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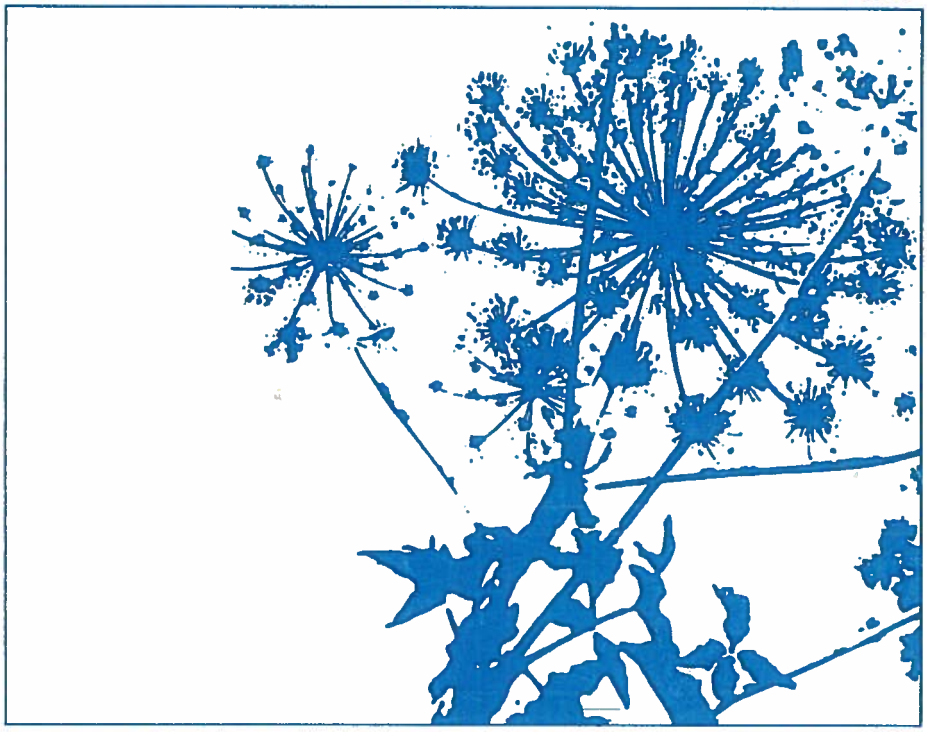

LONGITUDINAL ANALYSES OF CARDIOVASCULAR RISK FACTORS

The Tromsø Study 1974 - 1995

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CONTENTS

ACKNOWLEDGEMENTS

My background lies in mathematical statistics and before I started my work at the Institute of Community Medicine (ISM) I knew nothing about the field of epidemiology. I have really learned to appreciate epidemiology and medical research. It has been satisfactory for me, as a statistician, to apply enhanced theory to practical examples and real data.

I would like to thank Elinor Ytterstad, my supervisor during my studies for my statistics degree, and Tormod Brenn who introduced to me ISM. Tormod share my background as a statistician and he has been extremely helpful in discussions of statistical problems and epidemiological issues.

I would also like to give sincere thanks to my supervisor Egil Arnesen for discussions, ideas, and constructive criticisms. Also, I am grateful to the steering committee of the Tromsø Study, with Egil as chairman, for giving me access to the Tromsø data.

The ISM environment comprises highly skilled research fellows and researchers on a top national as well as international level. It has been a privilege to be a member of such an experienced and helpful group. The thesis couldn't have been finished without their contribution. I am especially indebted to the co-authors of my papers. Thanks to Bjarne Koster Jacobsen for his ability to fill my manuscript drafts with red ink, Henrik Schirmer for his ideas and his optimism, and Inger Thune for always being enthusiastic and supportive.

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Finally and most importantly I am indebted to my life companion and friend Tone, who with love has supported me. The last year has been hectic and eventful for us both. Magnus was born, we moved into a new house, and the final spurt of the thesis forced me to spend too many evenings at work.

LIST OF PAPERS

The thesis is based on the following papers:

I. Tracking of blood pressure in adult men: the Tromsø Study 1974 – 1986. J Epidemiol Biostat 1998;3(3):269-276.

II. Impact of body weight on blood pressure with a focus on sex differences. The Tromsø Study, 1986 – 1995. Arch Intern Med 2000;160:2847-2853.

III. Tracking of cardiovascular risk factors. The Tromsø Study, 1979 – 1995. Am J Epidemiol 2001;154(5):418-426.

IV. Change of serum lipids and body mass index by age, sex, and smoking status. The Tromsø Study 1986 – 1995. Submitted.

1 BACKGROUND

Although the mortality of coronary heart disease has decreased in most western countries in the last two decades it is still the most common cause of death. Positive changes in well-known cardiovascular risk factors (blood pressure, cholesterol, smoking habits) may partly explain the decrease(1-5). The decline could also be due to decreased incidence of first coronary event, decreased recurrence of coronary event, or decreased case fatality rates. Thus, important factors seem to be a combination of primary prevention and improvements in acute coronary care(1, 4-9). Despite the decreased incidence of coronary events, the incidence of obesity has increased in western societies. This may be a paradox because obesity is well understood as a risk factor for cardiovascular disease(10-16). However, changes in dietary intake and changes in physical activity should be addressed in order to understand the association between disease and the obesity epidemic.

1.1 Changes in risk factors and cardiovascular disease

The majority of studies who have estimated the contribution of changes in risk factors to trends in coronary heart disease have analysed data from cross-sectional studies(1, 3-5, 9, 17). The estimated changes in risk factors have been based on ecological studies and not based on longitudinal changes calculated from cohort studies. Population-based decreases in the most important risk factors have been associated with a population-based decrease in cardiovascular mortality. However, a statistical significant association may not necessarily express causality. Some of the decrease could be explained by other factors, which coincided with the cardiovascular intervention. Multivariate analyses from longitudinal cohort studies may give us further information on the association between cardiovascular disease and its risk factors. Although several studies have assessed longitudinal changes of body weight and blood pressure as cardiovascular risk factors, the results have been inconsistent(12, 15, 18-25). Assessments of longitudinal changes in serum lipids have been scarcely reported(26).

In order to assess the association between cardiovascular risk factors and the disease, the mutual association between the risk factors should be addressed. Knowledge of possible associations between two characteristics may help us to find preventive actions to reduce cardiovascular disease risk. If two characteristics are associated with cardiovascular disease, a risk reduction in one characteristic may also result in improved profile in the other characteristic. Other factors (extraneous variables) could confound these associations or be

effect modifiers. Although the main goal is to reduce the risk of cardiovascular disease, intermediate steps of changing the level of extraneous variables or changing the variables of interest in restricted areas of an extraneous variable could be of importance.

1.2 Tracking

Tracking of a characteristic is defined as the ability to maintain the same position within a distribution over time(27, 28), or the ability to predict future values from earlier measurements(29). In the literature there is no consensus of a single method of assessing tracking. A number of methods may be employed (30). Studies on tracking of cardiovascular risk factors have been published(31-43). However, the majority has investigated tracking during childhood(31-36), or from adolescence into adulthood(33, 37-42). Most of the studies of tracking concerning young adulthood or middle aged individuals either lack assessments and comparisons between the most common cardiovascular risk factors(37, 38, 42, 43), lack comparison between the sexes(37), or they are based on selected groups of individuals and not on a general population. In order to analyse trends or fluctuations over time for a given characteristic, knowledge about tracking may be of importance. The concept of tracking may also help us to examine possible associations between a characteristic's development over time and cardiovascular disease.

2 AIMS OF THE THESIS

- To assess the stability of cardiovascular risk factors over time, and to assess sex differences.
- To investigate the association between change of body weight with change of blood pressure, and to assess sex differences.
- To estimate possible predictors for tracking of cardiovascular risk factors.
- To assess the association between change of body weight and change of serum lipids grouped by baseline age, baseline weight and by change of smoking status.

3 SUBJECTS AND METHODS

3.1 Data source

Between 1974 and 1994-95 four health surveys have been carried out in the municipality of Tromsø, northern Norway. The first survey, carried out be the University of Tromsø in 1974 and called the Tromsø Heart Study, comprised men only and was initiated in order to investigate predictors and prevalence of coronary heart disease. The following three cardiovascular surveys, in 1979-80, in 1986-87 and in 1994-95, included both men and women and were carried out in co-operation with the National Health Screening Service. All persons invited received a mailed letter of invitation along with a questionnaire on the reverse side (appendices B-E). The procedures and the questionnaires in each survey were mainly the same. The questionnaires included the following topics:

- Current or previous history of cardiovascular diseases.
- Physical activity, at work and at leisure.
- Smoking habits.
- Ethnic origin.
- Family history of cardiovascular diseases.

At each survey the participants met to a physical examination. Specially trained personnel measured blood pressure and non-fasting blood samples were taken. Height and weight were determined and the questionnaire was checked. A few follow-up questions were asked and the participants were given a second questionnaire, which they were asked to answer at home and return by airmail. The second questionnaire included the following topics:

- Dietary habits, including intake of alcohol.
- Current or previous history of illnesses.
- Family history of illnesses.
- Social and psychological conditions.

The Tromsø Study in 1974, also referred to as Tromsø I

The whole male population (n=8867) between 20 and 49 years of age (born 1925 – 1954) were invited to this first survey in 1974. A total of 6595 attended the examination, 74.4% response rate. The method for measuring blood pressure is presented in paper I. The methods for measuring height, weight and serum lipids are presented in detail elsewhere(44).

Table 1. Number of participants according to examination year, age and sex. The Tromsø Study.

Men												
Age	1974			1979-80			1986-87			1994-95		
	Invited	Attended	%	Invited	Attended	%	Invited	Attended	%	Invited	Attended	%
20–24	1662	1265	76.1	1784	1028	57.6	2075	1160	55.9			
25–29	1995	1538	77.1	2261	1477	65.3	2210	1318	59.6	2920	1515	51.9
30–34	1741	1362	78.2	2279	1714	75.2	2327	1583	68.0	2651	1556	58.7
35–39	1250	925	74.0	1786	1422	79.6	2261	1710	75.6	2474	1649	66.7
40–44	1095	768	70.1	1211	1001	82.7	1893	1485	78.4	2324	1681	72.3
45–49	1124	737	65.6	1077	912	84.7	1318	1076	81.6	2094	1604	76.6
50–54				1085	924	85.2	1048	892	85.1	1595	1306	81.9
55–59							990	836	84.4	1077	918	85.2
60–64							415	353	85.1	906	796	87.9
65–69										810	691	85.3
70 +										1630	1149	70.5
Total	8867	6595	74.4	11483	8478	73.8	14537	10413	71.6	18481	12865	69.6
Women												
20–24				1999	1382	69.1	2103	1303	62.0			
25–29				2286	1734	75.9	2194	1572	71.6	3138	1794	57.2
30–34				2087	1784	85.5	2367	1848	78.1	2681	1798	67.1
35–39				1539	1376	89.4	1988	1681	84.6	2359	1811	76.8
40–44				1088	998	91.7	1722	1526	88.6	2138	1718	80.4
45–49				958	868	90.6	1177	1059	90.0	1981	1665	84.0
50–54							961	874	90.9	1449	1281	88.4
55–59							367	326	88.8	1025	941	91.8
60–64										855	774	90.5
65–69										970	860	88.7
70 +										2482	1651	66.5
Total	8867	6595	74.4	9957	8142	81.8	12879	10189	79.1	19078	14293	74.9

The Tromsø Study in 1979-80, also referred to as Tromsø II

Invited residents were all men born between 1925 and 1959 (aged 20 – 54) and all women born between 1930 and 1959 (aged 20 – 49). The invited population comprised 21440 individuals and the response rate was 77.5%, 16620 men and women(45). All details concerning the methods of measuring cardiovascular risk factors are given in paper III.

The Tromsø Study in 1986-87, also referred to as Tromsø III

A total of 27416 individuals, all men born between 1925 and 1966 and all women born between 1930 and 1966, were invited to this third survey. The response rate was 75.1%, 20602 participants. In addition, a 10% random sample of youths aged 12 to 19 years was invited(46). The methods of measuring the variables used in this thesis are given in paper II and III.

The Tromsø Study in 1994-95, also referred to as Tromsø IV

Invited were all 37559 individuals aged 25 and above who were resident in the municipality. A total of 27158 men and women attended the survey, 72.3% response rate. The methods of measuring the variables used in this thesis are given in paper II and III.

Table 1 shows the number of invited and attended participants according to examination year, age and sex. In the last three surveys the attendance rate increased with age and women had a higher attendance rate than men.

3.2 Cohorts

Each of the four surveys may be defined as a cohort that may be followed until a specified illness or death. The surveys may also be connected in order to assess longitudinal changes in cardiovascular risk factors such as blood pressure, BMI, and serum lipids. Figure 1 shows a flowchart of the participants in three cohorts. The first cohort consists of all men who attended the first survey in 1974. The second cohort consists of all participants followed from the 1979-80 survey. The third cohort consists of all persons who attended the third survey in 1986-87. Table 2 lists the surveys and number of persons included in each paper.

Table 2. Data sources.

	Persons examined in	Number
Paper I	Tromsø I, II, and III	4195
Paper II and Paper IV	Tromsø II and IV.	15624
Paper III	Tromsø II, III and IV, or two out of the three.	18372

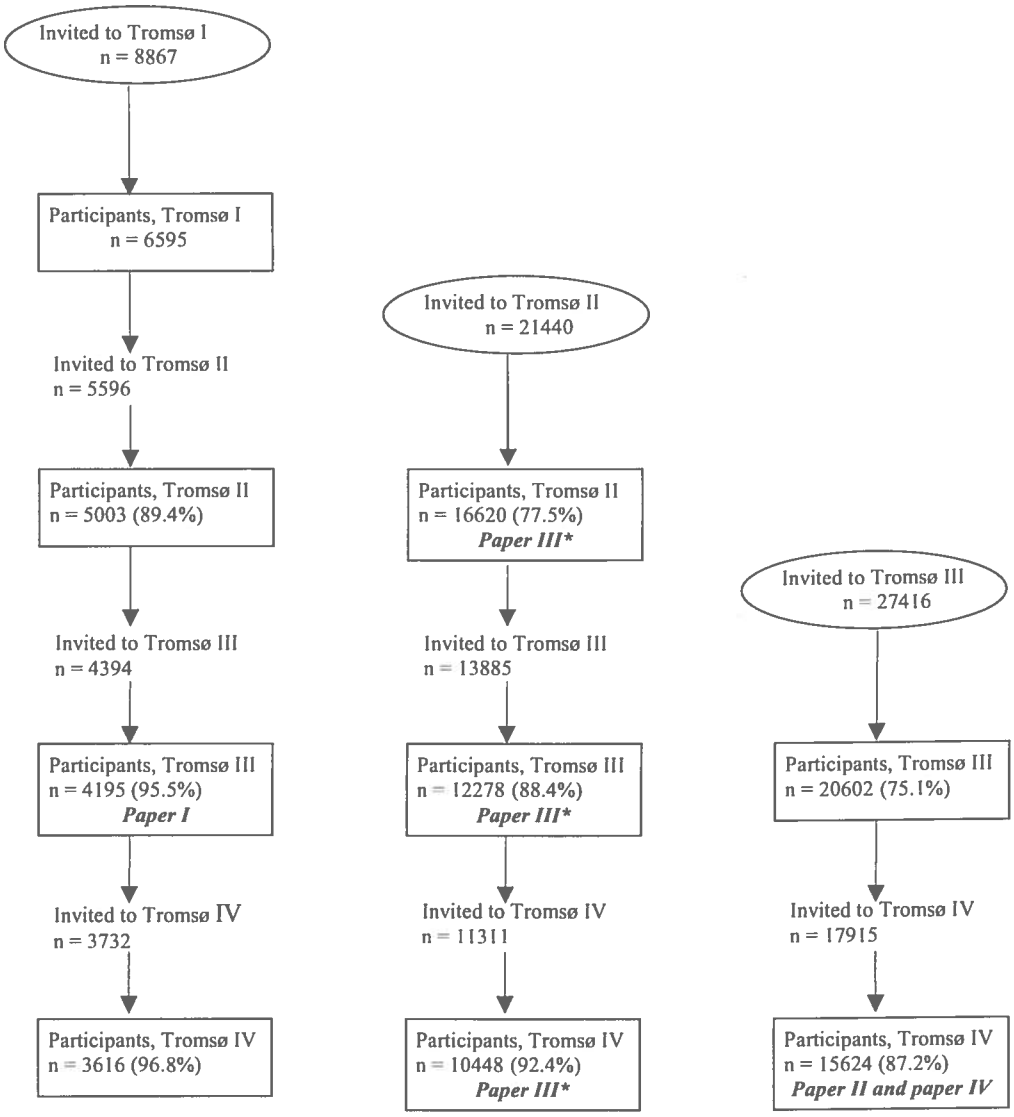


Figure 1. Flowchart of participants in the Tromsø Study.**

* Paper III comprises those who participated in at least two out of the last three surveys, n =18372 persons.

