Make a cross in the box where "YES" fits best.

	YES
Butter	☐
Normal margarine	☐
Vegetable margarine	☐
Soft margarine	☐

3. How many slices of bread do you usually eat daily? Make a cross in the box where "YES" fits best.

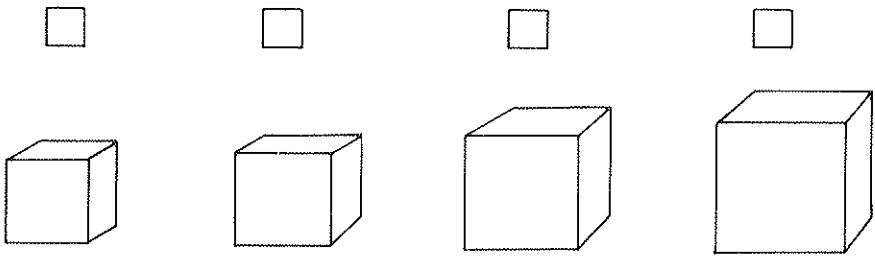
	YES
Less than 2 slices	☐
2-6 slices	☐
7-12 slices	☐
13 slices or more	☐

4. What type of milk do you usually drink? Make a cross in the box where "YES" fits best.

	YES
Do not drink milk	☐
Whole milk, sweet or sour	☐
Skimmed milk, sweet or sour	☐
Mixed skimmed and whole milk	☐

5. The drawing below shows cubes of butter or margarine in a true scale. Make a cross for the cube which most resembles the amount you use on one slice of bread. If in doubt, try buttering a slice.

Do not use butter or margarine ☐



6. How many glasses/cups of milk do you usually drink daily? Make a cross in the box where "YES" fits best. YES

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

7. How many cups of coffee do you usually drink daily? Make a cross in the box where "YES" fits best. YES

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

8. Are you teetotaller? YES ☐ NO ☐

If no,
How often do you drink beer? Make a cross in the box where "YES" fits best.

Never,or a few times per year ☐
1-2 times per month ☐
About once a week ☐
2-3 times a week ☐
About daily ☐

How often do you drink wine? Make a cross in the box where "YES" fits best.

Never,or a few times per year ☐
1-2 times per month ☐
About once a week ☐
2-3 times a week ☐
About daily ☐

How often do you drink spirits? Make a cross in the box where "YES" fits best.

Never,or a few times per year ☐
1-2 times per month ☐
About once a week ☐
2-3 times a week ☐
About daily ☐

9. How often during the last 12 months have you drunk so much beer,wine or spirits that you have become intoxicated? Make a cross in the box where "YES" fits best. YES

Never intoxicated or not during the last year ☐
A few times during the year ☐
1-2 times per month ☐
1-2 times a week ☐
3 times or more per week ☐

10. How often does your dinner consist of fish or fish dishes? Make a cross in the box where "YES" fits best. YES

Less than once a week ☐
1-2 times a week ☐
3-4 times a week ☐
5-6 times a week ☐
7 times a week ☐

11. How often do you use fruits or vegetables? Make a cross in the box where "YES" fits best. YES

Never use fruits or vegetables ☐
A few times per year ☐
1-2 times per month ☐
About once a week ☐
2-3 times a week ☐
About daily ☐

12. How many times per month do you eat boiled or fried sausages, meat balls, or other minced meat? Make a cross in the box where "YES" fits best. YES

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

APPENDIX PAPER III

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THE TROMSØ HEART STUDY: FOOD HABITS, SERUM TOTAL CHOLESTEROL, HDL CHOLESTEROL, AND TRIGLYCERIDES

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Jacobsen, B. K. (Institute of Community Medicine, U. of Tromsø, 9001 Tromsø, Norway), and D. S. Thelle. The Tromsø Heart Study: food habits, serum total cholesterol, HDL cholesterol, and triglycerides. *Am J Epidemiol* 1987;125:622–30.

Associations between food habits and total serum cholesterol, high density lipoprotein (HDL) cholesterol, and serum triglycerides were examined in 7,410 men and 7,257 women in Tromsø, Norway, following a screening in 1979–1980. High body mass index was associated with high serum cholesterol, high triglycerides, and low HDL cholesterol. Positive associations were observed between high serum cholesterol and high coffee consumption, use of butter or hard margarine, not selecting low-fat milk, and low bread consumption. The HDL cholesterol level was virtually independent of the dietary items recorded. Use of low-fat milk and frequent use of fish dishes for dinner seemed to be related to low serum triglyceride levels.

cholesterol; food habits; lipoproteins, HDL cholesterol; triglycerides

High total serum cholesterol and low high density lipoprotein (HDL) cholesterol are both associated with increased risk for coronary heart disease (1, 2). The role of serum triglycerides as an independent risk factor is more debatable, but high triglyceride levels have in some populations been associated with elevated risk for ischemic heart disease (3). The food habits are, through their effects on the blood lipid levels, one of several factors that may influence the risk for coronary heart disease.

However, although associations between the diet on the group level and blood lipids have been known for a long time (4), conflicting results have emerged when the same associations have been evaluated within different populations (5–8). The purpose of this study is to examine in the free-living population of Tromsø, Norway, the associations between food habits and total serum cholesterol, HDL cholesterol, and serum triglycerides.

In a previous paper from the Tromsø population, a rather strong positive association was observed between coffee drinking and total serum cholesterol (9). The present paper presents this association with adjustment for other food habits and describes other relationships between food habits and blood lipids in the same population.

MATERIALS AND METHODS

In 1979–1980, all men and women aged 20–54 and 20–49 years, respectively, 21,329 subjects altogether, were invited to take part in the second cardiovascular population study in Tromsø. A total of 16,621 persons attended the screening. The examination consisted of the administration of a questionnaire concerning previous dis-

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Abbreviations: HDL cholesterol, high density lipoprotein cholesterol; P/S ratio, ratio between intake of polyunsaturated and saturated fatty acids.

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This study was carried out in cooperation with the National Health Screening Service, Oslo, Norway.

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eases, symptoms possibly caused by atherosclerotic diseases, living habits, and social conditions, as well as measurements of blood pressure, weight, and height, and a venous nonfasting blood sample for lipid and blood glucose analyses. This study was to a large extent a replication of the first Tromsø Heart Study in 1974 and the cardiovascular county surveys, and the methods and details have been described in previous papers (9, 10).

A second questionnaire concerning food habits, previous diseases, and social and psychologic conditions was administered to those who attended the screening. It was filled in at home and returned by mail. A total of 7,410 men and 7,257 women completed this questionnaire. The nutritional part of the questionnaire covered questions about kind and quantity of bread normally used, type and quantity of table fat and milk, coffee drinking, alcohol habits, and the use of fish, ground meat, and fruits and vegetables. These dietary items had been selected since they provide information about some of the most important contributors of the intake of fat and energy. A number of dietary items, e.g., poultry and ice cream, have been omitted in this survey because they are not important parts of the daily diet in this population. The information about the nutritional habits collected in the study is too sparse to compute the energy or fat intake of each individual.

The validity of the data on dietary habits has been assessed in a subgroup of 528 men, 30–54 years old at screening. The data in the questionnaire were compared with data from a dietary history survey conducted 1–2 years after the screening. High concordance was found between the two methods for questions concerning types of foods most commonly eaten. For food items used every day in easily recalled units, and for the questions about use of alcohol, the concordance between the two dietary survey methods was quite good (Kendall's tau ≥ 0.50). For other food items, the concordance was less satisfactory (Kendall's tau ≥ 0.25) (unpublished observations).

Total serum cholesterol was measured directly by the enzymatic oxidase method, using a commercial kit (Boehringer 148393, Boehringer-Mannheim, Mannheim, West Germany). HDL cholesterol was assayed by the same procedure after precipitation of lower density lipoproteins with heparin and manganese chloride. Triglycerides were enzymatically determined as glycerol (Boehringer 15725, Boehringer-Mannheim, Mannheim, West Germany). All laboratory assessments were performed by the Division of Clinical Chemistry, University Teaching Hospital of Tromsø.

To determine the food habits which contributed significantly to the "explanation" of the variation of the dependent variables, total serum cholesterol, HDL cholesterol, and triglycerides, multiple regression analysis using SPSS (11) was performed. The three variables which convey information about use of alcohol were first forced into the equation, and, for the rest of the independent variables, forward selection was used, including variables if F-to-enter ≥ 3.85, corresponding to $p \leq 0.05$. For each dependent variable, a second multiple regression analysis was run with the alcohol variables and the other variables which contributed significantly to the regression in one or both sexes. The results from these analyses are given in the tables as unstandardized and standardized regression coefficients and p values for the associations. The standardized regression coefficient (B_{st}) provides a way to compare the relative effects on the dependent variable of each independent variable when these are measured in different units (as in these analyses). The B_{st} is computed from the unstandardized coefficient (B) for each independent variable X with standard deviation (SD X) as $B_{st} = B$ (SD X/SD Y) where SD Y is the standard deviation of the dependent variable in question. The p values are two-tailed throughout.

The three dependent variables were total serum cholesterol, HDL cholesterol, and serum triglycerides. The independent variables were age (five-year age groups), ciga-

rette smoking (cigarettes per day), body mass index (kg/m^2), leisure time physical activity, work time physical activity (both graded from 1–4 with increasing activity), use of beer (never or a few times/year, 1–2 times/month, once a week, 2–3 times a week, about daily), use of wine and of spirits (both coded as for beer), type of bread (brown bread, white bread), type of table fat (soft margarine, hard margarine or butter), milk-drinker (no, yes), glasses of milk per day (<1, 1–2, 3–4, ≥5), use skimmed milk or mixtures of whole fat and skimmed milk (no, yes), number of slices of bread per day (<2, 2–6, 7–12, ≥13), amount of table fat on each slice of bread (0, 3, 6, 9, 12 g), number of cups of coffee per day (<1, 1–4, 5–8, ≥9), frequency of use of fish dishes for dinner (<1, 1–2, 3–4, 5–6, 7 times per week), frequency of use of fruits and vegetables (never or a few times/year, 1–2 times/month, once a week, 2–3 times/week, about daily), frequency of use of ground meat (<1, 1–2, 3–4, 5–8, >8 times per month). In the analysis for serum triglycerides, time since last meal (<1, 1–2, 2–4, 4–8, >8 hours) was also used as an independent variable.

Because of missing values for some of the subjects, 6,647 men and 6,297 women (of the 7,410 men and 7,257 women who gave some information about the diet) were included in the first multiple regression analysis with all the 19 (for serum triglycerides, 20) independent variables. A somewhat higher number of subjects are included in the final regression analyses when not all independent variables are used.

Results

Table 1 shows the distribution of intake of some selected food items included in this study. As explained in the footnote, due to missing cases, the numbers of subjects included in the analyses vary. The two highest categories for bread and fish consumption are combined due to few subjects who eat ≥13 slices of bread or who have fish for dinner every day. Women were more apt to use soft margarine and low-fat milk than were men, who, on the other hand, used more bread and coffee. More than 90 per cent of the subjects in this population have fish for dinner at least once a week. The results from the multiple regression analyses are given in tables 2–4.

Table 1

*Distribution (in per cent) of intake of some selected food items in the Tromsø Heart Study, 1979–1980**

Food item	Men	Women
Type of table fat		
Butter or hard margarine	28.2	25.7
Soft margarine	71.8	74.3
Use of low-fat milk		
No	73.2	61.3
Yes	26.8	38.7
Slices of bread per day		
<2	2.1	9.6
2–6	60.5	86.0
≥7	37.4	4.4
Cups of coffee per day		
<1	6.9	7.8
1–4	32.5	42.7
5–8	44.6	40.0
≥9	16.0	9.6
Fish dishes for dinner (times per week)		
<1	7.0	7.4
1–2	45.1	46.1
3–4	44.6	43.9
5–7	3.2	2.6

* Due to missing cases, the numbers of men and women included in the analyses vary from 7,169 to 7,369 men and from 6,962 to 7,225 women.

Body mass index (kg/m^2) was significantly and positively associated with serum total cholesterol and triglyceride level and inversely associated with the HDL cholesterol concentration. A 5 per cent increase in body mass index (equivalent to 3.8 kg for a man 1.77 m tall and 3.0 kg for a woman 1.64 m tall) was associated in men with 0.08 mmol/liter (3 mg/100 ml) increase in total serum cholesterol, 0.03 mmol/liter (1 mg/100 ml) decrease in HDL cholesterol, and 0.12 mmol/liter (11 mg/100 ml) increase in serum triglycerides, and in women with 0.06 mmol/liter (2 mg/100 ml) increase in total serum cholesterol, 0.02 mmol/liter (1 mg/100 ml) decrease in HDL cholesterol, and 0.05 mmol/liter (4 mg/100 ml) increase in serum triglycerides.

TABLE 2

Associations between food and life-style habits and total serum cholesterol (mmol/liter). Unstandardized (B) and standardized regression coefficients (B_{st}), 6,711 men and 6,397 women, Tromsø, 1979–1980†

Variable	Men		Women	
	B	B_{st}	B	B_{st}
Age group	0.23	0.34***	0.24	0.32***
Body mass index	0.07	0.15***	0.05	0.15***
Daily cigarette smoking	0.00	0.02	0.01	0.05***
Leisure time physical activity	−0.08	−0.05***	−0.01	−0.00
Use of beer	−0.05	−0.04**	−0.05	−0.03*
Use of wine	−0.04	−0.02	−0.10	−0.06***
Use of spirits	0.02	0.02	−0.01	−0.01
Type of table fat	0.27	0.10***	0.27	0.10***
Coffee drinking	0.20	0.13***	0.15	0.10***
Slices of bread	−0.16	−0.07***	−0.09	−0.03**
Use of low-fat milk	−0.05	−0.02	−0.12	−0.05***
Use of fruits and vegetables	−0.02	−0.02	−0.07	−0.05***
Use of fish	0.05	0.03*	0.05	0.03*

* $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$.

† Mean total serum cholesterol concentration (and standard deviation) was 6.00 (1.28) and 5.64 (1.16) mmol/liter for men and women, respectively. Adjusted R^2 was 0.253 and 0.218, for the analyses for men and women, respectively.

Table 2 gives the results for total serum cholesterol. The strongest associations with the food habits recorded in this study were the positive associations with coffee drinking and use of butter or hard margarine. A weak positive association was seen for fish consumption. Negative associations were noted for bread, and, in women, for use of low-fat milk and consumption of fruits and vegetables.

Total serum cholesterol in men and women who used butter or hard margarine was approximately 0.27 mmol/liter (10 mg/100 ml) higher than in subjects who selected soft margarine. The difference in total serum cholesterol for subjects who drank little coffee (<1 cup/day), compared to those with high coffee consumption (≥9 cups/day), was approximately 0.60 mmol/liter (23 mg/100 ml).