**Percentages reflects the response rate.

4 MAIN RESULTS

"Tracking of blood pressure in adult men: the Tromsø Study 1974-1986."

Tracking of systolic and diastolic blood pressure was assessed using the cohort who attended the first survey in 1974. This cohort comprised 4183 men aged 20 – 49 years in 1974 who met at three consecutive examinations (Tromsø I – Tromsø III). Tracking was assessed by three different methods: Pearson's correlation coefficient, Foulkes and Davis' tracking index and calculation of the proportion of participants who either remained in the same sextile group at all three examinations or the proportions of participants who changed sextile group relative to the baseline examination. A moderate degree of tracking was found in all of six 5-year age groups for all three methods. The youngest participants had the lowest coefficients for both systolic and diastolic blood pressure. Otherwise, there was no clear age trend. Estimation of intrasubject variation according to sextile group at baseline showed the largest variation in the first and the last sextile. This trend was apparent in all age groups although the youngest participants had the largest degree of variation of blood pressure.

"Impact of Body Weight on Blood Pressure with a Focus on Sex Differences. The Tromsø Study, 1986 – 1995."

Our objective in this paper was to study the relationship between change of systolic and diastolic blood pressure with BMI change and baseline BMI in more than 15000 men and women. In all age groups in men and women, an increase in systolic and diastolic blood pressure, and in BMI was observed between Tromsø III and Tromsø IV. Systolic blood pressure increased approximately linearly by age, whereas the increase in diastolic blood pressure was not associated with age. The increase in BMI was highest in the youngest age groups, and higher for women than for men after the age of 25. A positive association was observed between blood pressure change and BMI change. BMI at baseline was only associated with systolic and diastolic blood pressure change in women. To prevent a blood pressure increase it seems to be more important for obese women not to increase their weight compared to both non-obese women and men in general.

"Tracking of cardiovascular risk factors. The Tromsø Study 1979 – 1995."

Tracking of systolic and diastolic blood pressure, BMI, HDL cholesterol, total cholesterol and triglycerides was studied using data from more than 17000 men and women who attended at least twice in Tromsø II – Tromsø IV. Tracking was assessed by different methods and comparisons were made between the sexes. For systolic and diastolic blood pressure, and BMI in women only, tracking was observed to increase with age. Although no clear age trend was observed for serum lipids, the youngest participants had the lowest degree of tracking. The significant highest coefficients were observed for BMI. The following coefficients in decreasing order were total cholesterol, HDL cholesterol, systolic blood pressure, diastolic blood pressure, and triglycerides, both in men and women. Tracking was also assessed as the ability to maintain a position in a high-risk group over time. The tracking coefficients were given as odds ratio estimates. The odds for men in the upper sextile of baseline BMI of being in the upper sextile at later examinations was 32 times higher than for men in the other five sextiles. The estimate for women was significantly higher than for men with an odds ratio of 38. The magnitude for the other risk factors were noticeable lower than for BMI. Sex differences were observed for systolic and diastolic blood pressure.

"Change of serum lipids and body mass index by age, sex, and smoking status. The Tromsø Study 1986 – 1995."

The association between change of BMI and change of serum lipids was assessed in more than 15000 men and women who attended the surveys in 1986-87 and 1994-95. A BMI increase was significantly associated with a decrease in HDL cholesterol and an increase in total cholesterol and triglycerides. The association was generally weaker in the oldest 10-year age group and also significantly weaker for women than for men. The observed association was modified by initial BMI. The estimated effects for change of HDL cholesterol and total cholesterol in persons in the upper part of baseline BMI were weaker than for persons in the middle or lower part of baseline BMI. Differences were also found between persons who were consistent smokers/non smokers and persons who changed their smoking habits between the two surveys. It was observed that the association between change of BMI and change of serum lipids was weaker in person who changed their smoking habits (significant p values in HDL cholesterol and triglycerides, both in men and women).

5 DISCUSSION

5.1 Statistical methods

5.1.1 Methods of tracking classification

In epidemiological literature tracking is used to describe the development of a certain characteristic over time. Different tracking indices are developed in order to classify tracking. Pearson's or Spearman's correlation coefficient is the most used tracking index in medical research. The advantage of this index is that it is easy to interpret and it is well known to most readers of medical journals. The drawback is that the coefficient can only be calculated from two points of time. Other methods, which handle three or more measurements per individual, may be employed. Methods that we have used in Paper I and III are listed below.

- Pearson's correlation coefficient (Paper I).
- Foulkes and Davis' tracking index(27) (Paper I). The index ranges from 0 to 1 and may be calculated from two or more measurements per individual. Tracking is defined to be present whenever the index is larger than 0.5.
- Each participant was categorised in a sextile group at each examination. The proportion of participants who remained in the same sextile throughout all of three examinations was calculated. The proportion of participants who changed one or two groups relative to the initial examination was also calculated. These proportions were compared to the estimated proportions given that no tracking was present; i.e. each participant was randomly categorised to one of six groups at each examination (Paper I and III).
- A regression model(47), which controls for dependencies between repeated observation and estimated by a technique called generalised estimating equations (GEE)(48) was presented (Paper III). The model for subject i at time point $t = t_2$ or t_3 is defined as

$$Y_{it} = \beta_0 + \beta_1 Y_{it_1} + \beta_2 t_1 + \beta_3 t + \sum_j \beta_{4j} X_{ijt} + \sum_k \beta_{5k} Z_{ik} + \varepsilon_{it},$$

- Y_{it} is the dependent variable for subject i at time t_2 or t_3
- t_1 is the baseline examination, t_2 and t_3 is the second and third examination, respectively
- β_0 is the intercept

- β_1 is the standardised regression coefficient used as the tracking index and Y_{it_1} is the initial value of the dependent variable for subject i at time t_1
- β_2 is the regression coefficient of time at the baseline examination
- β_3 is the regression coefficient of time and t is time of examination of the dependent variable (t_2 or t_3)
- β_{4j} is the regression coefficient of the time dependent covariate j and X_{ijt} is the time dependent covariate j for subject i
- β_{5k} is the regression coefficient of the time independent covariate k and Z_{ik} is the time independent covariate k for subject i
- ε_{it} is the measurement error of subject i.

The concept of tracking may also be employed to assess the degree of maintenance of the position in a high risk group of a certain risk factor over time. Tracking in the upper level (lower for HDL-cholesterol) was thus presented by a model(49), which may be interpreted as an ordinary logistic regression analysis(50), and estimated using GEE (Paper III).

$$\text{Model: } \log it[P(Y_{it}=1)] = \beta_0 + \beta_1 Y_{it_1} + \beta_2 t_1 + \beta_3 t + \sum_j \beta_{4j} X_{ijt} + \sum_k \beta_{5k} Z_{ik} + \varepsilon_{it},$$

where e^{β_1} is the odds ratio estimate of tracking in a high risk group of a specified risk factor. The other β's are coefficients for time dependent and time independent covariates.

5.1.2 Change in risk factors

Multiple linear regression models were used to analyse the relationship between blood pressure change and BMI change (Paper II), and between change of serum lipids and BMI change (paper IV). We used data from the last two Tromsø studies to calculate change as the difference between two measurements. However, given that we also had access to three or four measurements per individual, the change estimates could have been calculated using data from more than two examinations. The obvious advantage using data from three or four

examinations compared to the presented results in paper II and paper IV, is the inclusion of one extra measurement for women and two extra measurements for men. If we don't restrain the inclusion criteria to attendance at all examinations, another advantage would have been an increase in number of individuals studied. Our decision not to include data from the first two examinations was based on several point of views:

1. If we included data from Tromsø I we would have had one more measurement for men but not for women. One focus in our analyses was to present sex specific results. We believe that sex comparisons should be performed between equal birth cohorts for men and women.
2. There was a difference in procedures of collecting data between the first and the last three surveys. In Tromsø I five specially trained secretaries and two physicians participated, but one person did all examinations. In Tromsø II – Tromsø IV the University of Tromsø, in co-operation with the National Health Screening Service (SHUS), carried out the examinations and different persons did the examinations at different stations.
3. There was a change in method of collecting blood pressure between Tromsø II and Tromsø III (paper I and paper III). Especially diastolic blood pressure would be affected by this change(51). Thus, excluding Tromsø II from the analyses eliminated the methodical problem of assessing longitudinal blood pressure change (paper II).
4. In including the last three surveys we would have included the same birth cohorts for men and women. However, a measure of change would not be straightforward. A likely choice would be to estimate a linear regression coefficient of longitudinal change for each person. Interpretation of results tend to get more complicated as the models get more advanced. We wanted to present our results for an audience who most likely would prefer the simplest statistical models.
5. In a separate set of analyses we included data from the last three surveys. Figure 2 shows the association with blood pressure change and BMI change estimated as a linear regression coefficient over time for each individual. Compared to paper II, the general impression and the conclusion remained virtually unchanged. This was apparent for the association between serum lipids change and BMI change, as well (results not shown).

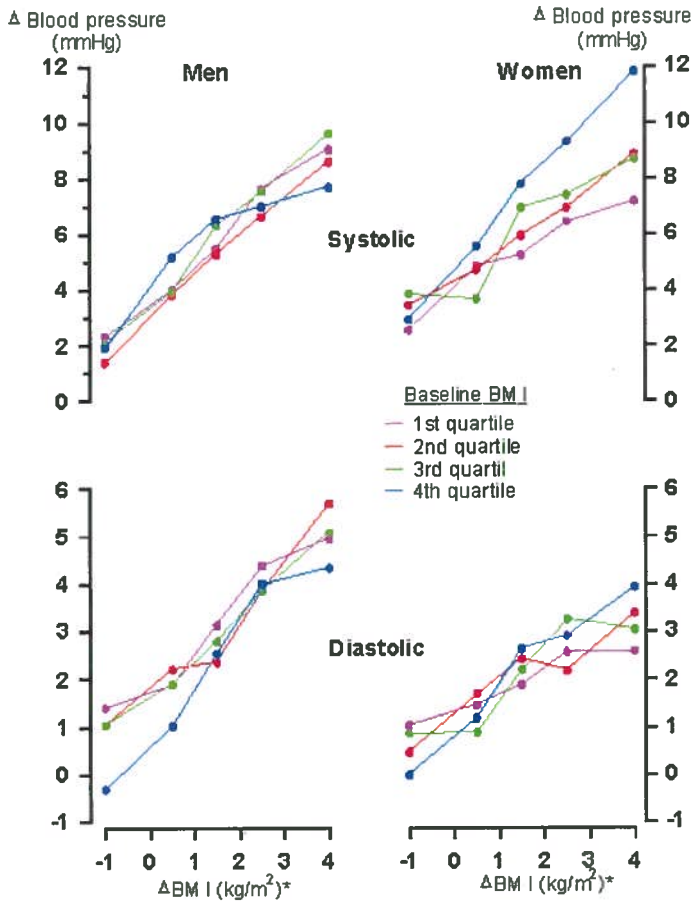


Figure 2. Change of systolic and diastolic blood pressure by change of BMI and quartiles of baseline BMI. The Tromsø Study

* Ten-year change estimated from linear regression models.

5.1.3 Model assumptions

Classical multiple linear regression models assume the error terms to be mutually independent identical distributed Gaussian variables. Model assumptions can be assessed by residual analyses. In all general linear models used in paper II and paper IV the model assumptions were checked and found to be sufficiently fulfilled.

The GEE models used in paper III require few assumptions about the distribution of the dependent variable. Some of the elements of GEE are listed below (see appendix A for further details).

- The GEE approach is a general method for fitting mathematical models to data involving repeated response measurements on the same subjects.
- The responses may be either discrete or continuous.
- The method allows the user to account for intra-subject correlations, often treated as nuisance parameters, among repeated observations.
- Different subjects can have different numbers of repeated measurements.
- Correlations are specified in the form of a working correlation matrix, which can have a variety of possible structures.
- The model parameters are estimated by iteratively solving a system of equations based on quasi-likelihood theory.
- In quasi-likelihood we only need to specify the relationship between the outcome mean and the covariates (referred to as the link function), and between the mean and the variance.
- The estimates for the regression parameters and their variances are consistent even under weak assumptions about the actual correlation matrix.

In paper III, where we assessed tracking in the upper levels of each risk factor, the dependent variable were categorised as binary responses. The link function, g, between the marginal expectation and the covariates was given as the logit function, $g(\mu_{ij}) = \ln[\mu_{ij} / (1 - \mu_{ij})]$, where μ_{ij} is the expectation of the dependent variable. For binary responses the variance is completely determined by the response mean. In cases where the response is close to Gaussian, the link may be given as the identity function, and the variance is a constant, independent of μ_{ij}. In situations with Gaussian responses, restricted maximum likelihood (REML) functions may be used instead of the quasi-likelihood theory. The covariance structure for the repeated measurements need still to be specified. The most common structures are compound symmetric, autoregressive order one, and unstructured(52). In the present analyses we used unstructured covariance pattern, which indicates that no mathematical pattern is imposed on the covariance matrix.

5.2 Methodological considerations

5.2.1 Validity

The validity of a study can be separated into two components, internal and external validity. Internal validity refers to the validity of inferences drawn from the population under study and prerequisite external validity, which refers to the generalizability of the study results. Possible biases resulting from internal validity are selection bias, information bias and confounding.

Selection bias

Selection bias is a bias that arises when individuals included in a study are not representatives of the target population for the study (53). The common element of such biases is that the relation between exposure and disease is different for those who participate and those who should be theoretically eligible for study(54). Since the whole population in the municipality of Tromsø was invited to the Tromsø Study, selection bias could be present due to non-responders. However, in population-based studies with a high response rate selection bias is normally not a large problem. The overall response rate in each of the four Tromsø studies is considered as high with rates in the range between 70 to 82 percent (table 1). A comparison between responders and non-responders showed a lower mean age among non responders and lower response rates for men than for women. It is not possible to compare other baseline characteristics between responders and non-responders. There are, however, other ways of assessing differences. Baseline characteristics between individuals who participated and dropped out of subsequent examinations were compared (paper I and paper II). Except for age and current smokers there were no significant differences between the two groups. Previous findings from the Tromsø Study showed agreeable results between individuals who returned and did not return the second questionnaire(55).

Information bias

Information bias can occur whenever there exist errors or misclassifications in the measurements of subjects, but the consequences of the errors are different, depending on whether the distribution of errors for one variable depends on the actual value of other variables(54). Misclassifications of discrete variables can be of two types; Differential misclassifications are error that depends on the values of other variables, and nondifferential misclassifications are errors that do not depend on other variables. Variables used in Paper I – Paper IV were, in addition to age and smoking, mainly the aforementioned cardiovascular risk

factors blood pressure, serum lipids and BMI. We have no indication of serious errors in these variables. Serum lipids were measured in a non-fasting state. The value of triglycerides may depend on the time since last meal(56). However, when we adjusted for time since last meal in the multivariate analyses it had no effect on the estimates of interest (paper III and paper IV). Other potential sources of bias could be seasonal variations or time of day. Values of blood pressure could especially depend on time of year and time of day. However, since there were no selection of time on study for each person, we believe that the factor did not influence the assessed relationships.

Confounding and interactions

In regression analyses one goal is to quantify the relationship of one or more independent variables to a dependent variable and is of particular interest when the research question concern disease etiology. The concepts of confounding and interaction are both relevant when we are trying to identify determinants of a disease. Confounding exists if meaningfully different interpretations of the relationship of interest result when an extraneous variable or a covariate is ignored or included in the data analysis(57). A confounder should be associated both with the independent variable and the response of interest. However, if a factor represent a step in the causal pathway between exposure and disease it should not be treated as confounding factor. There are ways of avoiding or adjusting for confounding. In our analyses we either stratified on possible confounders such as age, sex, and smoking, or we included the possible confounding variable in the regression model as a covariate. Interaction is the condition where the relationship of interest is different at different levels of the extraneous variable(57). In Paper II the relationship of interest was between change of BMI and change of blood pressure. Interaction was assessed for BMI change and baseline age and BMI change and baseline BMI. In paper IV the relationship of interest was between BMI change and change of serum lipids. Interactions were assessed for BMI change and baseline BMI, BMI change and baseline age, and for BMI change and change of smoking status.

Generalizability

Generalization may depend on a study group's being a representative subgroup of the target population. This definition would then limit the population to those individuals who might have been included in the study. However, generalization is not simply a matter of statistical generalization. To assess statements of more universal associations we have to gather information from different populations. In the Tromsø Study we assessed associations

between cardiovascular risk factors and also the stability of risk factors over time. Other studies and other study populations have addressed these associations, maybe not in the same subgroups and with the same range of risk factors as the present results. It is important to compare results between different population. Associations between risk factors may vary due to differences in dietary habits, ethnic differences or differences in other characteristics. Although the participants in the Tromsø Study are not statistically representatives for the population of Norway, we believe that the inferences drawn from the study could be generalised to the Norwegian population. In Tromsø, the incidence of cardiovascular disease, mortality, education, and lifestyle is in accordance with data from other parts of Norway(58). A relative high proportion of the population in the municipality of Tromsø comprises a homogeneous set of individuals. Although some of the inhabitants are of Sami or Finnish origin, few ethnic differences are present.

5.3 Risk factors

In medicine there are two principal, and mutually incompatible, interpretations of the term risk. 1: The probability, or chance, that an individual without disease will develop disease over a defined age or time interval. 2: A combination of the chance of an adverse effect and its severity(53). Statisticians and biologists usually favour the first definition. Risk factors usually relate to specific characteristics of populations, and relate to the increase of the individual's probability of experiencing and adverse reaction, disease, or other medical problems. A risk factor should not be interpreted as a factor of causality. Although a statistically significant association is observed between a characteristic and a disease, the characteristic may not be a causation of the disease. Causality may be determined by a commonly used list of criteria (59), which was introduced in order to answer the fundamental question: "is there any other way of explaining the set of facts before us, is there any other answer more likely than cause and effect?"

Risk factors for cardiovascular disease are assessed in this thesis. The stability of such factors over time was investigated in paper I and paper III. Associations between change of BMI with change of blood pressure and serum lipids were addressed in paper II and paper IV. Other risk factors such as sex, age, or daily smoking were also assessed, either as covariates in multivariate analyses or in strata specific analyses.

5.4 Obesity and cardiovascular risk factors

An expert consultation on obesity was convened by WHO in Geneva in 1997(60). It was recognised that overweight and obesity in adults represents a rapidly growing threat to the health of populations, and are prevalent in both developing and developed countries. In fact, overweight and obesity are now so common that they are replacing the more traditional public health concerns such as undernutrition and infectious diseases as some of the most significant contributors to ill health.

In cross-sectional and in longitudinal cohort studies height and weight are widely used measures of body composition. Consequently, BMI is a widespread measure and is considered to provide the most useful population level measure of obesity. Although BMI can be used to estimate population based prevalence of obesity and the risk associated with it, it does not account for the wide variation in the nature of obesity between different individuals.

In the Tromsø Study BMI the prevalence of overweight and obesity has increased in every birth cohort during 15 – 20 years of follow-up(61). Similar findings are presented in other studies(62-65). Screening of persons aged 40 – 42 years in eight Norwegian counties between 1994-96 to 1997-99 showed that the prevalence of obesity increased in practically all segments of the population(64). The Coronary Artery Risk Development in Young Adults (CARDIA) cohort experienced substantial weight gains from 1985-1986 to 1995-1996 in men and women in different ethnic groups aged 18 –30 years at baseline(62). Data from the National Health and Nutrition Examination Survey (NHANES) documented a substantial increase in overweight among adults in a series of national surveys in USA(63). Secular adverse trend of obesity is also documented world-wide(60).

The obesity epidemic may result in adverse risk profile and increased incidence of major diseases. Obesity is well established as a risk factor for non communicable diseases such as cardiovascular disease and non-insulin dependent diabetes mellitus (NIDDM), and also other health problems including various psychosocial consequences(60, 66-71). The secular increase of obesity should therefore be followed by increase in other diseases. A paradox may be the observed cardiovascular decline in western societies, and also the improved risk profile in other risk factors such as blood pressure and serum lipids(1, 5, 6, 8, 65, 72-75). However, the decline in the incidence of coronary disease may have been slowed by the increasing prevalence of obesity. Furthermore, factors that may support the decline are positive changes in dietary intake and improved medical surveillance and primary and secondary intervention. We know that high intake of saturated fat is harmful to health. In western countries there has been a shift towards larger intake of mono- and polyunsaturated

fatty acids, which favours the risk profile along with lower prevalence of smokers(75-77). Unsaturated fatty acids may also have a positive influence on blood coagulation and modifies the thromboembolic disease process.

There is a further need of assessing the impact the increased prevalence of obesity has on the disease process and also its association with intermediate risk factors.

5.4.1 Blood pressure

High levels of systolic and diastolic blood pressure is associated with increased risk of coronary heart disease and stroke(78-84). The decline in coronary events over the last decades has been accompanied with a decline in blood pressure levels(2, 4, 65, 74). Despite an increase in obesity and a decline in blood pressure positive associations have been documented between the two characteristics(85). Significant associations between characteristics measured cross-sectionally should also be assessed in longitudinal follow-up studies. In paper II we documented positive associations between longitudinal weight change and systolic and diastolic blood pressure change. Significant association was observed in all age groups and in different levels of baseline BMI. Baseline BMI was also associated with blood pressure change. However, the association was much weaker than with BMI change and significant in women only.

5.4.2 Total cholesterol

Total cholesterol is documented to be one of the most pronounced risk factors for cardiovascular disease (78, 86-88). The improved profile of total cholesterol over the past decades has been documented to account for a large part of the cardiovascular decline(4, 89). The dietary influence on serum lipids is widely documented. Saturated fatty acids, which raises cholesterol levels, may be substituted in the diet by other nutrients such as poly- and monounsaturated fatty acids and carbohydrates. Several studies have reported a relatively stable mean intake of dietary fat(74, 90). However, a significant decrease in consumption of higher-fat animal products has been observed. Consequently, the decline in total cholesterol is believed to be associated with an increase in the ratio of polyunsaturated to saturated fatty acids(90). Although there is a positive association between cholesterol decrease and improved diet, a direct association between body weight and total cholesterol are observed in a numerous of studies(91-94). Longitudinal associations between changes in these two

characteristics are also documented(95, 96), and were further explored in different strata of sex, age, baseline BMI, and change of smoking status (paper IV). The most important result was that individual increase in BMI leads to increased levels of total cholesterol.

5.4.3 High density lipoprotein cholesterol

An inverse relationship between HDL cholesterol and cardiovascular events have been documented in several studies(78, 87, 97, 98). However, in contrast to total cholesterol a favourable secular trend of HDL cholesterol has not been reported. HDL cholesterol levels have either fallen or remained unchanged(90, 99). The observed decline in HDL cholesterol may be explained by an adaptation to a diet lower in fat and may be a reflection of the decrease in total cholesterol. Changes in body weight have been associated to changes in HDL cholesterol(96, 100). In paper IV we further elucidated this relationship in strata of sex, age, baseline BMI, and change of smoking status.

5.4.4 Triglycerides

High levels of triglycerides are also linked to incidence of cardiovascular disease(87, 88, 101, 102). The associations are, however, not assessed in the same numbers as for total cholesterol and results are somewhat inconsistent, especially in men(103). Studies have documented that the strength of the association is dependent on cholesterol levels(104, 105). A meta-analyses of population-based prospective studies concluded, however, that triglycerides is a risk factor for cardiovascular disease in a general population, independent of HDL cholesterol(106). Studies of secular trends have shown adverse development of triglyceride levels(90, 107). Less attention has been given to the influence of diet. However, high levels of triglycerides are closely correlated to low levels of HDL cholesterol. Due to this correlation, the association between triglycerides and coronary heart disease often become non significant when adjusted for HDL cholesterol in multivariable analyses. In the past, triglycerides have gradually been accepted as a cardiovascular risk factor. Longitudinal analyses of change of triglycerides have been scarcely presented. We found that increase of BMI was significantly associated with increase of triglycerides in all strata of sex, age, initial BMI, and change of smoking habits (paper IV).

5.4.5 Sex differences

The incidence of coronary heart disease is severalfold higher in men than in women, depending on age. However, the relative impact of risk factor levels is not reported to differ between the sexes for many of the established risk factors. For instance, Njølstad et. al. did not observe sex differences in the relative risk for myocardial infarction for systolic blood pressure, HDL cholesterol, total cholesterol, triglycerides, and BMI(78). A difference in impact of smoking was, however, reported. The sex differences in stroke incidence and mortality do not follow the differences in coronary heart disease. In the Finnmark Study it was only observed a 36 percent higher stroke incidence in men(79), and Selmer reported only a slightly higher stroke mortality in men than in women in all age groups younger than 80 years of age(80). Although several studies have assessed the association between anthropometric variables (including BMI) and other cardiovascular risk factors in both men and women, few studies have focused on sex differences. Sex specific results from the Framingham Offspring Study showed that the prevalence of adverse levels of most CHD risk factors increased significantly by an increase in each one unit of BMI(91). Although no test for sex differences was presented, the estimates and their confidence intervals between the sexes coincided enough to give evidence of no sex difference. Studies with focus on sex differences in the association between BMI change and risk factor change are also missing. In paper II and paper IV one of our aim was to address sex differences. We observed that a BMI increase was significantly stronger associated with serum lipids increase in men compared to women. The strongest sex difference was observed for change of triglycerides, and the weakest difference for change of HDL cholesterol. For change of systolic and diastolic blood pressure the same pattern of sex difference was observed. However, the predicted increase in blood pressure induced by the increase in BMI was modified by baseline BMI in women but not in men. Women in the upper quartile of baseline BMI had a higher increase in blood pressure compared to women in the first quartile of baseline BMI, and also compared to men in general.

The observed sex differences for cardiovascular events are still debated. Some have hypothesised that the abdominal body fat distribution could explain the sex difference. Larsson et. al. concluded that body fat distribution or a factor highly correlated with waist:hip ratio, may help to explain the sex difference in coronary heart disease(108). Others have discussed the role of menopause and oral contraceptive use(105). Cigarette smoking, hypertension and hypercholesterolemia are risk factors for coronary heart disease in both sexes. Observed differences in these factors have not explained the observed coronary sex

difference. High levels of HDL cholesterol, which are protective against coronary events, are reported higher throughout life in women than in men. In men and women with NIDDM the cardiovascular difference is markedly reduced(109).

5.5 Stability of cardiovascular risk factors

Tracking coefficients is also referred to as stability coefficients(40). A high degree of stability does not necessarily mean that a characteristic is constant over time. The stability refers to a constant position in the characteristic's distribution over time. We found that the stability of blood pressure, BMI, and serum lipids tended to be lowest for adults early in their twenties (paper I and paper III). However, this is in contrast to the fact that the variability in each risk factor increases with age. Thus, despite lower standard deviations in early adulthood a higher degree of tracking was not observed.

In addition to the methods of tracking classification presented in paper I and paper III several other approaches can be found in the literature(30). Parametric and nonparametric methods may be employed. Spearman's and Pearson's correlation coefficient are widely used. Another approach is to divide the characteristic of interest into percentile groups or groups according to some predetermined cut point. When only two time points are available it is then reasonable straightforward to calculate the percent of subjects who stayed in the same group in both examinations. The problem of using the latter method is that the degree of tracking may highly depend on the grouping of data. Furthermore, when more than two time points are available it becomes more and more complicated to classify tracking according to each subject's movements between the groups in the different follow-up examinations. We divided the risk factors into six groups (sextiles) at each of three examinations (paper I and paper III). Each subject's movement between the sextile groups was registered. We had to determine a definition of tracking or no tracking. Persons who "tracked" were those who stayed within the same sextile at all examinations. Persons who moved one or two groups away from the baseline sextile group were also classified as "trackers". The obvious problem in using this definition of tracking is the difficulty of comparing the results with other studies. A comparison could only be valid with studies that have characteristics measured with the same number of time points. The range and variation in the measurements should be of equal magnitude and the time span between each examination should be the same as in our study. The number of time points and length of time span is, however, a general problem when we compare tracking results between studies.

Other nonparametric methods are Cohen's kappa, Kendall's coefficient of concordance, or a tracking index given by Nishio et al.(30). Examples of parametric tracking methods are also given in the review by Twisk et al.(30). We used Foulkes and Davis' tracking index to assess the stability of systolic and diastolic blood pressure in men (paper I). The Foulkes and Davis' index determine the probability that two individuals selected at random will have growth curves that do not cross over the considered time period. The estimated probability is simply the number of curves that do not cross divided by the total number of pairwise permutations of growth curves. The index obviously ranges between 0 and 1, and a value greater than 0.5 indicates tracking because two randomly selected growth curves would then be more likely not to cross. We used growth curves given as polynomial of second degree. The tracking results varied around 0.5 depending on the given age group. Consequently, our data indicated results close to no tracking of systolic and diastolic blood pressure. Results from the other two methods used in paper I indicated, however, a moderate degree of tracking. Our experience was that the Foulkes and Davis' index, estimated from three time points, did not give us a satisfactory answer of the degree of tracking. The problem could be the fitting of individual growth curves. What is the correct individual growth function of systolic and diastolic blood pressure change over time?