Total serum cholesterol for those who used butter or hard margarine and drank ≥9 cups of coffee per day, compared with those who used soft margarine and had a low coffee consumption (<1 cup/day), was 6.57 mmol/liter (n = 374) versus 5.42 mmol/liter (n = 345) for men and 6.25 mmol/liter (n = 189) versus 5.26 mmol/liter (n = 377) for women. Thus, the difference was 1.15 mmol/liter (44 mg/100 ml) for men and 0.99 mmol/liter (38 mg/100 ml) for women. This comparison is adjusted for age group, body mass index, alcohol use, cigarette smoking, leisure time physical activity, use of low-fat milk, number of slices of bread, and consumption of fish and fruits and vegetables by analysis of covariance. About 60 per cent of this difference is due to coffee consumption, the other 40 per cent to type of table fat. For women, but not for men, we observed a tendency toward a stronger effect of coffee drinking among the users of butter or hard margarine.

In the multiple regression analysis, HDL cholesterol was positively associated with use of butter or hard margarine as table fat, and negatively associated with use of fruits and vegetables for men (table 3). However, the influence of these food habits was modest, the difference in HDL cholesterol being approximately 0.04 mmol/liter (1–2 mg/100 ml) between users of butter or hard margarine and users of soft margarine.

TABLE 3

Associations between food and life-style habits and HDL cholesterol (mmol/liter). Unstandardized (B) and standardized regression coefficients (B_u), 6,796 men and 6,458 women, Tromsø, 1979–1980†

Variable	Men		Women	
	B	B_u	B	B_u
Age group	0.03	0.12***	0.05	0.19***
Body mass index	−0.03	−0.16***	−0.02	−0.15***
Daily cigarette smoking	−0.00	−0.07***	−0.01	−0.17***
Leisure time physical activity	0.01	0.03*	0.02	0.03**
Work time physical activity	0.03	0.07***	0.01	0.02
Use of beer	0.03	0.08**	0.03	0.05***
Use of wine	0.01	0.01	0.04	0.07***
Use of spirits	0.06	0.13***	0.06	0.10***
Type of table fat	0.04	0.04***	0.03	0.03**
Use of fruits and vegetables	−0.02	−0.04**	0.00	0.01

* $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$.

† Mean HDL cholesterol concentration (and standard deviation) was 1.45 (0.44) and 1.74 (0.41) mmol/liter for men and women, respectively. Adjusted R^2 was 0.068 and 0.097 for the analyses for men and women, respectively.

TABLE 4

Associations between food and life-style habits and serum triglycerides (mmol/liter). Unstandardized (B) and standardized regression coefficients (B_u), 6,877 men and 6,593 women, Tromsø, 1979–1980†

Variable	Men		Women	
	B	B_u	B	B_u
Age group	0.02	0.04**	0.01	0.02
Body mass index	0.10	0.28***	0.04	0.23***
Daily cigarette smoking	0.01	0.06***	0.01	0.11***
Leisure time physical activity	−0.06	−0.05***	−0.04	−0.04***
Time since last meal	−0.11	−0.12***	−0.06	−0.11***
Use of beer	−0.04	−0.04**	−0.00	−0.01
Use of wine	0.00	0.00	−0.02	−0.03
Use of spirits	−0.01	−0.01	−0.03	−0.03*
Amount of table fat	0.03	0.03*	0.04	0.05***
Use of low-fat milk	−0.08	−0.04**	−0.10	−0.08***
Glasses of milk	0.02	0.01	0.03	0.03**
Use of ground meat	0.05	0.05***	0.02	0.03*
Use of fish	−0.06	−0.04***	−0.02	−0.03*
Type of bread	0.03	0.01	0.08	0.03*
Slices of bread	0.04	0.02*	0.01	0.01

* $p \leq 0.05$; ** $p \leq 0.01$; *** $p \leq 0.001$.

† Mean serum triglyceride concentration (and standard deviation) was 1.63 (0.97) and 1.08 (0.58) mmol/liter in men and women, respectively. Adjusted R^2 was 0.109 and 0.091 for the analyses for men and women, respectively.

In the multiple regression analysis, the variation in serum triglyceride level was significantly associated with a number of different food habits for one or both sexes (table 4). For both sexes, statistically significant ($p \leq 0.05$) positive associations were seen for the amount of table fat on each slice of bread and the frequency of use of ground meat, whereas, for fish consumption and use of low-fat milk, negative associations were seen. However, none of these associations were very strong. Sub-

TABLE 5

Correlation coefficients between some independent variables included in this analysis, 6,647 men and 6,297 women, Tromsø, 1979–1980

Women	Men				
	Leisure time physical activity	Use of low-fat milk	Type of table fat	Coffee drinking	Slices of bread
Leisure time physical activity		0.08	−0.04	−0.12	0.12
Use of low-fat milk	0.10		−0.13	−0.09	−0.07
Type of table fat	0.00	−0.08		0.07	−0.03
Coffee drinking	−0.08	−0.05	0.05		0.04
Slices of bread	0.01	−0.05	0.01	0.01	

$p < 0.001$ if $r > 0.04$.

jects who did not use table fat had approximately 0.15 mmol/liter lower serum triglycerides than those who spread the table fat lavishly, and a similar difference was found between those who frequently eat fish for dinner (>4 times a week) and those who seldom eat fish (<1 time a week). It should be noted that time since last meal contributed significantly to the regression.

Some of the independent variables were statistically significantly correlated, and table 5 gives the correlation coefficients between some selected independent variables. The table suggests that cholesterol-lowering habits tend to aggregate. However, no simple correlation coefficient exceeded that between some of the alcohol variables ($r \leq 0.48$), and most correlation coefficients had values far below this level.

DISCUSSION

The information about food habits used in this study was collected from a self-administered questionnaire. No effort was made to obtain quantitative information about the diet, a virtually impossible task with the available resources in a population study with more than 14,000 individuals.

Stepwise regression analysis of such a large data set with up to 20 independent variables will nearly always give some statistically significant associations. Thus, in the following we will emphasize relationships with low p values.

Table 5 demonstrates that some of the variables which are associated with, for example, total serum cholesterol, are intercorrelated. In a cross-sectional study, there is a risk of confounding due to intercorrelation between the independent variables. This demands great care when interpreting associations, particularly those that are unexpected. Interrelations between two or more variables can take care of part of the variance originally explained by one of them, and the variable may turn out with the opposite sign in the multiple regression analysis. Furthermore, the confounding effects of other variables, not examined in the study, cannot, of course, be ruled out. Thus, some of the associations described in this paper, e.g., the association between coffee drinking and high level of serum cholesterol, may to some extent reflect an association between a set of cholesterol-increasing food items including coffee drinking.

The dependent variables in this study, particularly HDL cholesterol and serum triglycerides, are not normally distributed. However, analyses with the logarithmic transformed variables (which are more normally distributed) did not change the main findings presented above.

Cross-sectional studies will never answer the question of time sequence, i.e., which of the associated variables came first, and therefore likely to be the cause of the other.

This is even more complicated when examining the relationship within a health-conscious population in which a number of subjects begin to change their food habits on their physicians' advice or their own initiative. An example is the negative association observed in women but not men between low-fat milk consumption and total serum cholesterol (table 2). This may be due to some men drinking skimmed milk because they have been told that they have a high serum cholesterol level. Due to the intervention, which was started in 1974, it is more likely that men rather than women in this population have been recommended to change their diet because of hypercholesterolemia (12).

Body mass index was positively associated with serum total cholesterol and triglycerides and negatively correlated with HDL cholesterol concentration. This is in accordance with previous findings (13). The standardized regression coefficients for these associations were higher than for the food items. However, a man 1.77 m tall would have to gain more than 12 kg in weight in order to increase his serum cholesterol to the level that would be comparable to a change from soft margarine to butter or hard margarine. The corresponding weight gain necessary for a woman 1.64 m tall is about 14 kg. An increase of 4–5 kg in body mass was associated with the same change in HDL cholesterol as a change of type of table fat. Because the body mass index is used as an independent variable in the analysis, the other variables discussed below all contribute independently to the regression.

The two strongest associations between food items and total serum cholesterol in this analysis are the associations with coffee consumption and type of table fat, whereas the other variables were of less importance. The association between coffee drinking and total serum cholesterol in this population has previously been reported (9). Population studies published before 1985 are summarized by Mathias et al. (14). Positive associations were later observed in three cross-sectional studies (15–17), and a causal relationship, at least with coffee brewed in the northern Norwegian manner, is suggested by two small experiments (18, 19). It is not likely that use of cream or milk in the coffee can explain this association, and there were no indications that the coffee drinkers had particular nutritional patterns that could explain their higher cholesterol levels (20). In the previous report (9), no adjustment was made for food habits. The present study indicates that the association between coffee drinking and serum cholesterol is independent of the other food habits recorded, and that the adjustment does not notably reduce the magnitude of the association (approximately 0.60 mmol/liter (23 mg/100 ml) between high (≥9 cups) and low (<1 cup) coffee consumption).

It is well known from other studies that fats with high polyunsaturated fatty acids compared with saturated fatty acids, i.e., with a high polyunsaturated to saturated (P/S) ratio, are hypocholesterolemic compared with butter or other fats with a low P/S ratio (21). This is also demonstrated in this study, although the difference is fairly modest—about 4–5 per cent. The associations between serum cholesterol and the fatty acid composition of the diet have been observed in some populations, e.g., the Western Electric Study (5) and among Terahumara Indians (6), but not in other studies, e.g., the Tecumseh Study (7) and the Zutphen Study (8). The combined effect of high coffee consumption and use of butter is considerable in the present study (≥1 mmol/liter (38 mg/100 ml) between the extreme categories) and likely to be of clinical importance.

The association found between the number of slices of bread used daily and the total serum cholesterol was found to be strongest for men. In this population, the habit of eating many slices of bread per day indicates a high energy intake, but is not associated with the percentage of energy from fat in the diet (unpublished observations).

The rather weak positive association between fish consumption and serum cholesterol is interesting in light of the negative association between fish consumption and risk for coronary heart disease reported from Zutphen, Holland (22). Previous studies have indicated that diets high in fatty fish reduce (23, 24) or do not change (25, 26) total serum cholesterol. In this study, we did not enquire about the type of fish eaten, and some of the most commonly eaten types of fish are indeed low in fat. Furthermore, eating fish for dinner is in this population often associated with other food habits, e.g., use of melted fats (instead of sauce), which also may be related to the serum cholesterol level.

In his review on diet and HDL cholesterol, Katan (27) states that the HDL cholesterol level increases when the proportion of the energy from fats increases and that it is essentially independent of the P/S ratio of the diet. Our findings suggest that the food habits, except for their effects on body weight, are of minor importance for the HDL cholesterol level in the Tromsø population, although small, statistically significant effects of diet, particularly the P/S ratio for table fat, were observed both in men and women. This is similar to the findings of Shepard et al. (28), who observed higher HDL cholesterol levels among participants on diets high in saturated fats than among participants on diets high in polyunsaturated fats.

The blood samples were nonfasting. This may be particularly important for the analyses of associations between serum triglycerides and food habits. Time since last meal was included as an independent variable, and it was highly significantly ($p < 0.001$) inversely associated with serum triglycerides in both sexes, the regression coefficient indicating more than 20 per cent lower serum triglyceride levels in subjects who had not eaten during the last eight hours compared with persons who had just eaten (<1 hour since last meal). Residual confounding may, however, exist and influence the results to the extent that food habits are correlated to time since last meal. We do not think that this is likely because time since last meal was only weakly correlated ($r \leq 0.05$) to any of the food habits recorded in this study.

The negative correlation of fish consumption and serum triglyceride level may support the hypothesis that diets high in eicosapentanoic acid are related to decreased triglycerides (23–26), probably because of the reduced rate of very low density lipoprotein production (29). However, for reasons mentioned above, the association should be viewed with scepticism until confirmed by other studies.

According to the present study, preference for low-fat milk is associated with low serum triglycerides. Frequent consumption of ground meat and use of much table fat were also associated with high triglyceride levels, but a more detailed analysis revealed that the dose-response relation for these two food items was less convincing.

In summary, this study confirms the adverse effects of high body mass index on blood lipids. Positive associations were seen between high serum cholesterol and high coffee consumption and the use of table fat with low P/S ratio, while negative associations were observed between serum cholesterol and bread and low-fat milk consumption. In this study, the HDL cholesterol level is hardly influenced by diet. Furthermore, an inverse association was found between the serum triglyceride level and frequent consumption of fish for dinner.

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APPENDIX PAPER IV

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THE TROMSØ HEART STUDY: THE RELATIONSHIP BETWEEN FOOD HABITS AND THE BODY MASS INDEX*

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Abstract—Associations between food habits and body mass index (BMI) (kg/m^2) were explored in a cross-sectional study with 7410 men and 7257 women. High BMI was most strongly associated with low bread consumption and use of low-fat milk. Weaker positive associations were seen for coffee, fish and ground meat consumption, and with use of table fat with a low P/S-ratio. Negative associations were seen for use of fruits and vegetables and amount of table fat at each slice of bread. Inconsistent relationships were noted for use of alcohol. The results suggest that individuals to some extent have changed their food habits in order to keep the BMI within limits they consider to be normal, and underline the need for adjustment for BMI when e.g. relationships between the diet and blood lipids are studied.

Alcohol Body mass index Cross-sectional studies Diet Overweight

INTRODUCTION

Overweight is associated with both increased blood lipids and blood pressure [1–3] and is also in other ways associated with increased morbidity. It is therefore important to investigate the relationships between amendable habits and the relative body weight. Several studies have indicated that the energy intake of obese individuals is not higher than that of individuals with normal body weight [4–6] and weak negative associations between the body mass index (BMI) (kg/m^2) and the energy intake have been observed in population studies [7, 8]. Keys noted in the "Seven Countries Study" [9] a strong negative association between the energy intake per kg body weight and the sum of skinfold thickness. The present study describes relationships between BMI and some food habits in a cross-sectional survey. The results are presented as associations between food items and BMI, rather than associations between intake of nutrients or energy and the relative weight. In this way, the study gives information about food habits which may explain the lack of positive association between BMI and the energy intake.

MATERIAL AND METHODS

In 1979–80, 21,329 subjects were invited to take part in a second survey in the municipality of Tromsø. This included all men born between 1925 and 1959 and all women born between 1930 and 1959 registered in the municipality. A total of 16,621 (78%) attended the screening. The examination comprised the administration of a questionnaire concerning previous diseases, symptoms possibly caused by atherosclerotic diseases, living habits and social conditions as well as measurements of blood pressure, weight and height (to the nearest half kilogram and centimeter) and a venous nonfasting blood sample for lipid analyses. This study was to a

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large extent a replication of the first Tromsø Heart Study in 1974 and the cardiovascular county surveys in Norway, and the methods and details have been described in a previous paper [10].