Knowledge about the development over time of cardiovascular disease risk factors is important because it may lead to early detection of increased cardiovascular risk. In that respect the concept of tracking plays a major role. Although tracking defines the stability of a characteristic over time, it also pertains to the predictability of earlier measurements to values measured later in life. If we are able to identify persons before they get an increased risk profile, it would benefit public health concerns. Early interventions are preferable compared to disease treatments later in life. Our results indicated moderate degree of tracking of blood pressure and serum lipids. The individual prediction in each of these factors would only be of moderate precision. Consequently, only population-based statements of later values predicted from earlier measurements could be precise.

Not surprisingly, tracking of BMI was pronounced higher than tracking of blood pressure and serum lipids (paper III). Men and women had a relatively constant position in the body weight distribution. Once achieved a position in the body weight distribution in early adulthood most people remain in that position later in life. An implication could be that it is hard to break out of the usual trend. Analyses have shown that persons who undergo a weight program positively loose weight at first, but after a period of time the probability of gaining weight up to the same initial level is extremely high(110).

Variability and measurement errors are factors that could lead to an underestimation of tracking. Blood pressure and serum lipids are characteristics that may vary according to time of day or time of year. The measurement precision in these variables is satisfactory, but we still believe that the measurement precision of body height and body weight is better. Since body height and body weight also are more constant according to seasonal variability, some of the observed difference in tracking between BMI and serum lipids and blood pressure could be explained by these differences.

Assessment of tracking in high-risk groups is maybe more of a public health interest than tracking in general. We estimated the odds ratio (OR) between persons who were in the upper sextile of a specified risk factor with persons in the other five sextiles of a risk factor to be in the upper sextile at later examinations (paper III). As with tracking in general, BMI had the pronounced highest estimates and triglycerides the lowest. One drawback of the log linear regression model is the simplification of the independent variables, which were divide in two categories (high risk sextile or not). Surely, persons who are located in the first sextile will most likely have lower odds of ending in the upper sextile than persons in the second to fifth sextile. The model does not separate persons in the five first sextiles at baseline. One way of omitting this problem is to implement the baseline risk factors as five dummy variables with the first sextile as the reference category. Another way is simply just to leave the risk factor as a continuos variable.

5.5.1 Predictors of tracking

In paper III we also tried to assess possible predictors for tracking. To our knowledge no other study has addressed this issue. We focused on tracking in the upper part of the distribution of each risk factor. A person was classified to "track" whenever he/she remained in the upper sextile at a later examination. Most of the specified independent baseline variables (age, systolic blood pressure, BMI, HDL cholesterol, total cholesterol, triglycerides, and current smokers) were significantly associated with tracking in each risk factor. In paper II and paper IV we documented a significant association between BMI change and blood pressure change or serum lipids change. What about the association between BMI and tracking of blood pressure or serum lipids? We observed that persons with increased BMI had increased odds of remaining in the high risk sextile in each risk factor. Consequently, persons with higher levels of BMI had lower odds of improving their risk profile compared to person with lower BMI levels. These results are well compatible with the fact of a positive association between BMI

and blood pressure and serum lipids. They also correspond well to the presented results that a BMI increase predicts increases in other cardiovascular risk factors. An important action is thus to reduce increased levels of BMI. However, given the apparent lack of substantial, long-term success at weight reduction, perhaps greater emphasis should be placed on prevention of obesity. There is a general agreement that increased physical activity, both at work and at leisure, is good for health and would contribute to a lower risk profile. However, it seems to be extremely hard to force an increase in physical activity on to a population. I have no simple solution for this problem. Maybe more extreme actions should be introduced?

5.5.2 Sex differences in tracking

There are few tracking studies that have included both adult men and adult women(38, 42, 43, 111, 112). Although sex specific results are reported, the focus has not been on sex differences. Cohorts have mostly been based on small or selected groups(38, 43, 111) and differences between different risk factors have not been reported(38, 42, 43, 111, 112). Rosner et al(43) and the Dormont High School Study(111) have documented blood pressure correlations slightly higher for females than for males. We did not document such a sex difference (paper III). However, for tracking in the upper part of the systolic and diastolic blood pressure distribution the coefficients were significant higher for women than for men. In the Cardia Study, white men had higher correlation coefficients for total cholesterol compared to white women(42). The same sex difference was also documented in the Värmland Cohort(112). These results are in agreement with ours. We found higher total cholesterol tracking coefficients in men than in women. But we also found lower tracking coefficients for HDL cholesterol in men compared to women. Therefore, we would like to emphasis that no common sex trend was observed for all the studied risk factors. We could not conclude of a general sex difference in tracking of cardiovascular risk factors.

6 FURTHER RESEARCH

Much is still unknown of future implications caused by the ongoing obesity epidemic. Further research of health consequences is needed. We have assessed the relationship between BMI and other cardiovascular risk factors. Analyses on the relationship between longitudinal change of risk factors and diseases are also warranted. Especially, if we focus on the association between BMI change and cardiovascular disease, it would be of importance to compare the associations in different levels of other factors. Maybe a BMI increase has a more adverse impact on cardiovascular risk above certain threshold values of factors such as blood pressure, total cholesterol, HDL cholesterol, or triglycerides. Each person's initial weight or initial BMI may modify the association. Sex differences or differences in strata of smoking habits could also be detected.

The degree of tracking of a characteristic is related to the characteristic's stability over time. The relation depends, however, on the time-related trend in the population. If, fore instance, a population-based increase or decrease in a factor is not observed, then persons who "track" will experience small changes over time for the given factor. On the other hand, if a secular increase is observed (as for BMI) persons who "track" will also experience a correspondingly increase. The association between tracking and change of risk factors should be addressed. Furthermore, if we observe a significant association between risk factor change and cardiovascular disease, will the degree of tracking also contribute as a disease predictor?

In paper III we assessed possible predictors for tracking. We feel that this topic could be further explored. Are there different characteristics between those who "tracks" and those who do not? Could it be that persons who have a high degree of tracking in one risk factor also have a high degree of tracking in other risk factors? Is there an association between tracking and change in other risk factors? Is there a connection between predictors for risk factor change and predictors for tracking? We have shown a strong association between BMI change and blood pressure change, and between BMI change and serum lipids change. How is the association between BMI change and tracking in these risk factors?

7 CONCLUSIONS

The present study has addressed longitudinal changes in cardiovascular risk factors and also assessed the association between BMI change with changes in other risk factors.

We showed a moderate to high degree of tracking for systolic and diastolic blood pressure, HDL cholesterol, total cholesterol, and triglycerides and a higher degree of tracking for BMI. Tracking was higher for total cholesterol compared to HDL cholesterol, especially in men. Tracking was slightly higher for systolic blood pressure than for diastolic blood pressure, but was lower compared to cholesterol. The lowest tracking coefficients were seen in triglycerides. Although we demonstrated some sex differences in tracking, a common pattern of difference was not observed. A common age trend was that persons in their early twenties had the lowest degree of tracking.

Tracking in high-risk groups compared to tracking in general showed mostly agreeable results with regard to differences between the risk factors. However, it was demonstrated significant higher coefficients for systolic blood pressure, diastolic blood pressure, and BMI in women than in men.

Baseline values of age, systolic and diastolic blood pressure, BMI, HDL cholesterol, total cholesterol, triglycerides, and current smoker were all significant predictors for tracking in high-risk groups for several of the considered risk factors.

Change of BMI was significantly associated with change of systolic and diastolic blood pressure. Obese women were more likely to increase their blood pressure with increasing BMI compared to lean women and men in general.

Change of BMI was also associated with change of serum lipids. The association was generally stronger in men than in women and weakest for persons at or above 50 years of age.

8 REFERENCES

1. Hunink MG, Goldman L, Tosteson AN, et al. The recent decline in mortality from coronary heart disease, 1980-1990. The effect of secular trends in risk factors and treatment. JAMA 1997;277:535-542.

2. Vartiainen E, Puska P, Pekkanen J, et al. Changes in risk factors explain changes in mortality from ischaemic heart disease in Finland. BMJ 1994;309:23-27.

3. Kuulasmaa K, Tunstall PH, Dobson A, et al. Estimation of contribution of changes in classic risk factors to trends in coronary-event rates across the WHO MONICA Project populations. Lancet 2000;355:675-687.

4. Sytkowski PA, Kannel WB, D'Agostino RB. Changes in risk factors and the decline in mortality from cardiovascular disease. The Framingham Heart Study. N Engl J Med 1990;322:1635-1641.

5. Burke GL, Sprafka JM, Folsom AR, et al. Trends in CHD mortality, morbidity and risk factor levels from 1960 to 1986: the Minnesota Heart Survey. Int J Epidemiol 1989;18:S73-S81.

6. Rosamond WD, Chambless LE, Folsom AR, et al. Trends in the incidence of myocardial infarction and in mortality due to coronary heart disease, 1987 to 1994. N Engl J Med 1998;339:861-867.

7. Salomaa V, Miettinen H, Kuulasmaa K, et al. Decline of coronary heart disease mortality in Finland during 1983 to 1992: roles of incidence, recurrence, and case-fatality. The FINMONICA MI Register Study. Circulation 1996;94:3130-3137.

8. Sverre JM. Secular trends in coronary heart disease mortality in Norway, 1966-1986. Am J Epidemiol 1993;137:301-310.

9. McGovern PG, Pankow JS, Shahar E, et al. Recent trends in acute coronary heart disease--mortality, morbidity, medical care, and risk factors. The Minnesota Heart Survey Investigators. N Engl J Med 1996;334:884-890.

10. Hubert HB, Feinleib M, McNamara PM, et al. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation 1983;67:968-977.

11. Selmer R, Tverdal A. Body mass index and cardiovascular mortality at different levels of blood pressure: a prospective study of Norwegian men and women. J Epidemiol Community Health 1995;49:265-270.

12. Rosengren A, Wedel H, Wilhelmsen L. Body weight and weight gain during adult life in men in relation to coronary heart disease and mortality. A prospective population study. Eur Heart J 1999;20:269-277.

13. Manson JE, Colditz GA, Stampfer MJ, et al. A prospective study of obesity and risk of coronary heart disease in women. N Engl J Med 1990;322:882-889.

14. Björntorp P. Obesity and the risk of cardiovascular disease. Ann Clin Res 1985;17:3-9.

15. Willett WC, Manson JE, Stampfer MJ, et al. Weight, weight change, and coronary heart disease in women. Risk within the 'normal' weight range. JAMA 1995;273:461-465.

16. Rimm EB, Stampfer MJ, Giovannucci E, et al. Body size and fat distribution as predictors of coronary heart disease among middle-aged and older US men. Am J Epidemiol 1995;141:1117-1127.

17. Dobson A, Filipiak B, Kuulasmaa K, et al. Relations of changes in coronary disease rates and changes in risk factor levels: methodological issues and a practical example. Am J Epidemiol 1996;143:1025-1034.

18. Peters ET, Seidell JC, Menotti A, et al. Changes in body weight in relation to mortality in 6441 European middle-aged men: the Seven Countries Study. Int J Obes Relat Metab Disord 1995;19:862-868.

19. Tervahauta M, Pekkanen J, Enlund H, et al. Change in blood pressure and 5-year risk of coronary heart disease among elderly men: the Finnish cohorts of the Seven Countries Study. J Hypertens 1994;12:1183-1189.

20. Galanis DJ, Harris T, Sharp DS, et al. Relative weight, weight change, and risk of coronary heart disease in the Honolulu Heart Program. Am J Epidemiol 1998;147:379-386.

21. Wannamethee G, Shaper AG. Weight change in middle-aged British men: implications for health. Eur J Clin Nutr 1990;44:133-142.

22. Walker M, Wannamethee G, Whincup PH, et al. Weight change and risk of heart attack in middle-aged British men. Int J Epidemiol 1995;24:694-703.

23. Sesso HD, Stampfer MJ, Rosner B, et al. Two-year changes in blood pressure and subsequent risk of cardiovascular disease in men. Circulation 2000;102:307-312.

24. Witteman JC, Grobbee DE, Valkenburg HA, et al. J-shaped relation between change in diastolic blood pressure and progression of aortic atherosclerosis. Lancet 1994;343:504-507.

25. Selmer R, Tverdal A. Changes in blood pressure as a predictor of coronary heart disease and stroke mortality: a 27-year follow-up of 15518 men and women in the City of Bergen, Norway. J Epidemiol Biostat 1996;1:41-50.

26. Pekkanen J, Nissinen A, Vartiainen E, et al. Changes in serum cholesterol level and mortality: a 30-year follow-up. The Finnish cohorts of the seven countries study. Am J Epidemiol 1994;139:155-165.

27. Foulkes MA, Davis CE. An index of tracking for longitudinal data. Biometrics 1981;37:439-446.

28. Mcmahan CA. An index of tracking. Biometrics 1981;37:447-455.

29. Ware JH, Wu MC. Tracking: Prediction of Future Values from Serial Measurements. Biometrics 1981;37:427-437.

30. Twisk JW, Kemper HC, Mellenbergh GJ. Mathematical and analytical aspects of tracking. Epidemiol Rev 1994;16:165-183.

31. Clarke WR, Schrott HG, Leaverton PE, et al. Tracking of blood lipids and blood pressures in school age children: the Muscatine study. Circulation 1978;58:626-634.

32. Webber LS, Cresanta JL, Voors AW, et al. Tracking of cardiovascular disease risk factor variables in school-age children. J Chronic Dis 1983;36:647-660.

33. Porkka KV, Viikari JS, Taimela S, et al. Tracking and predictiveness of serum lipid and lipoprotein measurements in childhood: a 12-year follow-up. The Cardiovascular Risk in Young Finns study. Am J Epidemiol 1994;140:1096-1110.

34. Webber LS, Srinivasan SR, Wattigney WA, et al. Tracking of serum lipids and lipoproteins from childhood to adulthood. The Bogalusa Heart Study. Am J Epidemiol 1991;133:884-899.

35. Guo S, Beckett L, Chumlea WC, et al. Serial analysis of plasma lipids and lipoproteins from individuals 9-21 y of age. Am J Clin Nutr 1993;58:61-67.

36. Freedman DS, Byers T, Sell K, et al. Tracking of serum cholesterol levels in a multiracial sample of preschool children. Pediatrics 1992;90:80-86.

37. Tate RB, Manfreda J, Krahn AD, et al. Tracking of blood pressure over a 40-year period in the University of Manitoba Follow-up Study, 1948-1988. Am J Epidemiol 1995;142:946-954.

38. Casey VA, Dwyer JT, Coleman KA, et al. Body mass index from childhood to middle age: a 50-y follow-up. Am J Clin Nutr 1992;56:14-18.

39. Kemper HC, Snel J, Verschuur R, et al. Tracking of health and risk indicators of cardiovascular diseases from teenager to adult: Amsterdam Growth and Health Study. Prev Med 1990;19:642-655.

40. Twisk JW, Kemper HC, van-Mechelen W, et al. Tracking of risk factors for coronary heart disease over a 14-year period: a comparison between lifestyle and biologic risk factors with data from the Amsterdam Growth and Health Study. Am J Epidemiol 1997;145:888-898.

41. Andersen LB, Haraldsdottir J. Tracking of cardiovascular disease risk factors including maximal oxygen uptake and physical activity from late teenage to adulthood. An 8-year follow-up study. J Intern Med 1993;234:309-315.

42. Iribarren C, Jacobs-DR J, Slattery ML, et al. Epidemiology of low total plasma cholesterol concentration among young adults: the CARDIA study. Coronary Artery Risk Development in Young Adults. Prev Med 1997;26:495-507.

43. Rosner B, Hennekens CH, Kass EH, et al. Age-specific correlation analysis of longitudinal blood pressure data. Am J Epidemiol 1977;106:306-313.

44. Thelle DS, Førde OH, Try K, et al. The Tromsø heart study. Methods and main results of the cross- sectional study. Acta Med Scand 1976;200:107-118.

45. Bønaa KH, Thelle DS. Association between blood pressure and serum lipids in a population. The Tromsø Study. Circulation 1991;83:1305-1314.

46. Bønaa KH, Arnesen E. Association between heart rate and atherogenic blood lipid fractions in a population. The Tromsø Study. Circulation 1992;86:394-405.

47. Twisk JW, Kemper HC, Mellenbergh DJ, et al. Factors influencing tracking of cholesterol and high-density lipoprotein: the Amsterdam Growth and Health Study. Prev Med 1996;25:355-364.

48. Zeger SL, Liang KY. Longitudinal data analysis for discrete and continuous outcomes. Biometrics 1986;42:121-130.

49. Twisk JW, Kemper HC, Mellenbergh GJ, et al. A new approach to tracking of subjects at risk for hypercholesteremia over a period of 15 years: The Amsterdam Growth and Health Study. Eur J Epidemiol 1997;13:293-300.

50. Hosmer DW, Lemeshow S. Applied logistic regression. New York: John Wiley & Sons, Inc, 1989.

51. Lund Larsen PG. Blood pressure measured with a sphygmomanometer and with Dinamap under field conditions -a comparison. Norwegian Journal of Epidemiology 1997;7:235-241.

52. Littel RC, Milliken GA, Stroup WW, et al. SAS System for Mixed Models. Cary, NC: SAS Institute Inc., 1996.

53. Encyclopedia of Biostatistics. Chichester: John Wiley & Sons, 2001.

54. Rothman KJ, Greeland S. Modern Epidemiology. Philadelphia: Lippincott-Raven, 1998.

55. Jacobsen BK, Thelle DS. The Tromsø Heart Study: responders and non-responders to a health questionnaire, do they differ? Scand J Soc Med 1988;16:101-104.

56. Cooper GR, Myers GL, Smith SJ, et al. Blood lipid measurements. Variations and practical utility. JAMA 1992;267:1652-1660.

57. Kleinbaum DG, Kupper LL, Muller KE, et al. Applied Regression Analysis and Other Multivariable Methods. Pacific Grove,CA: Duxbury Press, 1998.

58. Statistics Norway. Statistical Yearbook 2000. Oslo, Norway: Statistics Norway, 2000.

59. Hill B. Principles of Medical Statistics. London: The Lancet Limited, 1971.

60. World Health Organization. Obesity. Preventing and Managing the Global Epidemic. Report of a WHO Consultation on Obesity, Geneva 3 - 5 June 1997. 1998.

61. Jacobsen BK, Njølstad I, Thune I, et al. Increase in weight in all birth cohorts in a general population: The Tromsø Study, 1974-1994. Arch Intern Med 2001;161:466-472.

62. Lewis CE, Jacobs DR, Jr., McCreath H, et al. Weight gain continues in the 1990s: 10-year trends in weight and overweight from the CARDIA study. Coronary Artery Risk Development in Young Adults. Am J Epidemiol 2000;151:1172-1181.

63. Kuczmarski RJ, Flegal KM, Campbell SM, et al. Increasing prevalence of overweight among US adults. The National Health and Nutrition Examination Surveys, 1960 to 1991. JAMA 1994;272:205-211.

64. Tverdal A. [Prevalence of obesity among persons aged 40-42 years in two periods]. Tidsskr Nor Laegeforen 2001;121:667-672.

65. Rosengren A, Eriksson H, Larsson B, et al. Secular changes in cardiovascular risk factors over 30 years in Swedish men aged 50: the study of men born in 1913, 1923, 1933 and 1943. J Intern Med 2000;247:111-118.

66. Coleman MP, Key TJ, Wang DY, et al. A prospective study of obesity, lipids, apolipoproteins and ischaemic heart disease in women. Atherosclerosis 1992;92:177-185.

67. Hu FB, Manson JE, Stampfer MJ, et al. Diet, lifestyle, and the risk of type 2 diabetes mellitus in women. N Engl J Med 2001;345:790-797.

68. Walker SP, Rimm EB, Ascherio A, et al. Body size and fat distribution as predictors of stroke among US men. Am J Epidemiol 1996;144:1143-1150.

69. Calle EE, Thun MJ, Petrelli JM, et al. Body-mass index and mortality in a prospective cohort of U.S. adults. N Engl J Med 1999;341:1097-1105.

70. Thune I, Lund E. Physical activity and risk of colorectal cancer in men and women. Br J Cancer 1996;73:1134-1140.

71. Thune I, Lund E. Physical activity and the risk of prostate and testicular cancer: a cohort study of 53,000 Norwegian men. Cancer Causes Control 1994;5:549-556.

72. Vartiainen E, Sarti C, Tuomilehto J, et al. Do changes in cardiovascular risk factors explain changes in mortality from stroke in Finland? [published erratum appears in BMJ 1995 Nov 18;311(7016):1339]. BMJ 1995;310:901-904.

73. Sytkowski PA, D'Agostino RB, Belanger A, et al. Sex and time trends in cardiovascular disease incidence and mortality: the Framingham Heart Study, 1950-1989. Am J Epidemiol 1996;143:338-350.

74. Posner BM, Franz MM, Quatromoni PA, et al. Secular trends in diet and risk factors for cardiovascular disease: the Framingham Study. J Am Diet Assoc 1995;95:171-179.

75. Hu FB, Stampfer MJ, Manson JE, et al. Trends in the incidence of coronary heart disease and changes in diet and lifestyle in women. N Engl J Med 2000;343:530-537.

76. Kris-Etherton PM, Yu S. Individual fatty acid effects on plasma lipids and lipoproteins: human studies. Am J Clin Nutr 1997;65:1628S-1644S.

77. Grimsgaard S, Bønaa KH, Bjerve KS. Fatty acid chain length and degree of unsaturation are inversely associated with serum triglycerides. Lipids 2000;35:1185-1193.

78. Njølstad I, Arnesen E, Lund Larsen PG. Smoking, serum lipids, blood pressure, and sex differences in myocardial infarction. A 12-year follow-up of the Finnmark Study. Circulation 1996;93:450-456.

79. Njølstad I, Arnesen E, Lund LP. Body height, cardiovascular risk factors, and risk of stroke in middle-aged men and women. A 14-year follow-up of the Finnmark Study. Circulation 1996;94:2877-2882.

80. Selmer R. Blood pressure and twenty-year mortality in the city of Bergen, Norway. Am J Epidemiol 1992;136:428-440.

81. Håheim LL, Holme I, Hjermann I, et al. Risk factors of stroke incidence and mortality. A 12-year follow-up of the Oslo Study. Stroke 1993;24:1484-1489.

82. Tverdal A. Systolic and diastolic blood pressures as predictors of coronary heart disease in middle aged Norwegian men. Br Med J Clin Res Ed 1987;294:671-673.

83. Cholesterol, diastolic blood pressure, and stroke: 13,000 strokes in 450,000 people in 45 prospective cohorts. Prospective studies collaboration. Lancet 1995;346:1647-1653.

84. MacMahon S, Peto R, Cutler J, et al. Blood pressure, stroke, and coronary heart disease. Part 1, Prolonged differences in blood pressure: prospective observational studies corrected for the regression dilution bias. Lancet 1990;335:765-774.

85. MacMahon S, Cutler J, Brittain E, et al. Obesity and hypertension: epidemiological and clinical issues. Eur Heart J 1987;8 Suppl B:57-70.

86. Cholesterol consensus: a trans-Atlantic perspective. Amsterdam, The Netherlands, 31-October-1 November 1991. Int J Cardiol 1992;37 Suppl 1:S1-37.

87. Stampfer MJ, Sacks FM, Salvini S, et al. A prospective study of cholesterol, apolipoproteins, and the risk of myocardial infarction. N Engl J Med 1991;325:373-381.

88. Håheim LL, Holme I, Hjermann I, et al. The predictability of risk factors with respect to incidence and mortality of myocardial infarction and total mortality. A 12-year follow-up of the Oslo Study, Norway. J Intern Med 1993;234:17-24.

89. Jousilahti P, Vartiainen E, Tuomilehto J, et al. Effect of risk factors and changes in risk factors on coronary mortality in three cohorts of middle-aged people in eastern Finland. Am J Epidemiol 1995;141:50-60.

90. Porkka KV, Raitakari OT, Leino A, et al. Trends in serum lipid levels during 1980-1992 in children and young adults. The Cardiovascular Risk in Young Finns Study. Am J Epidemiol 1997;146:64-77.

91. Lamon-Fava S, Wilson PW, Schaefer EJ. Impact of body mass index on coronary heart disease risk factors in men and women. The Framingham Offspring Study. Arterioscler Thromb Vasc Biol 1996;16:1509-1515.

92. Reeder BA, Senthilselvan A, Despres JP, et al. The association of cardiovascular disease risk factors with abdominal obesity in Canada. Canadian Heart Health Surveys Research Group. CMAJ 1997;157 Suppl 1:S39-S45.

93. Denke MA, Sempos CT, Grundy SM. Excess body weight. An underrecognized contributor to high blood cholesterol levels in white American men. Arch Intern Med 1993;153:1093-1103.

94. Van Horn LV, Ballew C, Liu K, et al. Diet, body size, and plasma lipids-lipoproteins in young adults: differences by race and sex. The Coronary Artery Risk Development in Young Adults (CARDIA) study. Am J Epidemiol 1991;133:9-23.

95. Bakx JC, van den Hoogen HJ, Deurenberg P, et al. Changes in serum total cholesterol levels over 18 years in a cohort of men and women: The Nijmegen Cohort Study. Prev Med 2000;30:138-145.

96. Wilson PW, Anderson KM, Harris T, et al. Determinants of change in total cholesterol and HDL-C with age: the Framingham Study. J Gerontol 1994;49:M252-M257.

97. Gordon DJ, Probstfield JL, Garrison RJ, et al. High-density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies. Circulation 1989;79:8-15.

98. Miller NE, Thelle DS, Førde OH, et al. The Tromsø heart-study. High-density lipoprotein and coronary heart- disease: a prospective case-control study. Lancet 1977;1:965-968.

99. Derby CA, Feldman HA, Bausserman LL, et al. HDL cholesterol: trends in two southeastern New England communities, 1981-1993. Ann Epidemiol 1998;8:84-91.

100. Hubert HB, Eaker ED, Garrison RJ, et al. Life-style correlates of risk factor change in young adults: an eight-year study of coronary heart disease risk factors in the Framingham offspring. Am J Epidemiol 1987;125:812-831.

101. Bass KM, Newschaffer CJ, Klag MJ, et al. Plasma lipoprotein levels as predictors of cardiovascular death in women. Arch Intern Med 1993;153:2209-2216.

102. Carlson LA, Bottiger LE. Ischaemic heart-disease in relation to fasting values of plasma triglycerides and cholesterol. Stockholm prospective study. Lancet 1972;1:865-868.

103. Stensvold I, Tverdal A, Urdal P, et al. Non-fasting serum triglyceride concentration and mortality from coronary heart disease and any cause in middle aged Norwegian women. BMJ 1993;307:1318-1322.

104. Tverdal A, Foss OP, Leren P, et al. Serum triglycerides as an independent risk factor for death from coronary heart disease in middle-aged Norwegian men. Am J Epidemiol 1989;129:458-465.

105. Castelli WP. The triglyceride issue: a view from Framingham. Am Heart J 1986;112:432-437.

106. Hokanson JE, Austin MA. Plasma triglyceride level is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol level: a meta-analysis of population-based prospective studies. J Cardiovasc Risk 1996;3:213-219.

107. Sjøl A, Grunnet K, Schroll M. Secular trends in serum cholesterol, high density lipoproteins and triglycerides 1964-1987. Int J Epidemiol 1991;20:105-113.

108. Larsson B, Bengtsson C, Björntorp P, et al. Is abdominal body fat distribution a major explanation for the sex difference in the incidence of myocardial infarction? The study of men born in 1913 and the study of women, Goteborg, Sweden [see comments]. Am J Epidemiol 1992;135:266-273.

109. Price JF, Fowkes FG. Risk factors and the sex differential in coronary artery disease. Epidemiology 1997;8:584-591.

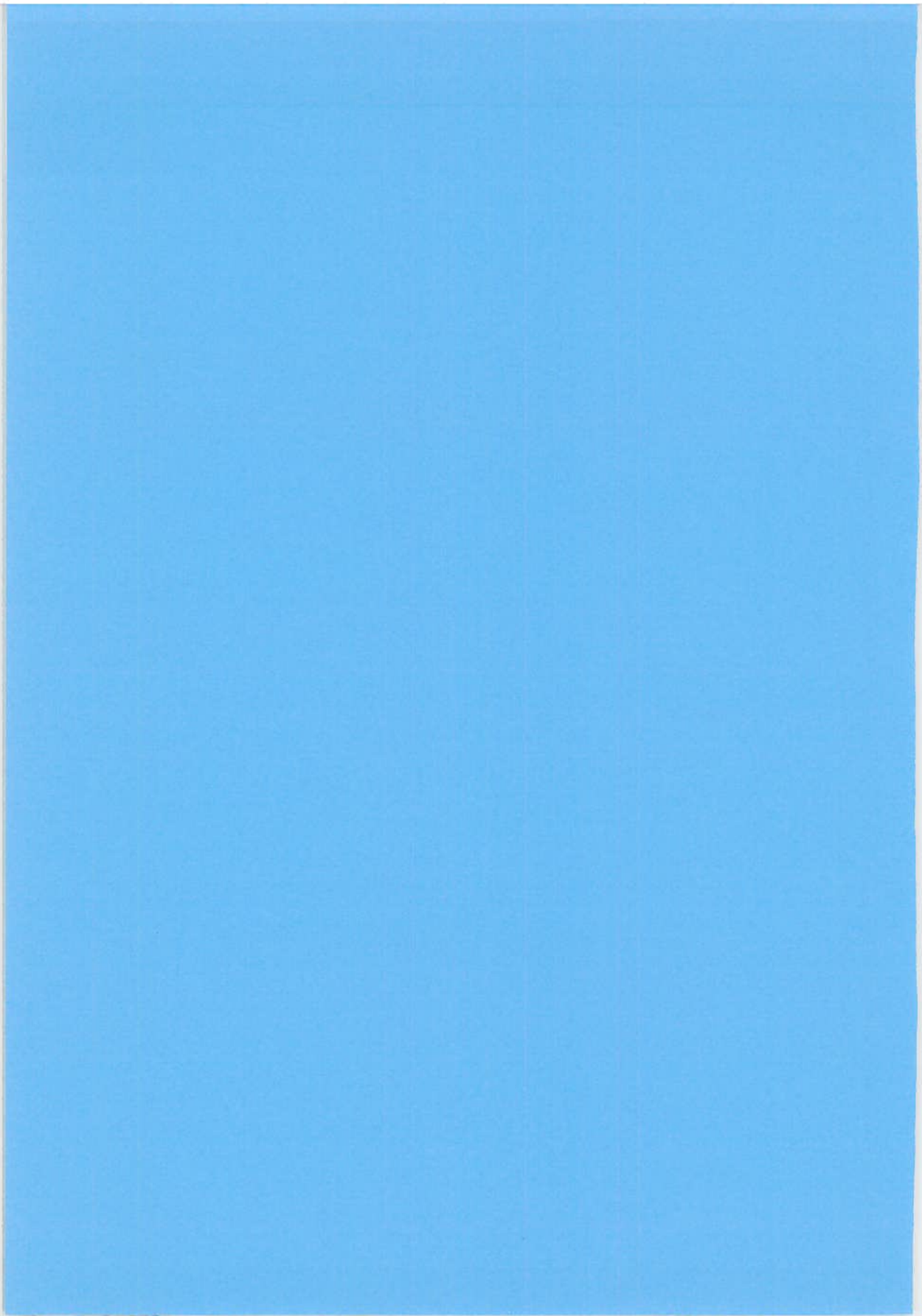
110. Grodstein F, Levine R, Troy L, et al. Three-year follow-up of participants in a commercial weight loss program. Can you keep it off? Arch Intern Med 1996;156:1302-1306.