A second questionnaire concerning food habits, previous diseases and social and psychological conditions was given to those who attended the screening. It was filled in at home and returned by mail. Altogether 7410 men and 7257 women completed this questionnaire. The nutritional part of the questionnaire covered questions about kind and quantity of bread normally used, type and quantity of table fat and milk, coffee drinking, alcohol habits and the use of fish, minced meat as well as fruits and vegetables. These dietary items had been selected as they provide information about some of the most important contributors of the intake of fat and energy. Fish consumption is relatively high, and mainly consumed as a dinner course. Coffee constitutes a major beverage in the Norwegian population, whereas alcohol consumption in general is relatively low. A number of dietary items, e.g. poultry and ice cream, were omitted from the frequency questionnaire because they are not important parts of the daily diet in this population. The information about the nutritional habits collected in this study is too sparse for computing the energy or fat intake of each individual.

The validity of the data on dietary habits has been assessed in a subgroup of 528 men, 30–54 years old at screening. The data in the questionnaire was compared with data from a dietary history survey conducted 1–2 years after the screening. High concordance was found between the two methods for questions concerning types of foods most commonly used. For food items used every day in easily recalled units, and for questions about use of alcohol, the correspondence between the two methods was good (Kendall's tau ≥ 0.50). For other food items, the concordance was less satisfactory (Kendall's tau ≥ 0.25) [11].

To examine the variation of the body mass index (BMI) (kg/m^2), a multiple regression analysis was performed using SPSS [12]. Stepwise forward selection was used, including a variable if F-to-enter > 3.85, corresponding to $p < 0.05$. After determination of the variables which contributed significantly to the regression for one or both sexes, the regression was run with these variables for both sexes. Unstandardized and standardized regression coefficients and p-values are given in the tables. The standardized regression coefficients (B_{st}) provide a way to compare the relative effects on the dependent variable of each independent variable when these are measured in different units (as in this study). The B_{st} is computed from the unstandardized coefficient (B) for each independent variable X with standard deviation SD X as $B_{st} = B$ (SD X/SD Y) where SD Y is the standard deviation of the dependent variable, in this study the body mass index.

The following variables were taken into account as possible determinants of the BMI: Age (5-year age groups), daily cigarette consumption (number of cigarettes/day), leisure time physical activity, work time physical activity (both graded from 1 to 4 with increasing activity), use of beer, wine and spirits (all three coded: never or a few times/year, 1–2 times/month, once a week, 2–3 times a week, about daily), type of bread (brown bread, white bread), type of table fat (soft margarine, hard margarine), use skimmed milk or mixtures of whole fat and skimmed milk (no, yes), glasses of milk per day (<1, 1–2, 3–4, ≥ 5), number of slices of bread per day (<2, 2–6, 7–12, ≥ 13), amount of table fat on bread (0, 3, 6, 9, 12 g), number of cups of coffee per day (<1, 1–4, 5–8, ≥ 9), frequency of use of fish dishes for dinner (<1, 1–2, 3–4, 5–6, 7 times per week), frequency of use of fruits and vegetables (less than once a week, about once a week, 2–3 times/week, about daily), frequency of use of minced meat (<1, 1–2, 3–4, 5–8, >8 times per month).

Due to missing data for some subjects, 6664 men and 6314 women are included in the multiple regression analyses.

RESULTS

Table 1 shows the distribution of intake of some selected food items included in this study. The highest consumption categories for bread consumption are combined due to few subjects who eat ≥ 13 slices of bread per day. Women were more apt to use low fat milk and not use table fat on the bread than men, who, on the other hand, used more bread and coffee.

Table 2 displays the results of the multiple regression analysis with BMI as the dependent variable. In both sexes, high BMI was associated with low bread consumption, use of low-fat milk, high coffee and minced meat consumption and with low table fat consumption. In addition, table fats with low P/S ratio were selected

Table 1. Distribtuion (in per cent) of intake of some selected food items in the Tromsø Heart Study (1979–1980)*

Food item	Men	Women
	(%)	
Use of low-fat milk		
No	73.2	61.3
Yes	26.8	38.7
Slices of bread per day		
< 2	2.1	9.6
2–6	60.5	86.0
≥ 7	37.4	4.4
Cups of coffee per day		
< 1	6.9	7.8
1–4	32.5	42.7
5–8	44.6	40.0
≥ 9	16.0	9.6
Amount of table fat (g) at each slice of bread		
0	7.1	16.9
3	42.5	58.2
6	32.4	18.5
9	13.6	4.4
12	4.5	2.1

*Due to missing cases, the number of men and women included in the analyses vary from 7325 to 7368 men and from 7176 to 7218 women.

by subjects with high BMI. The oldest individuals had the highest BMI, and high BMI was also positively associated with high physical activity at work, low physical activity in leisure time and non-smoking. Inconsistent relationships were seen for the alcoholic beverages. Note, however, that the regression coefficients are rather low. Apart from age, only changes in bread and milk consumption as well as wine consumption (only in women) can independently influence the BMI more than 5%. A 5% change in BMI corresponds to approximately 3.8 kg for a 1.77 m tall man and 3.0 kg for a woman who is 1.64 m tall. This is the mean height of men and women in this study.

In both sexes, the strongest relationships observed were those between high BMI and low consumption of bread and use of low fat milk (skimmed milk or mixtures of skimmed and whole fat milk). Individuals who eat less than two slices of bread per day had about 5 kg higher body weight than those who eat more than six slices per day. In men, a weak positive association was seen between BMI and the number of glasses of milk per day. In women, the opposite tendency was evident. However, the major difference (about 3 kg) was found between subjects who selected low-fat milk compared to those who used whole fat milk or did not drink milk. As shown in Table 1, about 27% of the men and 39% of the women used low fat milk.

The positive relationship between coffee consumption and BMI was observed in both sexes. The same was true for the associations between BMI and ground meat and table fat with low P/S-ratio. All of these relationships were more prominent in women than men. The negative association with the amount of table fat was statistically significant for women only. A more detailed analysis of this relationship revealed that subjects who used most table fat had a somewhat higher BMI than subjects who indicated their use in the next lower consumption category (9 g). The major difference in BMI (corresponding to approximately 2 kg) was

Table 2. Body mass index regressed on food and life style habits. Unstandardized (B) and standardized regression coefficients (B_{st}): 6664 men and 6314 women

	Men		Women	
Mean of BMI (SD)	24.24 (2.81)		22.49 (3.21)	
Adjusted R^2	0.133		0.147	
	B	B_{st}	B	B_{st}
Age group	0.31	0.20[a]	0.48	0.23[a]
Daily cigarette consumption	−0.02	−0.06[a]	−0.03	−0.06[a]
Leisure physical activity	−0.15	−0.04[a]	−0.14	−0.03[b]
Work time physical activity	0.14	0.05[a]	0.34	0.07[a]
Use of beer	−0.28	−0.10[a]	−0.14	−0.03[b]
Use of wine	−0.13	−0.03[b]	−0.41	−0.09[a]
Use of spirits	0.23	0.07[a]	−0.04	−0.01
Slices of bread	−0.93	−0.18[a]	−0.81	−0.09[a]
Use of low fat milk	0.82	0.13[a]	1.12	0.17[a]
Glasses of milk	0.09	0.03[c]	−0.15	−0.04[b]
Coffee drinking	0.26	0.07[a]	0.33	0.08[a]
Use of fish	0.22	0.05[a]	0.10	0.02
Use of ground meat	0.09	0.03[b]	0.13	0.04[a]
Type of table fat	0.20	0.03[b]	0.33	0.05[a]
Amount of table fat	−0.07	−0.02	−0.26	−0.07[a]
Use of fruits and vegetables	−0.02	−0.01	−0.18	−0.04[a]

[a]$p \leq 0.001$; [b]$p \leq 0.01$; [c]$p \leq 0.05$.

found between those who used table fat and those who did not.

The relationships between BMI and the alcoholic beverages were inconsistent. In men, a decrease in BMI with increasing beer and decreasing spirits consumption was seen. These associations were hardly significant in women. On the other hand, a relatively strong negative association between wine consumption and BMI was seen in women, the body weight of women who drank wine more than once a week was approximately 2.5 kg lower than that of women who never drank wine or drank wine only a few times a year.

In order to assure that the observed relationships were not only due to weight reducing activity among the most obese, we excluded in a separate set of analyses the individuals with BMI in the highest quartile. This exclusion did not change the main findings described above. However, for nearly all variables, the regression coefficients were reduced compared to the analysis with all men and women, but there were only four exceptions to the rule that the sign of the regression coefficients was the same. In contrast to the results for the entire population, in the lower-BMI-population the association between BMI and leisure physical activity was found to be positive in both sexes (more physical activity in leisure time, higher BMI). Furthermore, in women, a positive association was found between BMI and use of spirits, making this relationship in line with the results for men. In men, a non-significant negative association between BMI and use of fruits and vegetables was changed to a non-significant positive one.

Furthermore, we investigated the relationships between the food items and BMI in different subgroups of the population. The different strata were for each sex: BMI quartile (I, II + III, IV) age (< 40 vs $\geqslant 40$ years), years of education ($\leqslant 7$, 8–12, $\geqslant 13$) leisure physical activity (sedate or some activity vs take part in some sort of sport) and smoking habits (no smoker, smoker). For the variables which contributed highly significantly ($p \leqslant 0.001$) to the regression for both sexes (slices of bread, use of low-fat milk and coffee consumption), the sign of the associations was unchanged in 23 of 24 analyses. For variables which were associated ($p \leqslant 0.001$) with BMI in only one of the sexes, no major discrepancies were observed for the sign of the regression coefficients. The most interesting difference was the positive association in women between BMI and amount of table fat used at each slice of bread in the highest BMI quartile. However, none of the associations which were in contrast to the findings for all subjects were statistically significant ($p > 0.60$).

DISCUSSION

Individuals who are overweight must have, or at least have had, a higher energy intake than energy expenditure. The negative association between energy intake and BMI observed in several studies [4–8], should therefore have a correlate in lower energy expenditures among the obese. However, there are indications that this is not the case. In a recent publication, Prentice *et al.* using a doubly labeled water ($^2H_2{}^{18}O$) method, showed that obese women have a higher energy expenditure, both because of higher basal metabolism and higher physical activity, than lean women [13]. Furthermore, the positive association between per cent of the body weight as fat, at given fat free mass, and resting metabolic rate described by Garrow and Webster [14] among women, does not support the hypothesis that obese individuals have a particularily low resting metabolic rate. A positive association between reported physical activity and measures of obesity was also seen in one cross-sectional study [8].

In the present study, adjustments were done, albeit in a crude manner, for physical activity in work and leisure. When excluding the individuals with BMI in the highest quartile, a positive association was seen between BMI and both of these indices of physical activity, suggesting that in subjects with low or normal BMI, subjects with higher BMI also have higher physical activity.

It was not possible to compute the energy intake or expenditures of each individual in this study, and epidemiogical studies using frequency questionnaires are probably not the most appropriate way to elaborate all aspects of the obviously complicated physiological and psychological mechanisms behind obesity. However, frequency questionnaires may give information about items which are indicators of high fat or energy intake. This was confirmed in a subgroup of the men in this population where high energy intake was found to be positively associated with the number of slices of bread, the use of whole fat milk, the amount of milk per day, and the amount of table fat on each

slice of bread (unpublished observations). Acknowledging the limitations of food frequency questionnaires, particularly short ones as used in this study, this confirms our belief that frequency questionnaires may be used to describe associations between certain food items and risk factors of disease and morbidity.

High BMI is mainly due to increased fatness [15], even if increased muscle mass may influence the relative body weight, as suggested by the positive association between heavy manual work and BMI.

The seemingly inconsistencies observed in this study with high BMI associated with low-fat-milk and low bread intake may be due to methodological difficulties. The main methodological flaw would be the validity of the information on food habits, particularly if subjects with increased BMI tended to underestimate their food intake, both with regard to quality (i.e. type of food) and quantity. It can not be excluded that overweight subjects underestimate their energy intake [13, 16] and that slim subjects may overestimate their intake. However, the results of the analyses for the different parts of the population are quite consistent, supporting the view that the conclusions presented here are not due to methodological difficulties because of particular habits in the obese, less educated, young, sedate or non-smoking part of the population.

The results may also reflect the problems of describing associations in cross-sectional studies where the interviewees are aware of the possible relationship between the dependent and the explanatory variables, and therefore change their habits. The awareness of the relationship between nutritional content and BMI which is apparent from the increasing number of organized slimming activities in the population must explain some of the findings such as the higher BMI among those preferring skimmed milk and the negative association between the amount of table fat and BMI in women. However, although not all of these regression coefficients were statistically significant, the signs of the coefficients were the same in the quartile of the subjects with the lowest BMI (BMI $\leqslant 22.3$ for men and $\leqslant 20.4$ for women) as in the analyses for all subjects, indicating that the associations are not solely a result of changed food habits among the overweight. Even among men and women with rather low body weight (< 71 kg for a 1.77 tall man and < 55 kg for a 1.64 tall woman), we find indications of weight reducing food habits.

This observation, that subjects who consider themselves to be somewhat overweight have taken measures to reduce the weight, is supported by some other studies. Ohlson and Harper [6] noted in their longitudinal study that the mean energy intake among women was reduced with advancing age from 25 years of age to mid-fifties, and that this reduction in energy intake was partly due to reduced servings of bread and potatoes per day, increased use of low-fat milk and decrease in the amount of fat used in the household. Prentice *et al.* [13] found that the energy expenditure of lean subjects was near identical with the self-reported energy intake, whereas the self-reported energy intake of obese women was 33% lower than the energy expenditure, attributing some of this difference to dieting. Baecke *et al.* [4] noted a negative association between the percentage of the body weight as fat (%BF) and use of fruits and vegetables for men and consumption of fats and sugar-rich products for women. This is similar to our findings, although we do not have any information about intake of sugar. Also Richardson [17] observed an inverse relationship between sugar intake and relative weight. Keen *et al.* [7] found, after adjusting for age, negative associations between the BMI and the intake of protein, carbohydrate, fat and sucrose. The relationships did not, however, achieve statistical significance in all subgroups.

In men (and in women when the women with BMI in the highest quartile were excluded) a positive association was seen between use of spirits and BMI, whereas negative correlations were most strongly seen for beer (in men) and wine (in women). The negative associations may illustrate the same effect of reduced energy intake (here alcohol) because of increased body weight. On the other hand, some studies do indicate that energy from alcohol is utilized less efficiently than energy from other energy sources [18, 19], i.e. substitution of other calories by alcohol may result in weight loss. Similar to the results from this study, a negative association between alcohol consumption and BMI was also seen in men in the HANES I study [20] and Jones *et al.* [21] found that although drinkers had higher energy intake, they were less obese than non-drinkers. Kromhout [5], in contrast to these findings, reported that men in the highest quartile of body weight consumed significantly more alcohol that men in the lowest quartile.