111. Yong LC, Kuller LH. Tracking of blood pressure from adolescence to middle age: the Dormont High School Study. Prev Med 1994;23:418-426.

112. Törnberg SA, Jakobsson KF, Eklund GA. Stability and validity of a single serum cholesterol measurement in a prospective cohort study. Int J Epidemiol 1988;17:797-803.

APPENDIX A

The Generalized Estimating Equation approach



The Generalized Estimating Equation (GEE) approach(48)

Let (y_{ij}, x_{ij}) be the observations for subjects $i = 1,\ldots,K$ and times t_{ij}, $j = 1,\ldots,n_i$, where y_{ij} is the response variable and x_{ij} is a $p \times 1$ vector of covariates. Let y_i be the $n_i \times 1$ vector $(y_{i1},\ldots,y_{in_i})'$ and x_i be the $n_i \times p$ matrix $(x_{i1},\ldots,x_{in_i})'$ for the ith subject.

In the quasi likelihood approach, a known transformation of the marginal expectation of the outcome is assumed to be a linear function of the covariates, and the variance is assumed to be a known function of its expectation. Let μ_i be the expectation of y_i and assume that

$$\mu_i = h(x_i\beta), \tag{1}$$

where β is the vector of regression parameters. The inverse of h is referred to as the link function. The variance of y_{ij} is expressed as

$$g(\mu_{ij})/\phi. \tag{2}$$

Let $R_i(\alpha)$ be the $n_i \times n_i$ working correlation matrix for each y_i, which is fully specified by the $s \times 1$ vector of unknown parameters α. The working covariance matrix for y_i is

$$V_i = A_i^{1/2} R_i(\alpha) A_i^{1/2}/\phi, \tag{3}$$

where A_i is a $n_i \times n_i$ diagonal matrix whose jth diagonal element is given by $g(\mu_{ij})$.

The GEE estimators is the solution of the score-like equation system

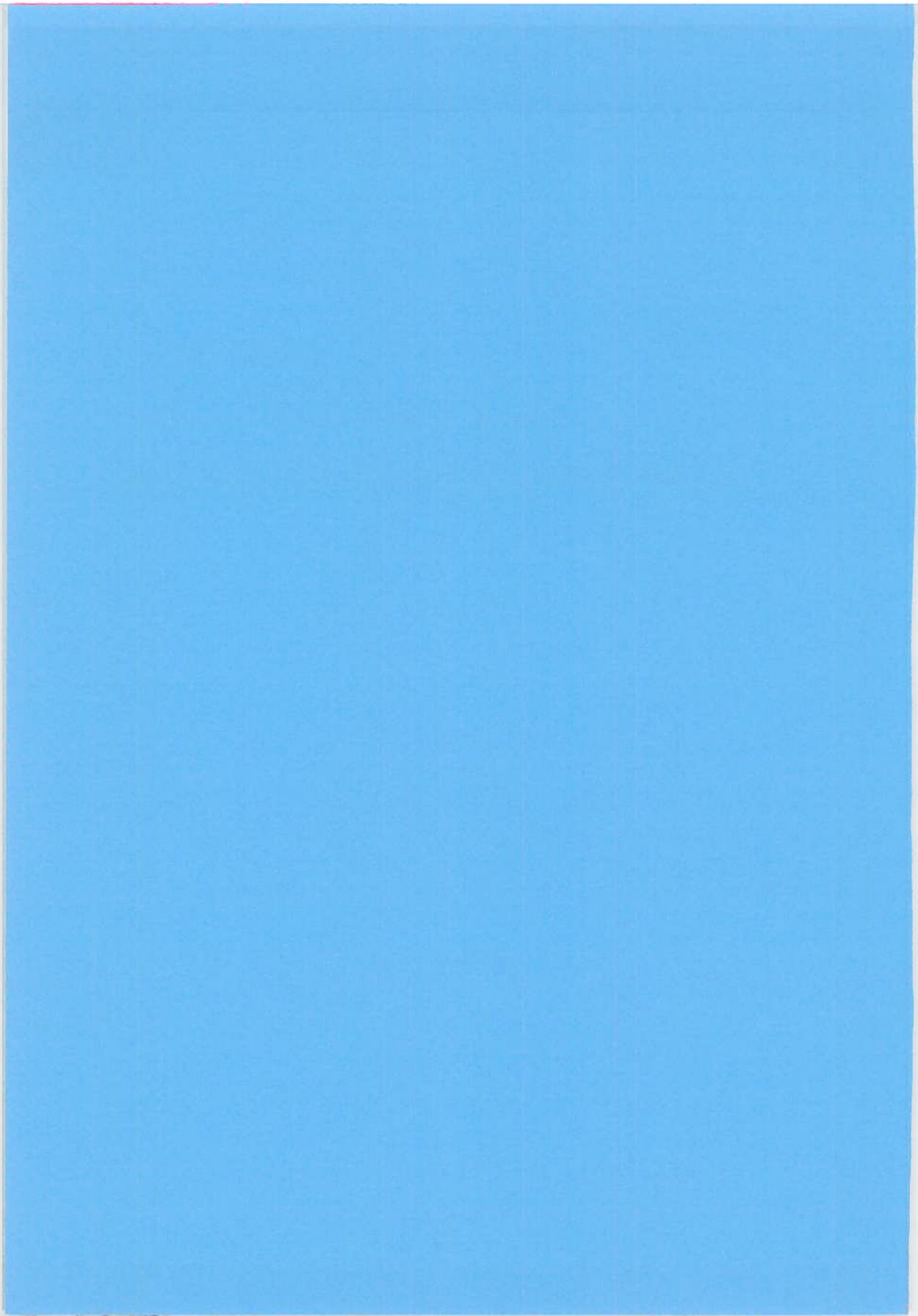
$$\sum_{i=1}^{K}\left[\frac{\partial\mu_i}{\partial\beta}\right]' V_i^{-1}[y_i - \mu_i] = 0 \tag{4}$$

Equation (4) is designed to guarantee consistency of the regression coefficients when the link function is correctly specified. It is not necessary for the working correlation matrix to be correctly specified to obtain a consistent and asymptotically Gaussian estimate for the regression parameters, or for estimating their variances consistently.

APPENDIX B

Questionnaire I Tromsø Study 1974

Original Norwegian version and English translation



MELDING OM SKJERMBILDEFOTOGRAFERING OG HJERTE-KARUNDERSØKELSE

(Gjelder bare den person brevet er adressert til)

Skjermbildefotograferingen kommer nå til Deres distrikt.

Tid og sted for Deres frammøte vil De finne nedenfor.

Denne gangen vil en del av befolkningen også få tilbud om hjerte-karundersøkelse. De tilhører denne gruppe. En orientering om undersøkelsen er gitt i vedlagte brosjyre.

Vennligst fyll ut spørreskjemaet på baksiden og ta det med til undersøkelsen. Ta også med tuberkulinkort eller helsebok; om De har.

Fravær bes eventuelt meldt på vedlagte seddel.

Undersøkelsen koster 1,– krone.

Med hilsen

HELSERÅDET FYLKESLEGEN
STATENS SKJERMBILDEFOTOGRAFERING

Født dato | Personnr | Kommune | Kretsnr

Møtested | Kjønn | Første bokstav etternavn | Dag og dato | Klokkeslett

A

Har De, eller har De hatt:

- Hjerteinfarkt? 33
- Angina pectoris (hjertekrampe)? 34
- Annen hjertesykdom? 35
- Åreforkalkning i bena? 36
- Hjerneslag? 37
- Sukkersyke? 38

Er De under behandling for:

- Høyt blodtrykk? 39

Bruker De:

- Nitroglycerin? 40

B

Får De smerter eller ubehag i brystet når De:

- Går i bakker, trapper eller fort på flat mark? 41
- Går i vanlig takt på flat mark? 42

Hvis De får smerter eller ubehag i brystet ved gange, pleier De da å:

- 1 Stanse? 43
- 2 Saktne farten? .....
- 3 Fortsette i samme takt? .....

Hvis De stanser eller saktner farten, forsvinner smertene da:

- 1 Etter mindre enn 10 minutter? 44
- 2 Etter mer enn 10 minutter? ....

Får De smerter i tykkleggen når De:

- Går? 45
- Er i ro? 46

Hvis De får leggsmerter, besvar da:

- Forverres smertene ved raskere tempo eller i bakker? 47
- Gir smertene seg når De stopper? .. 48

Har De vanligvis:

- Hoste om morgenen? 49
- Oppspytt fra brystet om morgenen? .. 50

C

Bevegelse og kroppslig anstrengelse i Deres **fritid**.
Hvis aktiviteten varierer meget f.eks. mellom sommer og vinter så ta et gjennomsnitt.

Spørsmålet gjelder bare det siste året.

Sett kryss i den ruten hvor „JA" passer best.

- 1 Leser, ser på fjernsyn eller annen stillesittende beskjeftigelse? 51
- 2 Spaserer, sykler eller beveger Dem på annen måte minst 4 timer i uken? .. (Heri medregnes også gang eller sykling til arbeidsstedet, søndagsturer m.m.)
- 3 Driver mosjonsidrett, tyngre hagearbeid e.l.? ..... (Merk at yirksomheten skal vare minst 4 timer i uken.)
- 4 Trener hardt eller driver konkurranseidrett regelmessig og flere ganger i uken? .....

D

- Røyker De daglig for tiden? 52

Hvis svaret var „JA" på forrige spørsmål, besvar da:

- Røyker De sigaretter daglig? ..... 53 (håndrullede eller fabrikkframstilte)

Hvis De ikke røyker sigaretter nå, besvar da:

- Har De røykt sigaretter daglig tidligere? . 54

Hvis De svarte „JA", hvor lenge er det siden De sluttet?

- 1 Mindre enn 3 måneder? 55
- 2 3 måneder - 1 år? .....
- 3 1 - 5 år? .....
- 4 Mer enn 5 år? .....

Besvares av dem som røyker nå eller har røykt tidligere:

- Hvor mange år tilsammen har De røykt daglig? ..... 56-57 — Antall år:
- Hvor mange sigaretter røyker eller røykte De daglig? Oppgi antall pr. dag 58-61 (håndrullede + fabrikkframstilte) — Ant. sigaretter:

Røyker De noe annet enn sigaretter daglig?

- Sigarer eller serutter/cigarillos? ... 62
- Pipe? 63

Hvis De røyker pipe, hvor mange pakker tobakk (50 gram) bruker De i pipa pr. uke? — Ant. tobakkp.

- Oppgi gjennomsnittlig antall pakker pr. uke. 64-66

E

- Har De vanligvis skiftarbeid eller nattarbeid? 67

Kan De vanligvis komme hjem fra arbeidet:

- Hver dag? 68
- Hver helg? 69
- Har De i perioder lengre arbeidsdager enn vanlig? ..... 70 (f.eks. under sesongfiske, onnearbeid)

Har De i løpet av siste året hatt:

Sett kryss i den ruten hvor „JA" passer best.

- 1 Overveiende stillesittende arbeid? .. 71 (f.eks. skrivebordsarb., urmakerarb., montering)
- 2 Arbeid som krever at De går mye? .. (f.eks. ekspeditørarb., lett. industriarb., undervisn.)
- 3 Arbeid hvor De går og løfter mye? .. (f.eks. postbud, tyngre industriarb., bygningsarb.)
- 4 Tungt kroppsarbeid? ..... (f.eks. skogsarbeid, tungt jordbruksarb., tungt bygningsarb.)

- Har De i løpet av de siste 12 mnd måttet flytte fra hjemstedet på grunn av forandring i arbeidssituasjonen? 72
- Er husmorarbeid Deres hovedyrke? 73
- Har De i løpet av de siste 12 mnd fått arbeidsledighetstrygd? 74
- Er De for tiden sykmeldt, eller får De attføringspenger? 75
- Har De full eller delvis uførepensjon? .. 76

F

- Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)? . 77
- Er to eller flere av Deres besteforeldre av finsk ætt? 78
- Er to eller flere av Deres besteforeldre av samisk ætt? 79

English translation of the questionnaire used in the cardiovascular disease study in Oslo* 1972-73, Norwegian counties 1974-78 (Finnmark, Oppland and Sogn og Fjordane) and Tromsø 1974.

English translation; Mr. Kevin McCafferty

Tick "yes/no" or "yes", as appropriate.

Part A

Have you, or have you had:
- a heart attack?
- angina pectoris (heart cramp)?
- any other heart disease?
- hardened arteries in the legs?
- a cerebral stroke?
- diabetes?

Are you being treated for:
- high blood pressure?

Do you use:
- nitroglycerine?

Part B

Do you have pain or discomfort in the chest when:
- walking up hills or stairs, or walking fast on level ground?
- walking at normal pace on level ground?

If you get pain or discomfort in the chest when walking, do you usually:
- (1) stop?
- (2) slow down?
- (3) carry on at the same pace?

If you stop or slow down, does the pain disappear:
- (1) within 10 minutes?
- (2) after more than 10 minutes?

Do you have pain in the calf while:
- walking?
- resting?

If you get pain in the calf, then:
- does the pain increase when you walk faster or uphill?
- does the pain disappear if you stop?

Do you usually have:
- cough in the morning?
- phlegm chest in the morning?

Part C

Exercise and physical exertion in *leisure time*. If your activity varies much, for example between summer and winter, then give an average. The questions refer only to the last twelve months.

Tick "YES" beside the description that fits best:
- (1) Reading, watching TV, or other sedentary activity?
- (2) Walking, cycling, or other forms of exercise at least 4 hours a week? (including walking or cycling to place of work, Sunday-walking, etc.)
- (3) Participation in recreational sports, heavy gardening, etc.? (note: duration of activity at least 4 hours a week).
- (4) Participation in hard training or sports competitions, regularly several times a week?

Part D*

Do you smoke daily at present?
If "Yes":
- Do you smoke cigarettes daily? (handrolled or factory made)

If you do not smoke cigarettes at present:
- Have you previously smoked cigarettes daily?

If "Yes", how long is it since you stopped?
- (1) Less than 3 months?
- (2) 3 months to 1 year?
- (3) 1 to 5 years?
- (4) More than 5 years?

For those who smoke or have smoked previously:

How many years altogether have you smoked daily? Number of years .....

How many cigarettes do you, or did you, smoke daily? Give number of cigarettes per day (handrolled + factory made)

Number of cigarettes .....

Do you smoke tobacco products other than cigarettes daily?

- cigars or cigarillos?
- a pipe?

If you smoke a pipe, how many packs of tobacco (50 grams) do you smoke per week? Give average number of packs per week.

Number of tobacco packs .....

Part E

Do you usually work shifts or at night?

Can you usually come home from work:

- every day?
- every weekend?

Are there periods during which your working days are longer than usual? (e.g.: fishing season, harvest)

*In Oslo preset groups of cigarettes smoked per day and packs of pipe tobacco smoked per day (see original questionnaire)

During the last year, have you had: (Tick "YES" beside description that fits best):

(1) mostly sedentary work? (e.g., office work, watchmaker, light manual work)
(2) work that requires a lot of walking? (e.g., shop assistant, light industrial work, teaching)
(3) work that requires at lot of walking and lifting? (e.g., postman, heavy industrial work, construction)
(4) heavy manual labour? (e.g., forestry, heavy farmwork, heavy construction)

During the last 12 months, have you had to move house for work reasons?

Is housekeeping your main occupation?

Have you within the last 12 months received unemployment benefit?

Are you at present on sick leave, or receiving rehabilitation allowance?

Do you receive a complete or partial disability pension?

Part F (alternatives: yes, no, don't know)

Have one or more of your parents or sisters or brothers had a heart attack (heart wound) or angina pectoris (heart cramp)?

In Finnmark and Tromsø only:

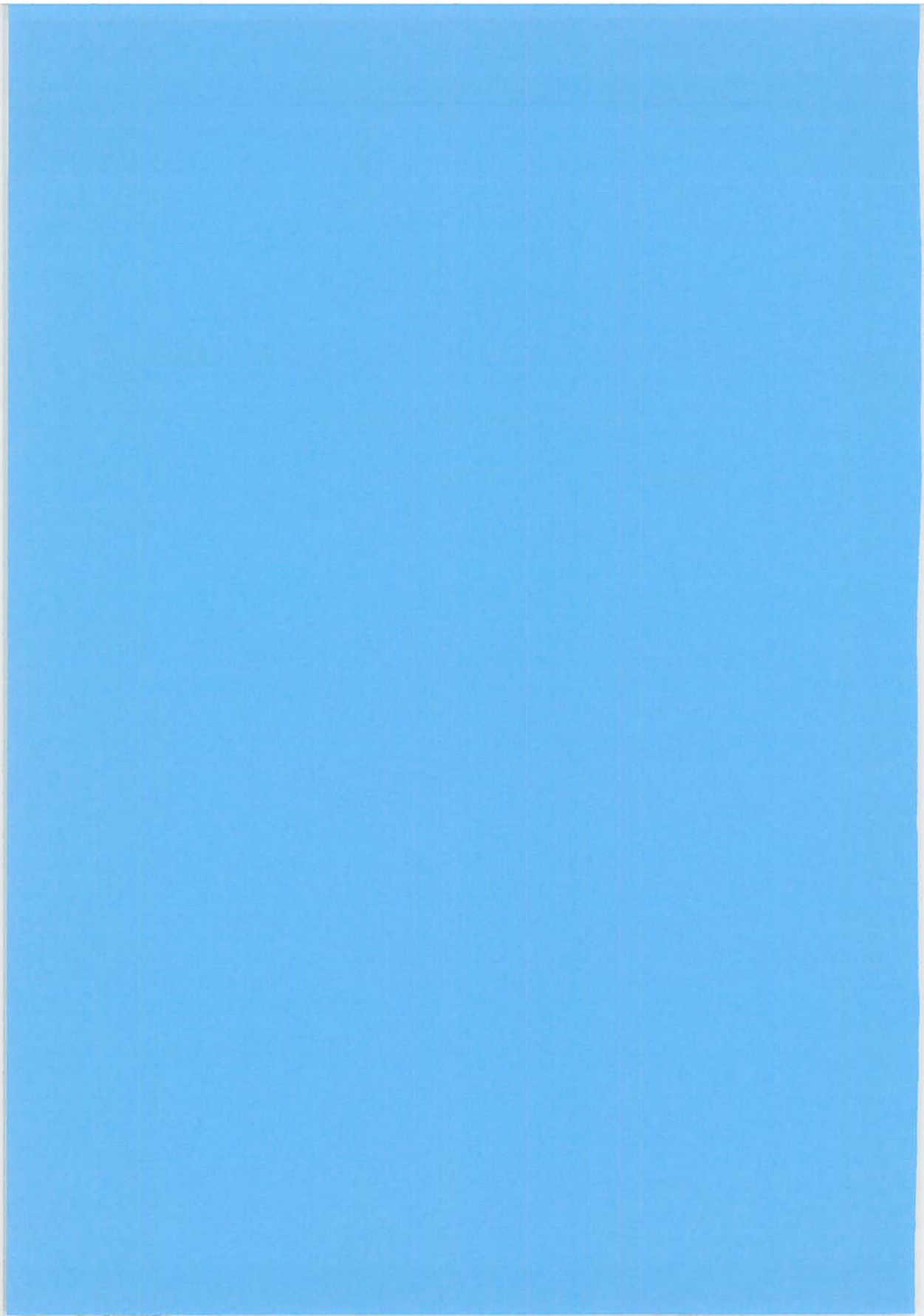
Are two or more of your grandparents of Finnish origin?

Are two or more of your grandparents of Lapp origin?

APPENDIX C

Questionnaire I Tromsø Study 1979-1980

Original Norwegian version and English translation



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Tid og sted for Deres frammøte vil De finne nedenfor.

Denne gangen vil en del av befolkningen få tilbud om hjerte-karundersøkelse. De tilhører denne gruppe. En orientering om undersøkelsen er gitt i vedlagte brosjyre.

Vennligst fyll ut spørreskjemaet på baksiden og ta det med til undersøkelsen. Ta også med tuberkulinkort eller helsebok, om De har.

Fravær bes meldt på vedlagte seddel.

Med hilsen

TROMSØ HELSERÅD FYLKESLEGEN I TROMS
FAGOMRÅDET MEDISIN, UNIVERSITETET I TROMSØ
STATENS SKJERMBILDEFOTOGRAFERING

Født dato	Personnr.	Kommune	Kretsnr.	
		TROMSØ	05	108

Møtested	Kjønn	Første bokstav etternavn	Dag og dato	Klokkeslett

A

Har De, eller har De hatt:

- Hjerteinfarkt? 33
- Angina pectoris (hjertekrampe)? 34
- Annen hjertesykdom? 35
- Åreforkalkning i bena? 36
- Hjerneslag? 37
- Sukkersyke? 38

Er De under behandling for:

- Høyt blodtrykk? 39

Bruker De:

- Nitroglycerin? 40

B

Får De smerter eller ubehag i brystet når De:

- Går i bakker, trapper eller fort på flat mark? 41
- Går i vanlig takt på flat mark? 42

Hvis De får smerter eller ubehag i brystet ved gange, pleier De da å:

- 1 Stanse? 43
- 2 Saktne farten? .....
- 3 Fortsette i samme takt? .....

Hvis De stanser eller saktner farten, forsvinner smertene da:

- 1 Etter mindre enn 10 minutter? 44
- 2 Etter mer enn 10 minutter? ....

Får De smerter i tykkleggen når De:

- Går? 45
- Er i ro? 46

Hvis De får leggsmerter, besvar da:

- Forverres smertene ved raskere tempo eller i bakker? 47
- Gir smertene seg når De stopper? .. 48

Har De vanligvis:

- Hoste om morgenen? 49
- [illegible] om morgenen? .. 50

C

Bevegelse og kroppslig anstrengelse i Deres fritid.
Hvis aktiviteten varierer meget f.eks. mellom sommer og vinter så ta et gjennomsnitt.

Spørsmålet gjelder bare det siste året.

Sett kryss i den ruten hvor „JA" passer best.

1 Leser, ser på fjernsyn eller annen stillesittende beskjeftigelse? 51

2 Spaserer, sykler eller beveger Dem på annen måte minst 4 timer i uken? ..
(Heri medregnes også gang eller sykling til arbeidestedet, søndagsturer m.m.

3 Driver mosjonsidrett, tyngre hagearbeid e.l.? .....
(Merk at yirksomheten skal være minst 4 timer i uken.

4 Trener hardt eller driver konkurranseidrett, regelmessig og flere ganger i uken? .....

G

Har noen i Deres husstand (utenom Dem selv) vært innkalt til nærmere undersøkelse hos distriktslegen etter forrige hjerte-kar undersøkelse? 80

D

Røyker De daglig for tiden? 52

Hvis svaret var „JA" på forrige spørsmål, besvar da:

Røyker De sigaretter daglig? 53
(håndrullede eller fabrikkframstilte)

Hvis De ikke røyker sigaretter nå, besvar da:

Har De røykt sigaretter daglig tidligere? . 54

Hvis De svarte „JA", hvor lenge er det siden De sluttet?

- 1 Mindre enn 3 måneder? 55
- 2 3 måneder - 1 år? .....
- 3 1 - 5 år? .....
- 4 Mer enn 5 år? .....

Besvares av dem som røyker nå eller har røykt tidligere:

Hvor mange år tilsammen har De røykt daglig? ..... 56-57 Antall år

Hvor mange sigaretter røyker eller røykte De daglig? Oppgi antall pr. dag 58-60 Ant. sigaretter
(håndrullede + fabrikkframstilte)

Røyker De noe annet enn sigaretter daglig?

Sigarer eller sarutter/cigarillos? ... 62

Pipe? 63

Hvis De røyker pipe, hvor mange pakker tobakk (50 gram) bruker De i pipa pr. uke? Ant. tobakkpk.

Oppgi gjennomsnittlig antall pakker pr. uke. 64-66

E

Har De vanligvis skiftarbeid eller nattarbeid? 67

Kan De vanligvis komme hjem fra arbeidet:

- Hver dag? 68
- Hver helg? 69

Har De i perioder lengre arbeidsdager enn vanlig? 70
(f.eks. under sesongfiske, onnearbeid)

Har De i løpet av siste året hatt:

Sett kryss i den ruten hvor „JA" passer best.

1 Overveiende stillesittende arbeid? .. 71
(f.eks. skrivebordsarb., urmakerarb, montering)

2 Arbeid som krever at De går mye? .
(f.eks. ekspeditørarb, lett industriarb., undervisn)

3 Arbeid hvor De går og løfter mye? ..
(f.eks. postbud, tyngre industriarb, bygningsarb)

4 Tungt kroppsarbeid? .....
(f.eks skogsarbeid, tungt jordbruksarb, tungt bygningsarb)

Har De i løpet av de siste 12 mnd måttet flytte fra hjemstedet på grunn av forandring i arbeidssituasjonen? 73

Er husmorarbeid Deres hovedyrke? 75

Har De i løpet av de siste 12 mnd fått arbeidsledighetstrygd? 74

Er De for tiden sykmeldt, eller får De attføringspenger? 75

Har De full eller delvis uførepensjon? .. 76

F

Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)? . 77

Er to eller flere av Deres besteforeldre av finsk ætt? 78

Er to eller flere av Deres besteforeldre av samisk ætt? 79

English translation of the questionnaire used in the cardiovascular disease study in Norwegian counties 1977-83 (Finnmark, Sogn og Fjordane, Oppland) and Tromsø 1979-80

English translation; Mrs. Anne Clancy and Mr. Kevin McCafferty

Tick "yes/no" or "yes", as appropriate.

Part A

Have you, or have you had:
- a heart attack?
- angina pectoris (heart cramp)?
- any other heart disease?
- arteriosclerosis of the legs?
- a cerebral stroke?
- diabetes?

Are you being treated for:
- high blood pressure?

Do you use:
- nitroglycerine?

Part B

Do you have pain or discomfort in the chest when:
- walking up hills or stairs, or walking fast on level ground?
- walking at normal pace on level ground?

If you get pain or discomfort in the chest when walking, do you usually:
- (1) stop?
- (2) slow down?
- (3) carry on at the same pace?

If you stop or slow down, does the pain disappear:
- (1) within 10 minutes?
- (2) after more than 10 minutes?

Do you have pain in the calf while:
- walking?
- resting?

If you get pain in the calf, then:
- does the pain increase when you walk faster or uphill?
- does the pain disappear if you stop?

Do you usually have:
- cough in the morning?
- phlegm chest in the morning?

Part C

Exercise and physical exertion in *leisure time*. If your activity varies much, for example between summer and winter, then give an average. The questions refer only to the last twelve months.

Tick "YES" beside the description that fits best:
- (1) Reading, watching TV, or other sedentary activity?
- (2) Walking, cycling, or other forms of exercise at least 4 hours a week? (including walking or cycling to place of work, Sunday-walking, etc.)
- (3) Participation in recreational sports, heavy gardening, etc.? (note: duration of activity at least 4 hours a week).
- (4) Participation in hard training or sports competitions, regularly several times a week?

Part D

Do you smoke daily at present?
If "Yes":
Do you smoke cigarettes daily? (handrolled or factory made)

If you do not smoke cigarettes at present:
Have you previously smoked cigarettes daily?

If "Yes", how long is it since you stopped?
- (1) Less than 3 months?
- (2) 3 months to 1 year?
- (3) 1 to 5 years?
- (4) More than 5 years?

For those who smoke or have smoked previously:
How many years altogether have you smoked daily? *Number of years* .....

How many cigarettes do you, or did you, smoke daily? Give number of cigarettes per day (handrolled + factory made)

Number of cigarettes .....

Do you smoke tobacco products other than cigarettes daily?
- cigars or cigarillos?
- a pipe?

If you smoke a pipe, how many packs of tobacco (50 grams) do you smoke per week? Give average number of packs per week.

Number of tobacco packs .....

Part E

Do you usually work shifts or at night?
Can you usually come home from work:
- every day?
- every weekend?

Are there periods during which your working days are longer than usual? (e.g.: fishing season, harvest)

During the last year, have you had: (Tick "YES" beside description that fits best):
(1) mostly sedentary work? (e.g., office work, watchmaker, light manual work)
(2) work that requires a lot of walking? (e.g., shop assistant, light industrial work, teaching)
(3) work that requires at lot of walking and lifting? (e.g., postman, heavy industrial work, construction)
(4) heavy manual labour? (e.g., forestry, heavy farmwork, heavy construction)

During the last 12 months, have you had to move house for work reasons?
Is housekeeping your main occupation?
Have you within the last 12 months received unemployment benefit?
Are you at present on sick leave, or receiving rehabilitation allowance?
Do you receive a complete or partial disability pension?

Part F (alternatives: yes, no, don't know)

Have one or more of your parents or sisters or brothers had a heart attack (heart wound) or angina pectoris (heart cramp)?

In Finnmark and Tromsø only:
Are two or more of your grandparents of Finnish origin?
Are two or more of your grandparents of Lapp origin?