If the main explanation to the findings

reported here is that the individuals respond to increase in body weight by changing the diet in order to reduce the energy intake, this underlines the need for adjusting for BMI when associations between food habits and other variables also related to BMI (e.g. blood lipids) are investigated. For instance, due to the well known positive association between BMI and serum total cholesterol [1, 2], given no association between serum total cholesterol and e.g. bread consumption, a negative association would be found if the analysis is not adjusted for BMI.

In summary, the present study suggests that most people in this population try to keep the body weight within limits they consider to be normal. This may be part of the explanation for the lack of positive association found between energy intake and BMI in several studies, and emphasize the need for adjustment for BMI when associations between food habits (and alcohol) and other variables associated with BMI are investigated.

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APPENDIX PAPER V

Acta Med Scand 1987; 222: 215–21

The Tromsø Heart Study: Is Coffee Drinking an Indicator of a Life Style with High Risk for Ischemic Heart Disease?

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ABSTRACT. Jacobsen BK, Thelle DS (Institute of Community Medicine, University of Tromsø, Tromsø, Norway). The Tromsø Heart Study: Is coffee drinking an indicator of a life style with high risk for ischemic heart disease? Acta Med Scand 1987; 222: 215–21.

Associations between coffee drinking, use of table fat with low contents of polyunsaturated fatty acids, preference for low-fat milk, use of fruits and vegetables, smoking and lack of physical activity in leisure time have been described in a cross-sectional study of 14 582 men and women. Coffee drinking was negatively related to the use of low-fat milk, use of table fat high in polyunsaturated fatty acids, use of fruits and vegetables, and positively associated with bread consumption. Three persons out of four with high coffee consumption (>8 cups/day) were daily smokers, in contrast to about a quarter of those with low coffee consumption (<1 cup/day). In women and young men, high coffee consumption was associated with low physical activity at leisure. The results suggest that high coffee consumption may be an indicator of a life style with high risk for coronary heart disease. *Key words: cigarette smoking, coffee, food habits, ischemic heart disease, physical activity.*

Although the mortality rates from ischemic heart disease (IHD) has been decreasing in Norway and some other Western countries over the last decade, it is still the major cause of death (1). With the increasing interest in individually oriented preventive actions (2, 3), the general practitioners' responsibility will be to identify subjects with a life style which may increase the risk of contracting IHD. High-risk identification implies the simultaneous assessment of a number of risk factors, even if more simplified methods have recently been suggested (4).

It may be, however, that even simpler questions about some particular habits, without going into a too detailed history, will reveal an atherogenic life style. Studies both from Norway (5) and elsewhere (6, 7) suggest that coffee consumption is associated with a diet high in fat and with a high proportion of the energy from fat. Whether coffee drinking per se increases the serum cholesterol is still a subject for debate (8). The association found in this population (9) is strong, and experiments give increasing evidence for a causal relationship between, at least, boiled coffee and increased serum cholesterol (10–12). One may, therefore, envisage at least three different mechanisms for the relationship between coffee drinking and total cholesterol; one as a direct effect on cholesterol metabolism (13), a second via other components of the diet (e.g. fat), and a third by interactions between coffee and other parts of the diet.

We have previously shown that the association between coffee consumption and total serum cholesterol found in this population (9) cannot be explained by associations between coffee consumption and other food habits (14). In this paper, we concentrate on the second of the three possible mechanisms for the coffee–serum cholesterol relationship outlined above, and discuss relationships between coffee consumption and some food habits associated with elevated total serum cholesterol in the Tromsø Heart Study (14) as well as cigarette smoking and low physical activity in leisure time.

Abbreviations: IHD = ischemic heart disease, P/S-ratio = ratio between intake of polyunsaturated fatty acids and saturated fatty acids.

Table I. *Distribution (%) of coffee consumption according to sex and age in the Tromsø Heart Study, 7 368 men, aged 20–54 years, and 7 213 women, aged 20–49 years*[a]

Age group	Men					Women				
		Cups of coffee/day					Cups of coffee/day			
	n	<1	1–4	5–8	>8	*n*	<1	1–4	5–8	>8
20–24	843	17.2	37.7	33.3	11.7	1 226	14.4	46.6	30.4	8.6
25–29	1 284	8.4	35.6	39.6	16.4	1 535	9.1	45.5	37.9	7.5
30–34	1 503	6.2	31.5	45.8	16.5	1 588	6.7	39.4	42.5	11.5
35–39	1 240	5.6	30.2	46.1	18.1	1 211	5.6	39.1	43.8	11.5
40–44	891	5.7	30.9	47.3	16.2	887	4.2	43.4	43.6	8.8
45–49	805	3.4	30.6	49.2	16.9	766	4.3	42.4	44.1	9.1
50–54	802	2.1	31.3	52.0	14.6	–	–	–	–	–
20–49	6 566	7.5	32.7	43.7	16.6	7 213	7.8	42.7	40.0	9.6
20–54	7 368	6.9	32.5	44.6	16.0	–	–	–	–	–

[a] The only female examined in the age-group 50–54 years is excluded in this table.

STUDY POPULATION AND METHODS

In 1979–80, 21 329 subjects were invited to take part in a health survey in the municipality of Tromsø. This included all men born between 1925 and 1959 and all women born between 1930 and 1959 registered in the municipality. 16 621 (78%) attended the screening. The examination comprised the administration of a questionnaire concerning previous diseases, symptoms possibly caused by atherosclerotic diseases, living habits (including physical activity in leisure time and smoking habits) as well as measurements of blood pressure, weight and height and a venous non-fasting blood sample for lipid and glucose analyses. This study was to a large extent a replication of the first Tromsø Heart Study in 1974 and the methods and details have been described in a previous paper (15).

A second questionnaire concerning questions on food habits, previous diseases and social and psychological conditions was given to those who attended the screening. It was filled in at home and returned by mail. 7 410 men and 7 257 women returned the questionnaire, but some individuals did not answer all questions. The nutritional part of the questionnaire covered questions about kind and quantity of bread normally used, type and quantity of table fat and milk, coffee drinking, alcohol habits and the use of fish and minced meat as well as fruits and vegetables. These food items had been selected as they provide information about some of the most important contributors of the intake of fat and energy. Coffee constitutes a major beverage in the Norwegian population, whereas alcohol consumption in general is relatively low. A number of dietary items, e.g. poultry and ice cream, were omitted from the

Table II. *Mean, age-adjusted percentage of the population who select low-fat milk, soft (high PUFA) margarine, >6 slices of bread/day and daily use of fruits and vegetables according to coffee drinking, Tromsø Heart Study, 1979–80*

Cups of coffee	Low fat milk				Soft margarine				>6 slices of bread/day			
	Men		Women		Men		Women		Men		Women	
	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*	%	*n*
<1	32.8	507	41.8	557	75.5	484	79.1	533	39.7	503	4.4	555
1–4	31.3	2 378	41.0	3 062	77.1	2 320	78.0	2 967	34.0	2 369	3.8	3 058
5–8	24.9	3 264	37.5	2 876	74.6	3 189	75.9	2 778	37.8	3 262	4.4	2 872
>8	19.9	1 172	31.3	686	69.0	1 146	70.5	650	42.4	1 165	7.0	687
p-value for linear trend	<0.001		<0.001		0.002		<0.001		0.13		0.02	

frequency questionnaire because they are not important parts of the daily diet in this population. The information about food habits collected in this study is too sparse for computing the energy or fat intake of each individual.

English translation of relevant parts of the questionnaire and information about the validity of the food consumption data assessed by comparison with data from a dietary history survey conducted 1–2 years after the screening in 528 men are given elsewhere (16).

One-way analyses of (co)variance were performed for each sex separately with the BMDP1V program (17). The analyses were done with the life style variables as the dependent variables, coffee as the grouping variable (and 5-year age groups as the covariate when age adjustment was performed). Differences between the coffee categories were tested for linear trend by using contrasts (-3, -1, 1, 3) between means of coffee consumption categories.

RESULTS

Table I shows the distribution of the coffee drinking habits according to age and sex in the Tromsø Heart Study. Men drank more coffee than women. Subjects in the youngest age group drank less coffee than the older subjects, but there was a reduced coffee consumption over the age of 40, especially in women. Table II demonstrates the relationships between coffee consumption and some food habits. Of the men who drank <1 cup of coffee per day, 33% used low-fat milk, in contrast to the 20% of men who drank >8 cups of coffee daily ($p<0.001$). The corresponding figures for women were 42 and 31%, respectively ($p<0.001$). A weaker gradient was found for use of table fat with high P/S-ratio. Of men with low coffee consumption, 76% used such table fat vs. 69% in men with high coffee consumption ($p=0.006$). In women, the corresponding figures were 79 and 71% ($p<0.001$). Bread and coffee consumption were positively associated. The p-values for linear trend were, however, less impressing ($p=0.13$ for men and $p=0.02$ for women). Coffee consumption and the use of fruits and vegetables were negatively associated, the frequency of daily users of fruits and vegetables in subjects with high coffee consumption was less than three quarters of that of subjects with low coffee consumption (p-value for linear trend <0.001).

Table III gives the associations between the proportion of the population who exercises to keep fit ≥4 hours/week and coffee consumption in different age groups. In women and relatively young men (<50 years old), high coffee consumption was associated with low physical activity. The opposite tendency, although not statistically significant, was observed in men in the 50–54-year age bracket.

The associations between coffee drinking and smoking are displayed in Table IV. Of those who drank >8 cups of coffee/day, 75% were daily smokers, whereas 20–25% of the indi-

Fruits and vegetables daily			
Men		Women	
%	*n*	%	*n*
52.1	510	73.8	560
47.5	2 386	68.8	3 077
40.5	3 279	63.7	2 883
38.1	1 179	52.7	689
<0.001		<0.001	

viduals who drank <1 cup were smokers. Among cigarette smokers, high coffee consumption was associated with a higher cigarette consumption. Smokers with very low coffee consumption tended to smoke somewhat more than smokers who drank 1–4 cups of coffee per day.

Table V gives the proportion of the subjects who do not smoke and have a low total serum cholesterol level (≤5.2 mmol/l or 200 mg/100 ml) according to the coffee consumption. While it is relatively rare (<1/12) to find such a person among subjects with high coffee consumption, more than one out of three of those who drink <1 cup of coffee/day fulfill both of these criteria.

DISCUSSION

Decaffeinated coffee is rarely used in Norway, and boiled coffee is the predominant type of coffee consumed in Tromsø. In northern Norway four out of five drink the coffee black (9). The relations described are therefore mainly with black, boiled coffee.

It may be concluded from the present analyses that knowledge of coffee consumption provides indirect information on each individual's atherogenic risk. Table V demonstrates clearly that in this population it is not very likely that a subject with high coffee consumption has total serum cholesterol as low as that recommended in a recent concensus report (3) and at the same time is a non-smoker. In this context, it is not of major importance whether or not coffee drinking itself is associated with increased risk for IHD (18–21). The reasons for the results displayed in Table V are the strong association between coffee consumption and total serum cholesterol in this population (9–11), even after adjustment for other food habits (14), the relationships between food habits associated with both high total serum cholesterol (14) and coffee consumption, and the association between smoking and coffee consumption.

A bias may have been introduced in this study as the subject already known to have IHD or other disease might have reduced the coffee consumption because of illness or because of doctor's advice (19, 20, 22). The study was, however, conducted in a relatively young popu-

Table III. *Mean percentage of the population who exercises ≥4 hours/week, Tromsø Heart Study, 1979–80*[a]

Age group	Cups of coffee/day <1 %	<1 *n*	1–4 %	1–4 *n*	5–8 %	5–8 *n*	>8 %	>8 *n*	*p*-value for linear trend
Men									
20–29	46.8	252	44.5	773	37.5	789	29.7	310	<0.001
30–39	43.8	162	39.6	848	35.3	1 259	25.2	469	<0.001
40–49	33.3	78	29.4	520	28.3	816	28.0	279	0.33
50–54	17.6	17	25.5	251	22.5	417	28.2	117	0.40
20–54	42.8	509	37.5	2 392	32.5	3 281	27.3	1 175	<0.001
Women									
20–29	14.3	315	12.4	1 269	10.0	952	9.5	220	0.05
30–39	16.1	174	15.5	1 095	13.4	1 206	12.8	321	0.23
40–49	17.1	70	13.2	710	12.3	724	8.1	148	0.05
20–49	15.2	559	13.7	3 074	12.0	2 882	10.7	689	0.009

[a] The only female examined in the age-group 50–54 years is excluded in this table.

lation, and except for the oldest age group, disease-related in coffee consumption would be unlikely to play an important role.

Solvoll and Løken (5) have evaluated the relationships between coffee drinking and different food habits in another Norwegian population comprising 13 214 men and women. They confirmed that individuals with high coffee consumption tended to have high bread consumption, use butter or hard margarine, butter the slice of bread lavishly and prefer whole-fat milk.

Although the interrelationships between coffee drinking and food habits may be culture-dependent to a great extent, coffee consumption is common in many countries and it may be worthwhile to look for such relationships at least in countries with similar food habits as the Norwegian. Studies from California (6, 7), a state which in most respects is quite different from the Tromsø community at 70° latitude North, suggest that some of the relationships observed here may be present also in other parts of the world. In men, Haffner and co-workers (6) found positive associations between coffee drinking and percentage of energy from fat, saturated fat and the cholesterol intake and a negative association with the P/S-ratio. In women, no significant associations were observed. Mathias and co-workers (7) reported negative associations between regular coffee consumption and the P/S-ratio of the diet.

A negative relationship between the proportion of the population who exercises and coffee consumption was observed by Mathias and co-workers in men, but not in women (7). The

Table IV. *Mean age-adjusted percentage of the population who smoke and mean cigarette consumption in cigarette smokers according to coffee consumption, Tromsø Heart Study, 1979–80*

	Smokers				Mean no. of cigarettes			
	Men		Women		Men		Women	
Cups of coffee	%	*n*	%	*n*	%	*n*	%	*n*
<1	25.0	509	20.9	559	13.1	117	10.8	135
1–4	34.8	2 394	34.3	3 077	12.5	786	9.5	1 064
5–8	54.0	3 284	56.8	2 885	14.4	1 714	11.4	1 612
>8	75.2	1 179	76.5	689	17.1	860	13.9	523
p-value for linear trend	<0.001		<0.001		<0.001		<0.001	

Table V. *Mean age-adjusted percentage of the population who do not smoke and have total serum cholesterol ≤5.2 mmol/l according to coffee consumption, Tromsø Heart Study, 1979–80*

	Non-smokers and low serum cholesterol			
	Men		Women	
Cups of coffee	%	*n*	%	*n*
<1	34.3	509	41.0	559
1–4	21.6	2 392	26.2	3 073
5–8	12.5	3 283	14.5	2 879
>8	5.3	1 177	7.8	689
p-value for linear trend	<0.001		<0.001	

association seen in this study was weak or absent in men over 39 years of age. The reason for this effect of age, which was not observed in women, may be that young men select physical activity as a part of a life style (in which low coffee consumption is another part), whereas in older men the level of physical activity is generally lower.

The positive association between coffee drinking and smoking is well known (20, 23, 24). The somewhat higher cigarette consumption level in smokers who do not drink coffee or drink less than one cup per day compared to those who drink 1–4 cups per day may be due to some individuals with somatic symptoms having stopped drinking coffee but continued smoking.

In conclusion, in this population of relatively young individuals with high coffee consumption, coffee drinking seems to be related to food-, leisure physical activity-, and smoking habits which are associated with elevated risk for IHD. Coffee drinking may therefore indicate an unhealthy life style. Similar relationships have been reported in other studies, and it is likely that the described associations are not unique for this population. Of course, we do not suggest that one question about coffee consumption can be a substitute for a more thorough interview, only that coffee consumption may be one of the questions to be included in this interview.

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APPENDIX PAPER VI

THE TROMSØ HEART STUDY: RISK FACTORS FOR CORONARY HEART DISEASE AND LENGTH OF EDUCATION.

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Abbreviation: HDL cholesterol, high density lipoprotein cholesterol.

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ABSTRACT

Jacobsen, B.K. (Institute of Community Medicine, University of Tromsø, 9001 Tromsø, Norway) and D.S. Thelle. The Tromsø Heart Study: risk factors for coronary heart disease and length of education. Am J Epidemiol 1988; 000; 000-00.

The relationships between length of education, life style variables and major risk factors for coronary heart disease were analyzed in 12,368 men and women in Tromsø, Norway. Subjects with the longest education tended to be less overweight, smoke less, be more physical active in leisure time and have food habits assumed to be less atherogenic (i.e. drink less coffee, use soft margarine and low fat milk and eat fruits and vegetables daily) than individuals with low education. Mean total serum cholesterol and systolic blood pressure were negatively, and high density lipoprotein (HDL) cholesterol in women positively, associated with educational level. The difference between the extreme groups of education (< 8 and > 16 years of education) was for total serum cholesterol 0.52 mmol/liter (20 mg/100 ml), for HDL-cholesterol 0.03 and 0.14 mmol/liter (1 and 5 mg/100 ml) in men and women, respectively, and for systolic blood pressure 1.9 and 5.6 mmHg in men and women, respectively. Adjustment of the relationships between length of education and total serum cholesterol and systolic blood pressure for several variables (including food habits) reduced the strength of the associations, which, however, were still statistically significant. For HDL cholesterol, a negative association was found in men when adjustments were done, and the positive association originally observed in women disappeared.

Key words: education, cholesterol, HDL cholesterol, blood pressure, food habits, physical activity, smoking,

Chronic disorders have always been more frequent in the poorer groups of the society, and the influence of social class as a determinant of disease was pointed out already by Rudolf Virchow in the last century. Coronary heart disease on the other hand gained reputation for being the better offs higher risk, as Sir William Osler noted in the Lancet in 1910, although the evidence for this may have been scarce (1).

This social gradient now seems to have diminished and may in some countries even be reversed (2-5). The reason for the lower coronary heart disease risk in the higher social classes remains obscure, but it is probable that changes towards a less coronary heart disease prone life style have to greater extent taken place in these classes.

High level of education is an indicator of high social class, and is associated with reduced cardiovascular morbidity in some studies (6-9). Marmot and coworkers (4) have shown that only parts of the difference in mortality between British civil servants with different grade of employment can be explained by a higher level of hypertension and cigarette smoking in subjects with the lowest level of education. Similar results have been reported from the Oslo Study (3). Liu and coworkers (8), on the other hand, found that the negative association between coronary heart disease mortality and level of education was not statistically significant when adjusted for blood pressure, serum cholesterol, smoking, relative weight and electrocardiogram abnormalities.

The present paper addresses the problem from a cross-sectional point of view, and describes how educational level is associated with risk factor levels and to what extent the observed differences in coronary risk factors can be explained by cigarette smoking, physical activity in leisure time, body mass index and the consumption of some specific food items.

MATERIAL AND METHODS

In 1979-1980, 21,329 subjects were invited to take part in a health survey in the municipality of Tromsø. This included all men born between 1925 and 1959 and all women born between 1930 and 1959 registered in the municipality. 16,621 (78 %) attended the screening. The examination comprised the administration of a questionnaire concerning previous diseases, symptoms possibly caused by atherosclerotic diseases, living habits (including physical activity in leisure time and smoking habits) as well as measurements of blood pressure, weight and height and a venous nonfasting blood sample for lipid and glucose analyses. This study was to a large extent a replication of the first Tromsø Heart Study in 1974, and the methods and details have been described in a previous paper (10).

Total serum cholesterol was measured directly by the enzymatic oxidase method, using a commercial kit (Boehringer 148393, Boehringer-Mannheim, Federal Republic of Germany). HDL cholesterol was assayed by the same procedure after precipitation of lower-density lipoprotein with heparin and manganese chloride. All laboratory

assessments were performed by the Division of Clinical Chemistry, University Teaching Hospital of Tromsø.

The blood pressure was read to the nearest even number of mmHg and measured twice with one minute interval with a mercury sphygmomanometer at the right upper arm with the subject in a sitting position. The lowest readings were recorded. The systolic blood pressure was measured when the first Korotkoff sound appeared (phase 1). The diastolic blood pressure was defined as the pressure at the disappearance phase of the Korotkoff sound (phase 5). If there was no phase 5, the pressure at phase 4 was recorded. The personell was trained according to the same program based on tape-recorded blood pressure sounds produced by London School of Hygiene and Tropical Medicine.

A second questionnaire concerning questions on food habits, previous diseases and social and psychological conditions (including the question: "How many years of education do you have?") was given to those who attended the screening. It was filled in at home and returned by mail. The question about length of education was answered by 14,426 men and women, but some individuals did not answer some of the other questions. The nutritional part of the questionnaire covered questions about kind and quantity of bread normally used, type and quantity of table fat and milk, coffee drinking, alcohol habits and the use of fish, minced meat as well as fruits and vegetables. English translation of relevant parts of the questionnaire is given elsewhere (11). These food items had been selected as they provide information about some of the most important contri-

butors of the intake of fat and energy. Coffee constitutes a major beverage in the Norwegian population, whereas alcohol consumption in general is relatively low. A number of dietary items, e.g. poultry and ice cream, were omitted from the frequency questionnaire because they are not important parts of the daily diet in this population. The information about the food habits collected in this study is too sparse for computing the energy or fat intake of each individual.

The validity of the data on dietary habits has been assessed in a subgroup of 528 men, 30-54 years old at screening. The data in the questionnaire were compared with data from a dietary history survey conducted 1-2 years after the screening. High concordance was found between the two methods for questions concerning types of foods most commonly used. For food items used every day in easily recalled units, and for the questions about use of alcohol, the concordance between the two dietary survey methods was quite good (Kendall's tau $\geq$ 0.50). For other food items, the concordance was less satisfactory, although statistically highly significant (Kendall's tau $\geq$ 0.25) (11).

In the questionnaire, physical activity in leisure time had been graded I to IV according to the following categories which best described his or her physical activity in leisure time: I: Reading, watching television, or some other sedentary past time, II: Walking, cycling, or some other form of physical activity for at least 4 hours per week, III: Exercises to keep fit, heavy gardening, etc. for at least 4 hours a week, IV: Hard training or participation in competetive sports, regularly and several times a week. In the analyses,

physical activity in leisure was dichotomized, combining code I and II into level 0, and code III and IV into level 1.

In most of the analyses, including all presented in the tables, the number of years of education was recoded into five education level groups, < 8, 8-10, 11-12, 13-16, and > 16 years at school. In the youngest age group examined at the screening, 20-24 years old, it was only possible for some individuals to have > 16 years of education, and we therefore excluded these men and women from the analyses, ending up with 6,440 men and 5,928 women. One woman, in the 50-54 year group, met without invitation. She is excluded in the present analyses. Because not all subjects answered all questions posed in the questionnaire, the number of individuals included change from one analysis to the next, e.g. in table 2 between 6,251 men and 5,727 women for information about use of soft margarine to 6,439 men and 5,924 women for information about smoking. In the multivariate analyses displayed in table 3-5, only subjects who gave information about all the variables included in the analyses are included.

Statistical analyses were done by SPSS (12). The associations between years of education and the different dependent variables were analysed by analysis of variance and tested for linear trend. Adjustment of the relationships between risk factors for coronary heart disease and years of education for age (five-year age groups), body mass index (kg/m^2), smoking habits, physical activity in leisure and food habits (including the frequency of alcohol consumption for analyses of HDL cholesterol and blood pressure) was done by analysis

of covariance (multiple classification analysis). In this type of analysis, the dependent variable can be continuous (e.g. serum cholesterol) or dichotomous (e.g. daily cigarette smoker) (13) and the independent variables are discrete variables (e.g. years of education coded into five groups), called factors, or covariates for which a linear scale is assumed.

RESULTS

Table 1 gives the relationships between level of education, sex and age. The younger part of the population had the longest education with 43.6 per cent of the men and 36.8 per cent of the women in the 25-29 age bracket having more than 12 years of education, whereas the corresponding figures for men and women aged 45-49 years were 14.9 and 10.1 per cent. There were more men than women who had longer education in all age groups.

Subjects with the longest education had lower mean body mass index. The difference in body mass index corresponded to approximately three kgs. difference in body weight between the extreme categories of education (Table 2). The associations between smoking, use of low fat milk and daily use of fruits and vegetables on one hand, and low education on the other were particularly impressive with more than twice as many daily smokers (61 vs. 27 per cent in men and 55 vs. 21 per cent in women) and less than half the frequency of users of low fat milk (17-26 per cent vs. 48-54 per cent) and daily use of fruits and vegetables (27-43 per cent vs. 68-88 per cent) in subjects with

only elementary school compared to those with more than 16 years education. Strong, statistically highly significant positive associations were also found between length of education and high physical activity in leisure (particularly in women) and low coffee consumption. Subjects with long education tend to use soft margarine (in contrast to butter or margarine with low ratio between the amount of polyunsaturated and saturated fatty acids) as table fat.

The associations between length of education, total serum cholesterol, HDL cholesterol, systolic and diastolic blood pressure were evaluated in the three age groups 25-34 years, 35-44 years and 45-54 (in women, 49) years. A negative relationship between educational level and total serum cholesterol was found for both sexes and in all three age groups, although not statistically significant for the oldest women. The difference between the extreme educational categories ranged from 0.34 to 0.79 mmol/liter (13 to 31 mg/100 ml) in men and 0.10 to 0.76 mmol/liter (4 to 29 mg/100 ml) in women. The age-adjusted figures are given in table 3.

When adjustments of the relationship between education and total serum cholesterol was done by first including body mass index, cigarette consumption and physical activity in leisure, and finally a number of dietary variables, the difference in serum total cholesterol was reduced, from 0.52 to 0.24, and 0.52 to 0.27 mmol/liter in men and women, (20 to 9, and 20 to 10 mg/100 ml) respectively. This corresponds to an approximate reduction of 50 percent. The association was, however, still statistically significant (table 3).

A positive association was found between length of education and HDL cholesterol in women, but not in men. The difference between the extreme education groups was approximately 0.14 mmol/liter (5 mg/100 ml) for women in all age groups, the p-value for linear trend was, however, not statistically significant in women 45-49 years at the examination. Table 4 shows the age-adjusted figures.

After first adjusting for age, body mass index, smoking and leisure physical activity, thereafter adding the frequency of alcohol consumption, type of table fat and use of fruits and vegetables, the association in women was not longer statistically significant, whereas in men a statistically significant negative association was found between HDL cholesterol and education with a 0.12 mmol/liter (5 mg/100 ml) lower HDL cholesterol concentration in men with > 16 years of education compared with men with less than eight ($p < 0.001$).

Systolic blood pressure was negatively related to level of education, this was particularly true in women where the difference in blood pressure between women in the extreme categories for education was 3.5 to 7.5 mmHg. The corresponding figures for men were 1.7 to 2.4 mmHg. The negative association between length of education and systolic blood pressure was statistically significant ($p < 0.05$) in all the six age-sex groups except for the oldest men. Diastolic blood pressure was unrelated to the length of education in men and negatively related in women, the difference between the extreme categories for education was 1.3 to 3.1 mmHg.

Table 5 shows the association between length of education and systolic blood pressure, first the age-adjusted association, then adjusted for body mass index and life style variables. The association was stronger and more consistent in women. A modest reduction of the difference was observed after the adjustment, implying that the independent variables only played a minor role in determining the blood pressure differences between the groups with different length of education. Adjustment for alcohol habits and bread consumption (bread consumption is strongly positively associated with systolic blood pressure in men in this cohort, data not shown) did not change these conclusions.

In men, there was no significant association between length of education and diastolic blood pressure, whereas women with < 8 years of education had 1.8 mmHg higher age-adjusted diastolic blood pressure than women with > 16 years of education. This difference was reduced to 1.6 mmHg, when adjusted for body mass index, physical activity in leisure, cigarette smoking, and frequency of alcohol consumption (data not shown).

DISCUSSION

Length of education is to some extent a marker of sosioeconomic status. Obviously, a subject's social class is determined by additional factors such as family background, income and occupation. Abramson and coworkers (14) found that associations between health and social class is not insensitive to the measure used, e.g.

education, occupation, income or household crowding. However, they conclude that if a single measure is used (as in this study), one of the major indicators is as good as the other.

In a cross-sectional study like the present, the problem of selection bias may be important. The negative association between length of education and total serum cholesterol and blood pressure could emerge if the subjects who did not give information about education (or did not attend the screening at all) had both low risk factors and low level of education. We do not find this likely as subjects who attended the screening, but did not return the questionnaire, had the same total serum cholesterol and systolic blood pressure and, in men, somewhat higher diastolic blood pressure than subjects who returned the questionnaire (unpublished observations). In addition, follow-up of non-responders to the first Tromsø Heart Study in 1974 did not show lower mortality from coronary heart disease than in men who met at the screening (15), suggesting at least not lower total serum cholesterol level in men who did not attend the screening.

Any difference in disease risk or risk factor levels between subjects with different educational background may be due to selection of low risk subjects to higher education, or that being exposed to longer education actually has an effect by itself. If the latter were true, one might argue that either the content of the curriculum had a health promoting effect, or that the intellectual training involved makes people more sensitive to the kind of health education message to which they have been exposed as adults. There is

a correlation between length of education and income, and it may also be that higher income makes it easier to choose a healthier life style. However, education seems to be more important than income in predicting both total mortality (3) and risk of coronary heart disease (3,7).

The striking age-related differences seen in table 1 with the younger subjects having experienced considerably more formal teaching than the older generation reflect an educational shift in Norway toward longer education. There is no doubt that higher education used to be a privilege for the better off classes in this society, and this is still true to some extent (16). It is therefore possible that the difference in risk factor level and lifestyle partly is familial, i.e., those with high education are offspring of healthy parents with high education who teach their children healthy lifestyles. If subjects who have parents with high education have low levels of risk factors over and above what can be explained by the life style factors included in this study, it is likely that selection can explain a fraction of the observed differences. Another possible, but less probable, source of bias could emerge if subjects with high risk for coronary heart disease (reflected in high total serum cholesterol, hypertension and smoking) tend to select less education.

Table 2 demonstrates that there are significant relationships between educational level and life style and food habits. For some variables like smoking, coffee drinking, preference for low fat milk and frequency of use of fruits and vegetables the relationships are rather strong. This suggests that subjects with longest education

have habits generally believed to be associated with low risk for coronary heart disease. These results are not surprising and are particularly for physical activity- and smoking habits and body mass index in accordance with other studies (9,17-21). The reason for the emphasis put on food habits displayed in table 2 is that in this population we found that total serum cholesterol was related to coffee and bread consumption, type of table fat, and, in women, use of low fat milk and use of fruits and vegetables. HDL cholesterol was related to alcohol consumption, type of table fat and, in men, use of fruits and vegetables (22). The association between length of education and bread consumption was not linear, and not shown in table 2.

The inverse relationship between total serum cholesterol and educational level is in contrast to some studies from the USA (8,23,24) where essentially no association was found, and with the Whitehall study (4) and British Regional Heart Study (25), in which positive associations between total serum cholesterol and social class were noted, but in accordance with studies from Ireland (9) and the negative relationship found between socioeconomic status and serum cholesterol in the Oslo Study (26).

The lower blood pressure among the higher educated is in variance with results from Germany (27) and from the Framingham study (24), but in accordance with the results from 158,906 men and women in the Hypertension Detection and Follow-up Program (28), and some other studies (9,18). Such differences probably reflect the dynamic situation in the industrialized populations with ongoing changes both

with regard to treatment for hypertension, diet and other health related habits.

The present material provided the opportunity for assessing the influence of some life style variables on the observed differences. The differences in serum total cholesterol and blood pressure did not completely disappear when such adjustments were undertaken, not surprising as both the background variables and the blood lipids and blood pressure are subject to random error. In this study, only information about some selected parts of the diet is included, and obviously other factors, including dietary variables not examined (e.g. intake of salt), may be operating. Information about use of other food items and food habits such as addition of fats to the meals would have been helpful. In the analyses of HDL cholesterol, the positive association between HDL cholesterol and length of education found in women disappeared when adjustments were done, and in men a negative association was seen. The reasons for this are the differences in habits displayed in table 2 as well as the higher alcohol consumption in the subjects with long education in this population.

Studies which have assessed the relationship between length of education and coronary heart disease risk factors adjusted for life style are scarce. Dyer and coworkers, however, found that the relationship between education and hypertension in white subjects remained statistically significant after adjusting for relative weight and heart rate (18). Regarding HDL cholesterol, Heiss and

coworkers found that the positive association between educational and HDL cholesterol levels in the Lipid Research Clinics Program Prevalence Study partly could be explained by differences in body mass index, smoking-, and alcohol habits and, in women, by use of gonadal hormone use (29).

The present study suggests that there are, at least in this population, relatively strong relationships between level of education and risk factors for coronary heart disease, as well as life style. The results are in accordance with the lower risk for coronary heart disease noted in subjects with high social class in Norway (3,26). Some of the difference in blood lipids and blood pressure, particularly for total serum cholesterol, demonstrated in this study can be explained by the life style variables recorded. We believe that the results underline the need for particular efforts in order to change the unhealthy habits, and thereby the risk of coronary heart disease, of the less educated.

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TABLE 1

Per cent distribution of length of education in 6,440 men, aged 25-54, and 5,927 women, aged 25-49, according to age group. Tromsø 1979-1980 *

	Men						Women					
Age group	N	Length of education (yr)					N	Length of education (yr)				
		< 8	8-10	11-12	13-16	>16		< 8	8-10	11-12	13-16	>16
25-29	1278	5.6	30.3	20.5	26.5	17.1	1536	4.8	37.7	20.8	27.8	9.0
30-34	1483	10.2	32.0	19.0	21.8	17.0	1580	7.8	45.7	17.1	20.4	9.0
35-39	1229	16.9	32.5	16.4	18.8	15.3	1197	18.0	47.5	13.8	13.4	7.3
40-44	884	29.9	33.0	14.9	12.0	10.2	866	34.9	40.9	10.9	10.2	3.2
45-49	791	39.8	32.0	13.3	10.2	4.7	748	47.3	30.9	11.8	7.4	2.7
50-54	775	43.9	30.5	10.3	10.5	4.9	-	-	-	-	-	-
25-49	5665	17.8	31.9	17.4	19.1	13.9	5927	18.0	41.4	15.8	17.7	7.0
25-54	6440	20.9	31.7	16.5	18.0	12.8	-	-	-	-	-	-

* The only female examined in the age-group 50-54 years is excluded in this table.

TABLE 2

Age-adjusted associations between length of education and mean body mass index (BMI), daily smokers, physical activity in leisure time * and some food habits. Men aged 25-54 years, and women aged 25-49 years. Tromsø 1979-1980

Length of education (years)	B M I		% smokers		% who exercise		% who drink > 4 cups of coffee/day		% who use soft margarine		% who drink low fat milk		% who eat fruits or vegetables daily	
	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women	Men	Women
< 8	24.7	23.5	61	55	28	11	73	65	66	67	17	26	27	43
8-10	24.7	22.9	57	51	31	12	68	57	71	75	22	35	37	62
11-12	24.5	22.4	47	42	34	13	60	49	76	78	30	43	49	74
13-16	24.3	22.3	39	27	38	15	56	37	75	78	36	51	55	83
> 16	23.8	22.1	27	21	39	18	46	32	75	69	48	54	68	88

In all analyses p-value for main effect $\leq$ 0.001.

* Exercises four or more hours per week.

TABLE 3

Relationships between length of education and total cholesterol. Adjusted for age and life-style factors. 6,050 men, aged 25-54, and 5,509 women, aged 25-49. Tromsø 1979-1980

Length of education (years)	Total serum cholesterol							
	Men				Women			
	N	I	II	III	N	I	II	III
< 8	1280	6.33	6.26	6.23	998	6.01	5.96	5.88
8-10	1924	6.27	6.22	6.21	2312	5.88	5.86	5.84
11-12	995	6.12	6.13	6.14	867	5.61	5.62	5.66
13-16	1086	5.95	6.00	6.01	959	5.52	5.58	5.64
> 16	765	5.81	5.95	5.99	373	5.49	5.56	5.61
p-value for main effect		***	***	***		***	***	***

I : Age-adjusted.

II : Adjusted for age, physical activity, cigarette smoking and body mass index.

III: Also adjusted for food habits included in table 2 and the number of slices of bread per day ($\leq$ 1, 2-6, $\geq$ 7).

*** $p \leq 0.001$

TABLE 4

Relationships between length of education and HDL cholesterol. Adjusted for age and life style factors. 5,939 men, aged 25-54, and 5,320 women, aged 25-49. Tromsø 1979-1980

Length of education (years)	HDL cholesterol Men N	I	II	III	Women N	I	II	III
< 8	1195	1.47	1.48	1.50	913	1.70	1.73	1.74
8-10	1898	1.46	1.47	1.48	2224	1.75	1.76	1.77
11-12	989	1.46	1.45	1.45	859	1.78	1.77	1.77
13-16	1088	1.47	1.46	1.45	950	1.80	1.77	1.75
> 16	769	1.44	1.41	1.38	374	1.84	1.80	1.75
p-value for main effect		NS	*	***		***	*	NS

I : Age-adjusted.

II : Adjusted for age, physical activity, cigarette smoking and body mass index.

III: Adjusted in addition for type of table fat, frequency of use of fruits and vegetables and alcohol.

NS $p > 0.05$, * $p \leq 0.05$, *** $p \leq 0.001$

TABLE 5

Relationships between length of education and systolic blood pressure. Adjusted for age and life-style factors. 6,075 men, aged 25-54, and 5,487 women, aged 25-49. Tromsø 1979-1980

Length of education (years)	Systolic blood pressure							
	Men				Women			
	N	I	II	III	N	I	II	III
< 8	1208	132.1	131.9	132.0	939	124.6	124.1	124.1
8-10	1933	130.4	130.2	130.3	2284	121.6	121.5	121.5
11-12	1016	130.1	130.1	130.1	886	120.4	120.7	120.7
13-16	1122	129.8	130.0	129.9	988	119.4	119.6	119.6
> 16	796	130.2	130.9	130.6	390	119.0	119.4	119.4
p-value for main effect		***	**	**		***	***	***

I : Age-adjusted.

II : Adjusted for age, physical activity, cigarette smoking and body mass index.

III: Adjusted in addition for alcohol and bread consumption ($\leq$ 1, 2-6, $\geq$ 7 slices of bread per day).

** $p \leq 0.01$, *** $p \leq 0.001$

APPENDIX PAPER VII

Coffee Drinking, Mortality, and Cancer Incidence: Results From a Norwegian Prospective Study [1,2]

Bjarne K. Jacobsen, [3,4] **Erik Bjelke,** [3] **Gunnar Kvåle,** [3] *and* **Ivar Heuch** [5]

ABSTRACT—Relationships between coffee consumption and occurrence of cancer as well as mortality were explored in a Norwegian study of 13,664 men and 2,891 women who in 1967–69 reported their coffee consumption. No statistically significant positive associations were found between coffee consumption and disease. A weak negative association was found with total cancer incidence even when the first 4 of the 11½ years of follow-up were excluded, and strong negative associations with coffee drinking were noted for cancer of the kidney and nonmelanoma skin cancer. For cancer of the pancreas and bladder, no increase in incidence was found among those with a high coffee consumption. In subjects less than 65 years of age at start of follow-up, coffee drinking showed a significant inverse association with colon cancer.—JNCI 1986; 76:823–831.

Coffee has been implicated in the causation of various serious diseases, e.g., IHD (*1*) and cancer of the bladder (*2*) and the pancreas (*3*). Inasmuch as coffee drinking is a common habit in many parts of the world, it is important to determine whether coffee has any adverse effects on health. Prospective studies have not indicated that coffee consumption enhances the risk of cancer to any high degree (*4–6*).

We report here the results from a prospective study of 16,555 individuals, mostly men, followed for 11½ years. During this period, 1,498 cases of cancer were diagnosed and 4,032 deaths occurred in the cohort. The results suggest that neither the total mortality rate nor the total cancer incidence is adversely influenced by coffee drinking.

SUBJECTS AND METHODS

In 1964 a questionnaire concerning cardiorespiratory symptoms and smoking habits was sent to two cohorts of Norwegian men, a probability sample of the entire male population, and a set of brothers of migrants to the United States. The response rate to this survey was 79%. In 1967, 89% of the surviving respondents returned another questionnaire providing information about dietary habits, including coffee consumption. During 1967–69, 76% of the spouses and siblings of individuals interviewed in a case-control study of gastrointestinal cancer completed a similar questionnaire. These persons gave no information about smoking habits. The present study is based on the composite cohort consisting of these 3 groups, representing approximately 48, 20, and 32% of the total sample. Details about the sample surveys are given elsewhere (*7*).

In the questionnaire the subjects were asked how many cups of coffee they usually drank each day, with the following alternatives provided: *a*) do not drink coffee, *b*) less than one cup/day, *c*) 1–2 cups/day, *d*) 3–4 cups/day, *e*) 5–6 cups/day, and *f*) 7 or more cups/day. In cases of ambiguous or incomplete response to this question, the subjects were sent another request to provide the relevant information. Inasmuch as only 7% of the respondents belonged to categories *a* or *b*, alternatives *a*, *b*, and *c* were combined in the present analysis; the levels of use were assigned scores as follows: 0) 2 or less cups/day, 1) 3–4 cups/day, 2) 5–6 cups/day, and 3) 7 or more cups/day.

The respondents were not asked about duration of coffee drinking habits or type of coffee consumed. In the Norwegian cohorts considered here, adult coffee consumption habits would normally be established by the age of 20 years; we would not expect the duration of this habit to vary much among individuals of the same age in our study. Decaffeinated coffee is seldom consumed in Norway, and use of instant coffee was rather uncommon in most of the follow-up period.

The analyses were confined to the 16,555 respondents who had provided information about coffee consumption. Some analyses were further restricted to the 10,517 men who responded in both the 1964 (smoking habits) and 1967 (dietary habits) surveys. The official birth number made it possible to link information about coffee consumption with data on cancer cases collected by the Cancer Registry of Norway and with information on deaths from the Central Bureau of Statistics. For each individual the follow-up period started with the month after the one in which the questionnaire on dietary habits had been received and lasted until December 31, 1978, i.e., on the average, 11½ years.

The statistical analyses were based on models for stratified logistic regression. Through stratification the

ABBREVIATIONS USED: ICD = International Classification of Diseases; IHD = ischemic heart disease.

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results were adjusted for age at start of follow-up (10-yr intervals), for sex, and for region and urban or rural place of residence. Many calculations were also carried out with additional adjustment for cigarette smoking status (never smoked; ex-smokers; or current smokers of 1–9, 10–19, or ≥20 cigarettes/day). In the models, the interest was centered on the probability of developing cancer or dying at the four given levels of coffee drinking. The logit of this probability could be expressed as a linear function of the score for coffee, with the slope having a common value β, but with the intercept allowed to vary over strata. The hypothesis $\beta=0$ corresponded to the situation where coffee consumption had no effect. The odds ratio for any score d of coffee drinking relative to the next lower score d-1 can be written as $\exp(\beta)$. This value also approximated the corresponding relative risk.

Calculations according to this model were done by using a computer program written by Thomas and Gart (*8*). This program applies a test for trend in proportions to the hypothesis $\beta=0$ and calculates a maximum likelihood estimate b of β, with a corresponding standard error. This estimate in turn produces an estimate R of the odds ratio $\exp(\beta)$, as well as an estimate R^3 of the odds ratio for level 3 relative to the lowest level 0 (≥7 cups of coffee/day vs. ≤2). This odds ratio R^3 is the relative risk given in the tables.

The program also finds the expected number of cancer cases at the various levels of coffee drinking, given no association with disease. When computing these values, the program incorporates the information about deaths occurring in the follow-up period (*9*). Similar adjustments are included in the calculation of P-values, which are two-sided throughout. The program was also used to test for first-order linear interactions between coffee consumption and one of the stratification variables, age or cigarette smoking.

Strata without cancer cases or in which all the respondents were cases provided no information, and such strata were automatically deleted. Therefore, the number of relevant cases included in our calculations may change from one analysis to the next. Each estimated odds ratio was found by applying the logistic model to the complete set of data corresponding to all levels of the study variable. However, comparing the observed/expected ratios at different levels of use gave an impression of the relative risks for the individual levels of coffee consumption.

The distribution of coffee consumption according to demographic variables and smoking habits is given in table 1. Men tended to drink more coffee than women; the young people, more coffee than old people. Residents in northern Norway drank far more coffee than those in the southern regions; and smokers, more than those who had never smoked regularly

Table 1 reflects a decrease in coffee consumption with advancing age, which has also been observed in other studies (*10*). It is, however, likely that this reduction, relatively speaking, was the same for most subjects. Therefore, such changes in coffee drinking habits did not necessarily invalidate the ranking of coffee consumption on the basis of information obtained at any particular age.

The reproducibility of the coffee intake data was assessed by two small surveys. The questionnaire was completed twice by 193 subjects providing information on coffee drinking habits, with an average interval of 3–4 months between replies. The simple correlation coefficient with the use of the original coding in the questionnaire was 0.77. Another 126 subjects were per

TABLE 1.—*Percent distribution of coffee consumption among the respondents and in different subgroups of the respondents*

Category of respondents	No. of respondents	Percent distribution according to coffee consumption, No. of cups/day			
		≤2 cups	3–4 cups	5–6 cups	≥7 cups
Total series	16,555	24.9	38.3	24.9	11.8
Sex					
Male	13,664	24.7	36.9	25.6	12.9
Female	2,891	26.3	45.3	21.7	6.8
Age, yr					
≤54	5,788	22.6	33.6	29.2	14.6
55–64	5,941	22.7	38.5	26.1	12.7
≥65	4,826	30.5	43.8	18.2	7.6
Residence					
Urban	6,493	27.7	39.7	22.7	9.9
Rural	10,062	23.2	37.4	26.3	13.1
Oslo	3,012	32.2	40.1	20.0	7.7
Other southern	12,044	24.7	39.2	25.2	10.9
Northern Norway	1,499	12.1	28.2	31.8	28.0
Cigarette smoking among men					
Never	4,219	30.7	38.7	21.6	9.0
Formerly	2,311	24.6	38.1	25.4	11.9
Currently					
1–9/day	1,693	20.6	37.6	29.1	12.6
10–19/day	1,746	16.6	32.0	31.3	20.2
≥20/day	548	13.9	29.4	31.6	25.2

TABLE 2.—*Associations between coffee drinking and concentrations of some substances in serum*[a]

Serum substances	Concentration according to coffee consumption; No. of cups/day				No. of individuals	Slope[b]	P[c]
	≤2 cups	3–4 cups	5–6 cups	≥7 cups			
Potassium, mmol/liter	4.37	4.47	4.52	4.50	433	0.059	.02
Cholesterol, mg/100 ml	275.3	282.2	290.7	289.5	438	5.74	.02
Creatinine, mg/100 ml	1.08	1.01	0.98	0.94	435	−0.045	<.001
Uric acid, mg/100 ml	4.90	4.59	4.33	4.43	416	−0.193	.001

[a] Blood samples drawn 2 yr after the dietary survey.
[b] Slope for blood parameter regressed on score for coffee drinking.
[c] Two-sided P-value for slope.

sonally interviewed and also answered the postal questionnaire. Here the correlation coefficient between the reported coffee intakes was 0.72 (*7*), higher than the corresponding values for the other dietary items.

Results from an investigation concerning validity of the coffee consumption data are shown in table 2. Coffee consumption reported in 1967 by a subsample of men living in Oslo was compared with some blood parameters determined 2 years later in a joint study with the Institute of Clinical Chemistry, University of Oslo (*7*). The biochemical measurements were carried out under a system of quality control involving Scandinavian interlaboratory surveys. Being a good source of potassium, coffee correlated positively with the serum value of this electrolyte. The positive correlation with total serum cholesterol, previously discussed in relation to colon cancer (*11*), was in accord with results from a larger study in Norway (*12*). High coffee consumption was also associated with low levels of serum creatinine and uric acid.

RESULTS

Coffee Drinking and Mortality

During the period of follow-up, 4,032 deaths occurred among the 16,555 respondents. As shown in table 3, the mortality in the first years of follow-up related strongly to coffee drinking habits, those with low coffee consumption having higher-than-expected mortality. This finding was true for total mortality as well as for deaths from cancer. When the 1,213 deaths that occurred in the first 4 years of follow-up were excluded, coffee consumption showed no association, either in positive or negative direction, with any particular major cause of death, including cancer and IHD (table 4). For most causes of death, adjustment for cigarette smoking led to a fall in the relative risk estimates, especially marked for deaths from cancer. In the small group represented by diseases of the digestive system, a departure from linear trend was indicated.

Coffee Drinking and Risk of Developing Cancer

Table 5 presents relationships between coffee drinking and the incidence of cancer of different organs and tissues, with and without control for cigarette smoking. In these analyses no part of the follow-up period was excluded. However, the significant negative associations reported later in this paper were upheld when the first 4 years were excluded.

Total cancer incidence was not adversely influenced by coffee drinking, and this is true whether or not the

TABLE 3.—*Coffee drinking and mortality by period of follow-up*

Period of study	Stratification group[a]	Observed/expected No. of deaths according to coffee consumption; No. of cups/day				Total No. of cases	Relative risk[b]	P[c]
		≤2 cups	3–4 cups	5–6 cups	≥7 cups			
All deaths								
Total period	I	1,119/1,079.0	1,643/1,638.4	844/892.2	426/422.3	4,032	0.95	.15
	II	695/655.0	1,030/1,011.8	564/605.2	294/311.0	2,583	0.84	.01
First 1½ yr	II	86/67.9	97/99.6	46/53.1	17/25.4	246	0.48	.002
Next 2½ yr	II	138/129.4	215/198.5	96/114.3	52/58.8	501	0.73	.04
Next 7½ yr	II	474/459.8	721/717.0	423/438.8	225/227.3	1,843	0.93	.36
Deaths with cancer								
Total period	I	216/229.5	368/354.3	198/203.3	104/98.9	886	1.14	.49
	II	140/130.0	220/215.0	131/139.1	72/78.8	563	0.89	.13
First 1½ yr	II	20/13.0	21/19.6	6/11.0	2/5.3	49	0.19	.003
Next 2½ yr	II	31/28.1	52/46.6	22/28.5	15/16.8	120	0.68	.19
Next 7½ yr	II	89/88.9	147/148.8	102/98.6	55/56.7	393	1.07	.99

[a] I: Stratified for sex, age (10-yr groups), and residence. II: Men only, stratified for age, residence, and cigarette smoking (never; ex-smoker; or 1–9, 10–19, or ≥20 cigarettes per day).
[b] Estimated odds ratio, ≥7 vs. ≤2 cups of coffee per day.
[c] Two-sided P-value for trend.

TABLE 4.—*Coffee drinking and mortality; deaths after first 4 years of follow-up by cause groups*

Cause of death (ICD-8 No's.)	Stratification group[a]	Observed/expected No. of deaths according to coffee consumption; No. of cups/day				Total No. of cases	Relative risk[b]	P[c]
		≤2 cups	3–4 cups	5–6 cups	≥7 cups			
All causes	I	743/746.3	1,153/1,138.0	609/633.1	315/302.6	2,820	1.02	.93
	II	474/459.8	721/717.0	423/438.8	225/227.3	1,843	0.93	.36
Infective and parasitic diseases (001–008, 0090, 010–136)	I	3/4.6	5/6.5	5/3.5	3/1.4	16	4.05	.08
	II	2/1.9	3/3.7	3/3.2	2/1.2	10	2.05	.63
Malignant neoplasms (140–209)	I	132/152.5	245/238.9	153/141.7	72/68.9	602	1.31	.09
	II	89/88.9	147/148.8	102/98.6	55/56.7	393	1.07	.99
Diseases of the circulatory system (390–458)	I	413/410.5	647/628.9	330/344.0	155/161.6	1,545	0.93	.39
	II	261/257.3	407/397.6	232/236.4	109/117.7	1,009	0.91	.36
IHD (410–413)	I	238/243.2	388/374.9	212/217.2	103/105.7	941	0.99	.84
	II	166/162.0	261/253.2	156/159.7	72/80.2	655	0.87	.29
Cerebrovascular disease (430–438)	I	108/99.8	150/153.0	73/74.6	30/33.6	361	0.82	.30
	II	60/60.5	90/86.9	45/46.0	21/22.6	216	0.93	.77
Diseases of the respiratory system (460–519)	I	66/61.6	96/91.1	31/43.7	26/22.7	219	0.82	.42
	II	43/38.9	59/56.7	25/30.7	17/17.7	144	0.74	.28
Diseases of the digestive system (0091–0099, 520–577)	I	19/17.3	24/24.7	5/12.5	12/5.5	60	1.25	.58[d]
	II	11/9.5	17/15.5	4/9.0	7/5.0	39	0.77	.64[e]
Diseases of the genitourinary system (580–629)	I	18/15.4	22/23.0	9/11.3	6/5.3	55	0.71	.59
	II	12/11.6	17/16.2	6/8.0	5/4.3	40	0.75	.86
Other causes and ill-defined conditions (rest, 210–796)	I	62/58.4	82/85.3	51/51.7	26/25.6	221	0.92	.79
	II	37/39.0	58/54.5	33/36.0	20/18.4	148	1.02	.85
Accidents, poisonings, and violence (E800–E999)	I	30/26.0	32/39.5	25/24.8	15/11.7	102	1.17	.75
	II	22/16.4	16/26.4	20/17.8	11/8.3	69	1.07	.79[d]

[a] I: Stratified for sex, age (10-yr groups), and residence. II: Men only, stratified for age, residence, and cigarette smoking (never; ex-smoker; or 1–9, 10–19, or ≥20 cigarettes per day).
[b] Estimated odds ratio, ≥7 vs. ≤2 cups of coffee per day.
[c] Two-sided P-value for trend.
[d] Departure from linear trend ($P<.05$).
[e] Linear interaction with smoking ($P<.05$).

first 4 years of follow-up were excluded. At the 5% level for two-sided tests, there were no statistically significant positive associations. However, relative-risk estimates above 2.0 were found for cancer of the cervix (9 cases), melanoma (19 cases), and leukemia (37 cases). When adjustment was done for cigarette smoking, the relative-risk estimate for lymphocytic leukemia was 3.8 (8 cases) and that for other and unspecified leukemia, 1.5 (17 cases). In this study, it was not possible to adjust for cigarette smoking among the women. After adjustment for alcohol consumption, however, the very high relative-risk estimate found for cancer of the cervix was reduced to 8.7 ($P=0.19$).

Coffee drinking was negatively associated with colon cancer for respondents younger than 65 years of age and positively associated for those 65 years or more at the start of follow-up (table 6). When additional adjustment was made for alcohol consumption (a risk factor for colon cancer in this study), a highly significant and strong tendency toward low coffee consumption was found among the relatively young colon cancer patients. In contrast, no negative association was found for cancer of the rectum.

Respondents with high coffee consumption had a low rate of renal cancer (tables 5, 7). The association was limited to cancers of the renal parenchyma. The odds ratio estimate was far below 1.0 in all analyses shown in the table, also when adjustment was made for cigarette smoking.

Data on the association between coffee drinking and nonmelanoma skin cancer are given in table 8. A negative association was found both for normally and not normally sun-exposed parts of the body and both for squamous and basal cell carcinoma. We observed a statistically significant interaction with cigarette smoking, the negative association being stronger among smokers.

In this study, coffee drinking was not associated with cancer of the bladder or pancreas (table 5).

DISCUSSION

This study provides further evidence against any strong association between coffee drinking and death from IHD or cancer (*5*). A tendency to lower coffee consumption among those who died in the follow-up period disappeared when we excluded deaths occurring during the first 4 years of follow-up. After such exclusion, no statistically significant association between coffee drinking and any main cause of death remained (table 4).

Given the strong association observed between coffee drinking and serum cholesterol level in several Norwegian populations (*12*), it is remarkable that no association is found between coffee consumption and IHD. The population studied by us consists, however, of rather old individuals, with 65% of the respondents above 54 years of age when the coffee consumption data were collected. As the data are sparse for younger

TABLE 5.—*Coffee drinking and incidence of cancer*

Primary site (ICD-7 No.'s.)	Stratification group[a]	Observed/expected No. of cancers according to coffee consumption; No. of cups/day				Total No. of cases	Relative risk[b]	P[c]
		≤2 cups	3-4 cups	5-6 cups	≥7 cups			
All persons with cancer (140-205)	I	384/384.3	619/603.2	335/347.8	160/162.7	1,498	1.00	.61
	II	254/230.3	378/371.0	233/240.7	105/128.1	970	0.79	.005
First 4 yr	II	59/58.7	109/94.4	58/58.8	17/31.1	243	0.64	.04
Next 7½ yr	II	193/170.1	268/275.1	174/180.9	88/97.0	723	0.80	.05
Buccal cavity and pharynx (140-148)	I	7/9.6	21/14.1	7/9.4	3/4.9	38	0.73	.53
	II	6/6.8	14/11.3	7/7.8	3/4.1	30	0.84	.65
Lip (140)	I	1/4.7	14/7.3	3/5.0	2/2.9	20	1.01	.96[d]
	II	1/3.3	10/6.0	3/4.2	2/2.5	16	1.23	.97
Other buccal cavity and pharynx (141-148)	I	6/4.8	7/6.9	4/4.3	1/2.0	18	0.49	.38
	II	5/3.4	4/5.3	4/3.6	1/1.6	14	0.54	.48
Digestive organs (150-157)	I	104/108.5	180/168.4	87/93.5	42/42.6	413	1.01	.86[e]
	II	66/57.9	95/91.4	48/54.5	25/30.2	234	0.71	.07
Esophagus (150)	I	4/4.1	7/6.0	1/3.4	3/1.5	15	1.19	.85
	II	1/1.9	5/2.8	0/1.3	1/1.0	7	0.79	.88
Stomach (151)	I	32/38.0	61/59.1	34/33.6	20/16.3	147	1.46	.21
	II	24/20.3	35/33.1	18/20.2	10/13.4	87	0.64	.13
Colon (153) (including rectosigmoid)	I	30/25.8	43/41.3	21/22.5	6/10.5	100	0.59	.10[e]
	II	16/13.2	22/22.0	12/12.7	5/7.1	55	0.62	.24
Rectum (154) (excluding rectosigmoid)	I	14/16.5	30/25.8	13/14.5	6/6.2	63	1.07	.94
	II	9/9.2	15/14.0	7/8.4	4/3.4	35	1.07	.99
Pancreas (157)								
All cases	I	17/17.0	32/26.4	9/13.8	5/5.8	63	0.70	.37
	II	11/10.0	16/15.1	8/9.0	3/3.9	38	0.71	.48
Histologically confirmed cases	I	9/10.5	21/16.1	4/8.9	5/3.5	39	0.99	.94
	II	5/5.4	11/8.3	3/5.9	3/2.4	22	0.88	.78
Respiratory system (160-164)	I	40/49.7	71/74.3	59/49.2	30/26.9	200	1.62	.05
	II	27/27.7	52/51.3	43/40.5	22/24.5	144	1.09	.87
Larynx (161)	I	4/2.7	4/4.5	4/3.1	0/1.7	12	0.32	.23
	II	3/2.3	3/3.6	4/2.9	0/1.2	10	0.50	.50
Trachea, bronchus, and lung (162-163)	I	35/44.8	63/66.3	50/42.8	29/23.1	177	1.82	.02
	II	22/22.7	46/43.7	34/34.3	21/22.2	123	1.09	.84
Breast and genitourinary organs (170-181)	I	143/120.9	188/194.7	89/107.4	50/46.9	470	0.78	.07
	II	94/76.3	115/119.8	62/72.1	33/35.7	304	0.68	.03
Female breast (170)	I	12/8.0	10/15.3	7/6.9	3/1.9	32	0.81	.73
Cervix (171)	I	0/1.6	4/4.3	3/2.1	2/1.0	9	10.6	.07
Corpus (172)	I	3/3.0	7/5.0	0/2.4	1/0.6	11	0.52	.55
Ovary (175)	I	5/3.2	5/5.6	1/2.4	1/0.8	12	0.35	.35
Prostate gland (177)	I	79/68.6	104/107.0	52/58.0	25/26.4	260	0.80	.18
	II	62/52.8	79/81.7	43/47.0	21/23.6	205	0.74	.14
Kidney (180)	I	14/11.2	25/17.9	3/10.4	2/4.5	44	0.25	.01
	II	11/8.1	17/12.2	2/7.4	1/3.3	31	0.15	.008
Bladder (181)	I	28/23.7	31/36.9	22/23.0	13/10.4	94	0.99	.99
	II	20/15.3	19/25.2	16/16.6	10/7.9	65	0.98	.88
Skin (190-191)	I	65/57.6	92/89.4	55/53.0	12/24.0	224	0.62	.03
	II	45/38.7	61/59.2	47/41.4	7/20.7	160	0.53	.01[d,f]
Melanoma (190)	I	1/5.2	10/7.8	7/4.3	1/1.7	19	2.63	.16
	II	0/2.7	5/5.2	7/3.0	0/1.2	12	3.47	.17[d]
Nonmelanoma (191)	I	64/52.9	82/82.4	50/49.2	11/22.6	207	0.56	.01
	II	45/36.6	56/54.8	42/38.9	7/19.7	150	0.47	.006[f]
Lymphatic and hematopoietic tissues (200-205)	I	21/27.2	48/41.7	23/23.3	11/10.8	103	1.33	.49
	II	14/17.0	31/28.0	18/17.6	8/8.4	71	1.21	.73
Lymphoma (200-202, 205)	I	8/10.6	19/16.9	9/10.0	6/4.6	42	1.55	.45
	II	6/7.0	13/11.5	7/7.6	4/3.9	30	1.19	.89
Multiple myeloma (203)	I	6/6.2	11/9.7	6/5.6	1/2.6	24	0.71	.58
	II	4/3.3	7/7.0	4/3.8	1/1.9	16	0.59	.50
Leukemia (204)	I	7/10.5	18/15.1	8/7.7	4/3.7	37	1.67	.41
	II	4/6.7	11/9.5	7/6.2	3/2.6	25	2.05	.31
Other and unspecified (192-199)	I	21/24.2	36/38.8	26/22.1	13/10.8	96	1.59	.19
	II	15/16.1	22/22.7	17/15.2	8/8.0	62	1.22	.70

[a] I: Stratified for sex, age (10-yr groups), and residence. II: Men only, stratified for age, residence, and cigarette smoking (never; ex-smoker; or 1-9, 10-19, or ≥20 cigarettes per day).
[b] Estimated odds ratio, ≥7 vs. ≤2 cups of coffee per day.
[c] Two sided P value for trend.
[d] Departure from linear trend ($P<.05$).
[e] Linear interaction with age ($P<.05$).
[f] Linear interaction with smoking ($P<.05$).

TABLE 6.—*Coffee drinking and incidence of colon cancer*[a]

Case category	Observed/expected No. of colon cancers according to coffee consumption: No. of cups/day				Total No. of cases	Relative risk[b]	P[c]
	≤2 cups	3–4 cups	5–6 cups	≥7 cups			
All cases of colon cancer	30/25.8	43/41.3	21/22.5	6/10.5	100	0.59	.10[d]
All cases of colon cancer also adjusted for alcohol consumption	29/25.3	41/38.6	21/22.8	6/10.5	97	0.54	.10
Age 35–64 yr at follow-up entry	19/11.8	20/19.0	12/14.2	2/8.0	53	0.22	.002
Age ≥65 yr at follow-up entry	10/13.4	21/19.6	9/8.6	4/2.4	44	1.96	.18

[a] Men and women, stratified for sex, age (10-yr groups), and residence.
[b] Estimated odds ratio, ≥7 vs. ≥2 cups of coffee per day.
[c] Two-sided P-value for trend.
[d] Significant interaction with age (P=.003).

respondents, generalizations of our findings to these age groups might be misleading. However, lack of association between coffee consumption and IHD has also been observed in other prospective studies [e.g., (*5*)].

The results reported in table 3 suggest that people who are ill and therefore at a higher risk than the normal risk for dying during the first years of follow-up had already reduced their coffee consumption at the time of registration. The alternative explanation that coffee should in particular improve survival among debilitated persons cannot be entirely ruled out, although such an effect could hardly produce contrasts of the magnitude seen in table 3. It has formerly been shown (*5, 13*) that patients with chronic illnesses tend to have lower coffee consumption than the general population. This represents a problem in the design and interpretation of case-control studies using hospital controls and emphasizes the need, in prospective studies on coffee consumption and mortality, for exclusion of deaths occurring shorly after the coffee consumption is reported. Otherwise, results from such studies with short duration of follow-up can be misleading.

Incidence data should be less influenced by disease-related changes in coffee consumption than mortality data. However, table 5 demonstrates that the relative-risk estimate for a cancer diagnosis in the course of the first 4 years of follow-up was lower than in the next 7½ years. This result is explained by a very low coffee consumption among those who developed cancer of the stomach or the pancreas in the first 4 years after registration. One can easily imagine that stomach cancer or its precursor conditions are associated with symptoms (pain in the abdomen) leading to reduced coffee drinking. It is perhaps more surprising that pancreatic cancer should show symptoms, leading to reduced coffee consumption, for a long time before the condition is discovered.

The very old age groups may present particular problems in the interpretation of the analyses. In addition to inaccurate registration of typical coffee consumption, related to changes in coffee-drinking habits, there are problems with lower response rates; and the accuracy of diagnosis may be poor when compared with that of the young and middle-aged. Further, there may be a bias in risk estimates due to deaths from other causes. However, separate analyses carried out excluding individuals 75 or more years of age at start of follow-up suggested that these problems did not affect our overall results to any significant extent. For the group 65–74 years old, there were no indications of any particular results deviating from those in the younger categories, except for cancers of the digestive organs (tables 5, 6).

A weak negative association between coffee drinking and total cancer incidence was found after adjustment for cigarette smoking in addition to the demographic

TABLE 7.—*Coffee drinking and incidence of renal cancer*[a]

Case category	Stratification group[a]	Observed/expected No. of renal cancers according to coffee consumption: No. of cups/day				Total No. of cases	Relative risk[b]	P[c]
		≤2 cups	3–4 cups	5–6 cups	≥7 cups			
All cases of renal cancer	I	14/11.2	25/17.9	3/10.4	2/4.5	44	0.25	.01
Cancers of renal parenchyma	I	13/9.6	22/15.9	3/9.4	1/4.1	39	0.19	.004
Cancers of renal parenchyma not first diagnosed at autopsy	I	11/8.6	20/14.2	3/8.5	1/3.8	35	0.21	.01
Age 35–64 yr at entry	I	7/4.8	12/8.1	3/6.2	0/2.9	22	0.15	.01
Men, age 35–64 yr at start of follow-up	I	6/4.1	10/6.6	3/5.5	0/2.7	19	0.15	.02
Men, age 35–64 yr at start of follow-up, also adjusted for cigarette smoking	II	5/3.0	8/5.2	2/4.8	0/1.9	15	0.08	.01

[a] I: Stratified for sex, age (10-yr groups), and residence. II: Men only, stratified for age, residence, and cigarette smoking (never; ex-smoker; or 1–9, 10–19, or ≥20 cigarettes per day).
[b] Estimated odds ratio, ≥7 vs. ≤2 cups of coffee per day.
[c] Two-sided P-value for trend.

TABLE 8.—*Coffee drinking and incidence of nonmelanoma skin cancer*[a]

Case category	Observed/expected No. of nonmelanoma skin cancers according to coffee consumption; No. of cups/day				Total No. of cases	Relative risk[b]	p[c]
	≤2 cups	3–4 cups	5–6 cups	≥7 cups			
All cases	45/36.6	56/54.8	42/38.9	7/19.7	150	0.47	.006[d]
Head	26/23.7	41/36.7	27/26.1	6/13.5	100	0.58	.07
Rest of body	14/9.0	12/14.2	10/9.0	1/4.8	37	0.28	.04
Squamous cell carcinoma	8/5.8	8/9.4	7/4.9	0/3.0	23	0.35	.16
Basal cell carcinoma	35/28.1	45/41.9	32/32.2	6/15.9	118	0.45	.007

[a] Men only, stratified for age (10-yr groups), residence, and cigarette smoking (never; ex-smoker; 1–9, 10–19, or ≥20 cigarettes per day).
[b] Estimated odds ratio, ≥7 vs. ≤2 cups of coffee per day.
[c] Two-sided P-value for trend.
[d] Significant interaction with smoking (P=0.04).

variables (table 5). Any residual confounding with smoking will tend to give falsely high relative-risk estimates of associations between coffee drinking and cancers in which cigarette smoking is a part of the etiology. In this study, however, with a large variation in coffee consumption among individuals and a low proportion of heavy smokers, analyses stratified by five categories of cigarette smoking should leave little residual confounding. The smoking habits in Norway have changed during the period of follow-up, but this can influence the results only if the tendency to stop smoking is related to the coffee consumption.

There was no statistically significant positive association between coffee drinking and cancer of any site. Relative-risk estimates above 2.0 were found for cancer of the cervix, malignant melanoma, and lymphocytic leukemia. These results are based on a relatively small number of cases, and information about several potential confounding variables is not available, making the interpretation difficult. However, a positive association between leukemia and coffee drinking has previously been reported (*14, 15*), although Whittemore et al. (*15*) found the strongest association for myeloid leukemia, whereas we observed the highest relative risk for the lymphocytic type. The result for cancer of the cervix may be explained by a life-style of which high coffee and alcohol consumption is a part. We are not aware of published results that could give support to a causal relationship between coffee drinking and cancer of the cervix.

A rather strong negative association between coffee consumption and colon cancer was found among individuals under 65 years of age at the start of follow-up (table 6). Negative associations have previously been observed in some case–control studies (*7, 16*). However, coffee drinking was positively associated with risk of colon cancer in the last 11 years of a prospective study involving a 21-year follow-up of Seventh-Day Adventists (*6*). The coffee consumption among Seventh-Day Adventists is considerably lower than that in the general Norwegian population, which may be one of the reasons for the discrepancy. Further, as suggested by the authors (*17*), Adventists who drink coffee do not adhere too strictly to the teaching of the church and a higher mortality in this group could simply reflect poor adherence to other features of the Adventist's life-style.

We have no obvious explanation for the significant interaction with age for colon cancer in this study. The interaction was linear over several age groups. The repeated findings of associations with cancer of the colon suggest that coffee consumption may influence the incidence of this cancer, and more research is certainly needed. No association was found between coffee drinking and cancer of the rectum.

Kidney cancer risk showed a strong negative association with coffee drinking in this study (table 7). Three case-control studies have previously shown no association between coffee consumption and risk of kidney cancer (*18–20*). Our finding needs to be confirmed by others before a possible causal association can be considered. Even if there is a causal relationship, the importance should not be exaggerated since renal cancer is not among the most common cancers.

Table 8 shows a strong negative association between coffee consumption and nonmelanoma skin cancer. UV irradiation is accepted as a risk factor for this usually benign form of skin cancer (*21*); and, if coffee drinkers tend to stay more indoors, a negative association may result. However, there are no indications that the association with coffee seen in our material is due to such confounding. In particular, a stronger association was observed considering only parts of the body that are usually not sun exposed. In contrast to the other forms of cancer, the registration of nonmelanoma skin cancer has been lacking in completeness in Norway, especially for basal cell carcinoma. However, stratification on demographic variables will reduce any potential bias introduced by incomplete registration; and, in view of the lower relative risk observed for squamous cell carcinoma, it seems unlikely that such factors can account for the general association found with coffee. The significant interaction with cigarette smoking, the apparent protective effect being stronger among smokers, needs further evaluation.

There have been reports linking coffee consumption to increased risk of cancer of the pancreas (*3*). We cannot

support this claim. Possible associations between the use of alcohol, tobacco, and coffee and the risk of pancreatic cancer in this cohort are discussed in greater detail in a separate report (*22*).

Some studies (*23, 24*) have shown associations between coffee drinking and ovarian cancer. However, other studies, both in the United States (*25*) and Athens (*26*) where the association first was found by Trichopoulos and co-workers, have failed to show statistically significant associations. The present study with only 12 cases of ovarian cancer does not indicate that coffee drinking increases the risk.

The question of whether coffee drinking is associated with any increased risk of bladder cancer has not been completely settled (*2, 6, 15, 27-29*). Morrison and co-workers (*27*), who observed no association of coffee drinking with bladder cancer in a large case-control study, emphasized the importance of detailed adjustment for cigarette smoking. The results in our study, most likely with minimal residual confounding by smoking, add further support to the hypothesis that no relationship exists between coffee drinking and bladder cancer.

Experimental work on effects of coffee on carcinogenesis is not easy to interpret as regards to the total effects of the different constituents of coffee. Nagao and co-workers have reported mutagens in coffee (*30*), but activation by coffee of an enzyme system that catalyzes the binding of electrophiles has also been reported (*31*). Caffeine is metabolized so rapidly in man that near lethal doses are required to enhance chromosome damage in vivo (*32*). In vitro studies on the effect of coffee on cancer risk are thus equivocal. In vivo experiments do not indicate an increased cancer rate in rats given large doses of caffeine (*33*) or instant coffee (*34*), and some experiments actually suggest that addition of green coffee beans to the diet may confer a protective effect (*35*). Thus both laboratory and epidemiologic studies indicate that, while a carcinogenic effect of coffee cannot be excluded, carcinogenic effect is not necessarily the only action of coffee on cancer development.

This study suggests that high intakes of coffee may be associated with low risk of carcinoma of the colon, the renal parenchyma, and the skin. These findings need, however, confirmation by other studies. The most important findings reported here are the lack of positive association between coffee drinking and any major cause of death and coffee not significantly increasing the incidence of any common cancer.

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