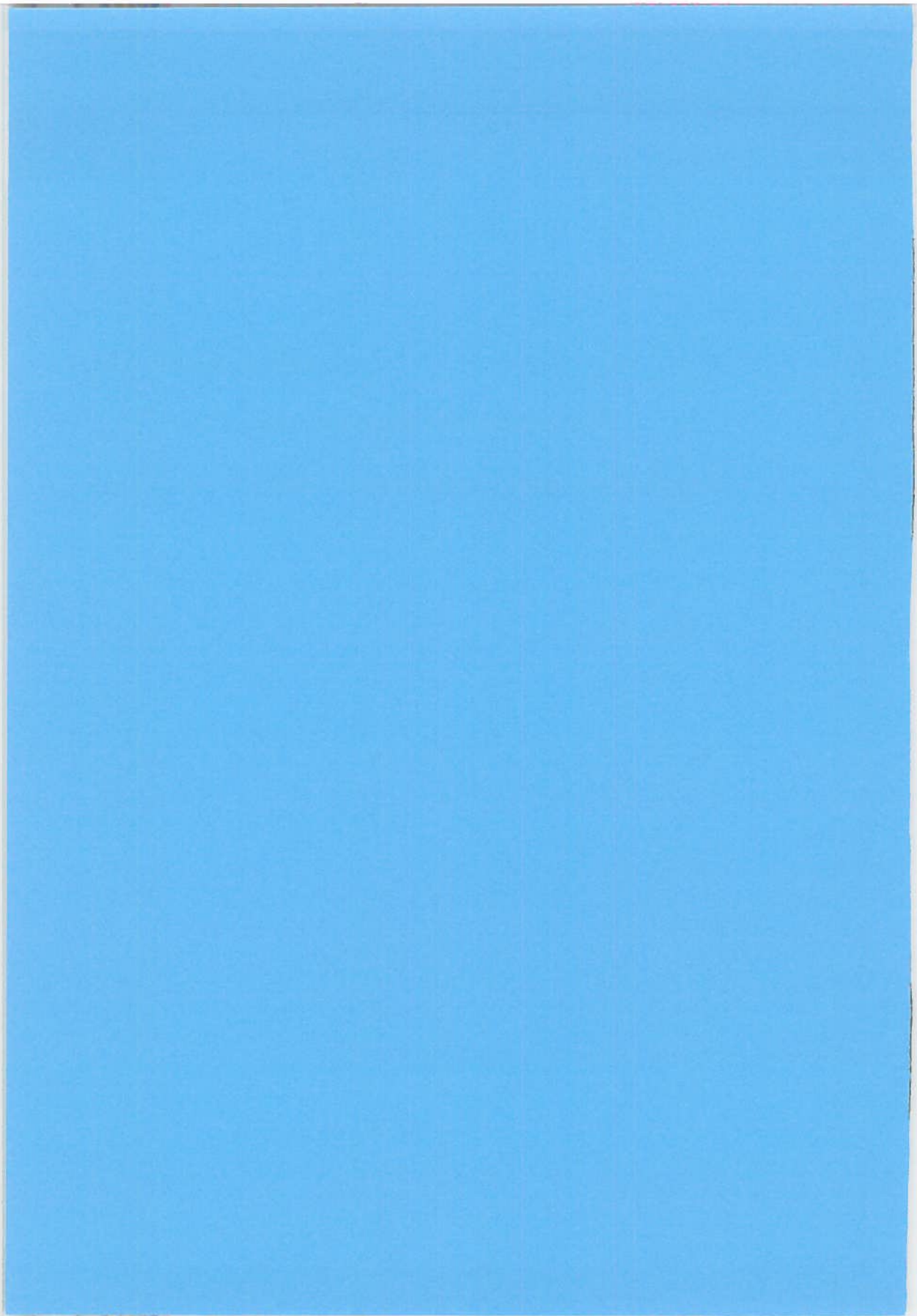
Part G

Has anyone in your household (other than yourself), been called in to a doctor for further medical examination after the previous cardiovascular disease survey?

APPENDIX D

Questionnaire I Tromsø Study 1986-1987

Original Norwegian version and English translation



HELSEUNDERSØKELSEN I TROMSØ

(Gjelder bare den person som brevet er adressert til.)

Helseundersøkelsen kommer nå til Deres distrikt.

Tid og sted for frammøte vil De finne nedenfor.

De finner en orientering om undersøkelsen i den vedlagte brosjyren.

Vi ber Dem vennligst fylle ut spørreskjemaet på baksiden og ta med dette til undersøkelsen.

Vi ber Dem eventuelt melde fra om fravær på den vedlagte fraværsmeldingen.

Med hilsen

KOMMUNEHELSETJENESTEN I TROMSØ
FYLKESLEGEN I TROMS UNIVERSITETET I TROMSØ
STATENS HELSEUNDERSØKELSER

Født dato | Personnr. | Kommune | Kretsnr.

Møtested | Kjønn | Første bokstav i etternavn | Dag og dato | Klokkeslett

HØYDE ␣␣␣ VEKT ␣␣␣␣ ANM 70 ␣	M ␣ P ␣ Ø ␣ KODE 75 ␣␣	AVVIK ␣ ARM ␣␣ MAN ␣ APP.NR. ␣␣ TSH 82 ␣
MÅLING 1	**MÅLING 2**	**MÅLING 3**
MAR ␣ 85 S ␣ 88	MAR ␣ 91 S ␣ 94	MAR ␣ 97 S ␣ 100
HR ␣ 103 D ␣ 106	HR ␣ 109 D ␣ 112	HR ␣ 115 D ␣ 118

A FAMILIE

	JA	NEI	VET IKKE
Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)? 12			

B EGEN SYKDOM

	JA	NEI
Har De, eller har De hatt:		
Hjerteinfarkt? 13		
Angina pectoris (hjertekrampe)? 14		
Hjerneslag? 15		
Sukkersyke? 16		
Er De under behandling for:		
Høyt blodtrykk? 17		
Bruker De:		
Nitroglycerin? 18		

C SYMPTOMER

	JA	NEI
Får De smerter eller ubehag i brystet når De:		
Går i bakker, trapper eller fort på flat mark? 19		
Går i vanlig takt på flat mark? 20		
Dersom De får smerter eller vondt i brystet ved gange, pleier De da:		
Stoppe? 21	1	
Saktne farten?	2	
Fortsette i samme takt?	3	
Dersom De stopper eller saktner farten, går da smertene bort:		
Etter mindre enn 10 minutter? 22	1	
Etter mer enn 10 minutter?	2	
Har De vanligvis:	JA	NEI
Hoste om morgenen? 23		
Oppspytt fra brystet om morgenen? 24		

D MOSJON

Bevegelse og kroppslig aktivitet i Deres fritid. Dersom aktiviteten varierer mye, f.eks. mellom sommer og vinter, så ta ett gjennomsnitt. Spørsmålet gjelder bare det siste året.

Sett kryss i den ruten som passer best.

Leser, ser på fjernsyn eller annen stillesittende beskjeftigelse? 25	1
Spaserer, sykler eller beveger Dem på annen måte minst 4 timer i uken? ..... (Her skal De også regne med gang eller sykling til arbeidsstedet, søndagsturer m.m.)	2
Driver mosjonsidrett, tyngre hagearbeid e.l.? .. (Merk at aktiviteten skal vare i minst 4 timer i uken.)	3
Trener hardt eller driver konkurranseidrett regelmessig og flere ganger i uken?	4

E SALT/FETT

Hvor ofte bruker De salt kjøtt eller salt fisk til middag?

Sett kryss i den ruten som passer best.

Aldri eller sjeldnere enn en gang i måneden 25	1
Inntil en gang i uken	2
Inntil to ganger i uken	3
Mer enn to ganger i uken	4

Hvor ofte pleier De å strø ekstra salt på middagsmaten?

Sett kryss i den ruten som passer best.

Sjelden eller aldri 27	1
Av og til eller ofte	2
Alltid eller nesten alltid	3

Hva slags margarin eller smør bruker De vanligvis på brødet?

Sett kryss i den ruten som passer best.

Bruker ikke smør eller margarin på brød 28	1
Smør	2
Hard margarin	3
Myk (Soft) margarin	4
Smør/margarin blanding	5

Hva slags fett blir vanligvis brukt til matlaging i husholdningen Deres?

Sett kryss i den ruten som passer best.

Smør eller hard margarin 29	1
Myk (Soft) margarin eller olje	2
Smør/margarin blanding	3

F RØYKING

	JA	NEI
Røyker De daglig for tida? 30		
Dersom svaret er «JA», svar da på dette:		
Røyker De sigaretter daglig? ..... 31 (håndrullede eller fabrikkfremstilte)		
Dersom De ikke røyker sigaretter nå, svar da på dette:		
Har De røykt sigaretter daglig tidligere? 32		
Dersom De svarte «JA», hvor lenge er det da siden De sluttet?		
Mindre enn 3 måneder? 33	1	
3 måneder – 1 år?	2	
1–5 år?	3	
Mer enn 5 år?	4	
Skal besvares av de som røyker nå eller som har røykt tidligere:		
Hvor mange år til sammen har De røykt daglig? 34		År
Hvor mange sigaretter røyker eller røykte De daglig?		
Gi opp antallet sigaretter daglig ..... 36 (håndrullede + fabrikkframstilte)		Sigaretter
Røyker De noe annet enn sigaretter daglig?		
Sigarer eller serutter/sigarillos? 40		
Pipe? 41		
Dersom De røyker pipe, hvor mange pakker tobakk (50 gram) bruker De i pipen på en uke?		
Gi opp gjennomsnittlig tall på pakker i uken 42		Tobakkspk.

G KAFFE

Hvor mange kopper kaffe drikker De vanligvis hver dag?

Sett kryss i den ruten som passer best.

Drikker ikke kaffe, eller mindre enn en kopp 45	1
1 – 4 kopper	2
5 – 8 kopper	3
9 eller flere kopper	4

Hva slags kaffe drikker De vanligvis hver dag?

Kokekaffe 46	
Filterkaffe 47	
Pulverkaffe 48	
Koffeinfri kaffe 49	
Drikker ikke kaffe 50	

H ARBEID

	JA	NEI
Har De i de siste 12 månedene fått arbeidsledighetstrygd? 51		
Er De for tiden sykemeldt, eller får De attføringspenger? 52		
Har De full eller delvis uførepensjon? 53		
Har De vanligvis skiftarbeid eller nattarbeid 54		

Har De i det siste året hatt:

Sett kryss i den ruten som passer best.

For det meste stillesittende arbeid? ..... 55 (f.eks. skrivebordsarb., urmakerarb., montering)	1
Arbeide som krever at De går mye? ..... (f.eks. ekspeditørarb., lett industriarb., undervisn.)	2
Arbeide der De går og løfter mye? ..... (f.eks. postbud, tyngre industriarb., bygningsarb.)	3
Tungt kroppsarbeid? ..... (f.eks. skogsarb., tungt jordbruksarb., tungt bygningsarb.)	4

	JA	NEI
Er husmorarbeid hovedyrket Deres? 56		

I ETTERUNDERSØKELSE

Har noen i husstanden Deres (utenom Dem selv) vært innkalt til nærmere undersøkelse hos lege etter den siste hjertekarundersøkelsen? 57	
Dersom denne helseundersøkelsen viser at De bør undersøkes nærmere: Hvilken almenpraktiserende lege ønsker De da å bli henvist til?	
Skriv navnet på legen her → 58	Ikke skriv her
Ingen spesiell lege	

QUESTIONNAIRE I, TROMSØ SURVEY 1986-87

English translation; Mrs. Anne Clancy and Mr. Kevin McCafferty

A FAMILY

Have one or both of your parents, or any of your siblings (brothers and sisters) had a heart attack or angina pectoris (heart cramp)?

	Yes	*No*	*Don't know*
	☐	☐	☐

B OWN ILLNESSES

Have you, or have you had:	*Yes*	*No*
A heart attack?	☐	☐
Angina pectoris (heart cramp) ?	☐	☐
A cerebral stroke?	☐	☐
Diabetes?	☐	☐

Are you receiving treatment for:	*Yes*	*No*
High blood pressure?	☐	☐
Do you use nitroglycerine?	☐	☐

C SYMPTOMS

Do you get pain or discomfort in the chest, when:	*Yes*	*No*
Walking up hills, stairs or walking fast on level ground?	☐	☐
Walking at ordinary pace on level ground?	☐	☐

If you get pain or discomfort in your chest when walking, do you usually :

	Yes
Stop	☐
Slow down	☐
Carry on at the same pace	☐

If you stop or slow down, does the pain disappear:

	Yes
After less than 10 minutes?	☐
After more than 10 minutes?	☐

D EXERCISE

Exercise and physical exertion in leisure time. If your activity varies much, for example between summer and winter, then give an average. The questions refer only to the last twelve months.

Tick "yes" in the most appropriate box:

	Yes
- Reading , watching TV or other sedentary activity?	☐
- Walking, cycling or other forms of exercise at least 4 hours a week? (including walking or cycling to place of work, Sunday walking ,etc.)	☐
- Participation in recreational sports, heavy gardening, etc.? (Note: duration of activity at least 4 hours a week)	☐
- Participation in hard training or sports competitions regularly several times a week?	☐

E SALT/ FAT

How often do you use salted meat or salted fish for dinner?

Tick the appropriate box	*Yes*
Never or less than once a month	☐
Once a week or less	☐
Twice a week or less	☐
More than twice a week	☐

How often do you add extra salt to your dinner ?

Tick the appropriate box	*Yes*
Rarely or never	☐
Sometimes or often	☐
Always or nearly always	☐

What type of margarine or butter do you usually use on your bread?

Tick the most appropriate box	*Yes*
Do not use margarine or butter on bread	☐
Butter	☐
Margarine	☐
Soft (soya) margarine spread	☐
Butter/ margarine mixtures	☐

What type of cooking fat do you normally use in your household ?

Tick the appropriate box.	*Yes*
Butter or hard margarine	☐
Soft (soya) margarine or oil	☐
Butter/ margarine mixtures	☐

F SMOKING

Do you smoke daily at present?	*Yes*	*No*

If "*Yes* ": ☐ ☐
Do you smoke cigarettes daily? ☐ ☐
(hand-rolled or factory made)
If you do not smoke cigarettes at present:

Have you previously smoked cigarettes on a daily basis?	*Yes* ☐	*No* ☐

If "*Yes*", how long is it since you gave up smoking ?

	Yes
More than 3 months?	☐
3 months to 1 year?	☐
1 - 5 years?	☐
More than 5 years?	☐

The following questions are to be answered by those who smoke at present or who have smoked previously.
How many years altogether have you smoked on a daily basis: .....

How many cigarettes do you smoke or did you smoke daily: .....
(hand-rolled + factory made)

Do you smoke anything else other than cigarettes daily?

	Yes
Cigars, cigarillos, cheroots ?	☐
Pipe?	☐

If you smoke a pipe, how many packets of tobacco (50 gr.) do you smoke in a week?
Give the average number of packets a week: .....

G COFFEE

How many cups of coffee do you usually drink daily?

Tick the most appropriate box	*Yes*
Do not drink coffee, or less than one cup	☐
1 - 4 cups	☐
5 - 8 cups	☐
9 or more cups	☐

What type of coffee do you usually drink daily?

Coarse ground coffee for brewing (boiled)	☐
Finely ground filter coffee	☐
Instant coffee	☐
Caffeine free coffee	☐
Do not drink coffee	☐

H EMPLOYMENT

Have you received unemployment benefit within the past 12 months?	*Yes* ☐	*No* ☐
Are you at present on sick leave, or receiving rehabilitation allowance?	☐	☐
Are you on a full time or partial disability pension?	*Yes* ☐	*No* ☐
Do you usually work shifts or do night work?	☐	☐

During the past year have you had :

Tick the most appropriate box.	*Yes*
- Mostly sedentary work? (office work, watchmaker, light manual work)	☐
- Work requiring a lot of walking? (shop assistant, light industrial work, teaching)	☐
- Work requiring a lot of walking and lifting? (postman, heavy industrial work, construction)	☐
- Heavy manual labour? (forestry, heavy farmwork, heavy construction)	☐

Is house-keeping your main occupation?	*Yes* ☐	*No* ☐

I FOLLOW - UP EXAMINATION

Has any one in your household (other than yourself) been called in to a doctor for further medical examination after the previous cardiovascular disease survey?	*Yes* ☐	*No* ☐

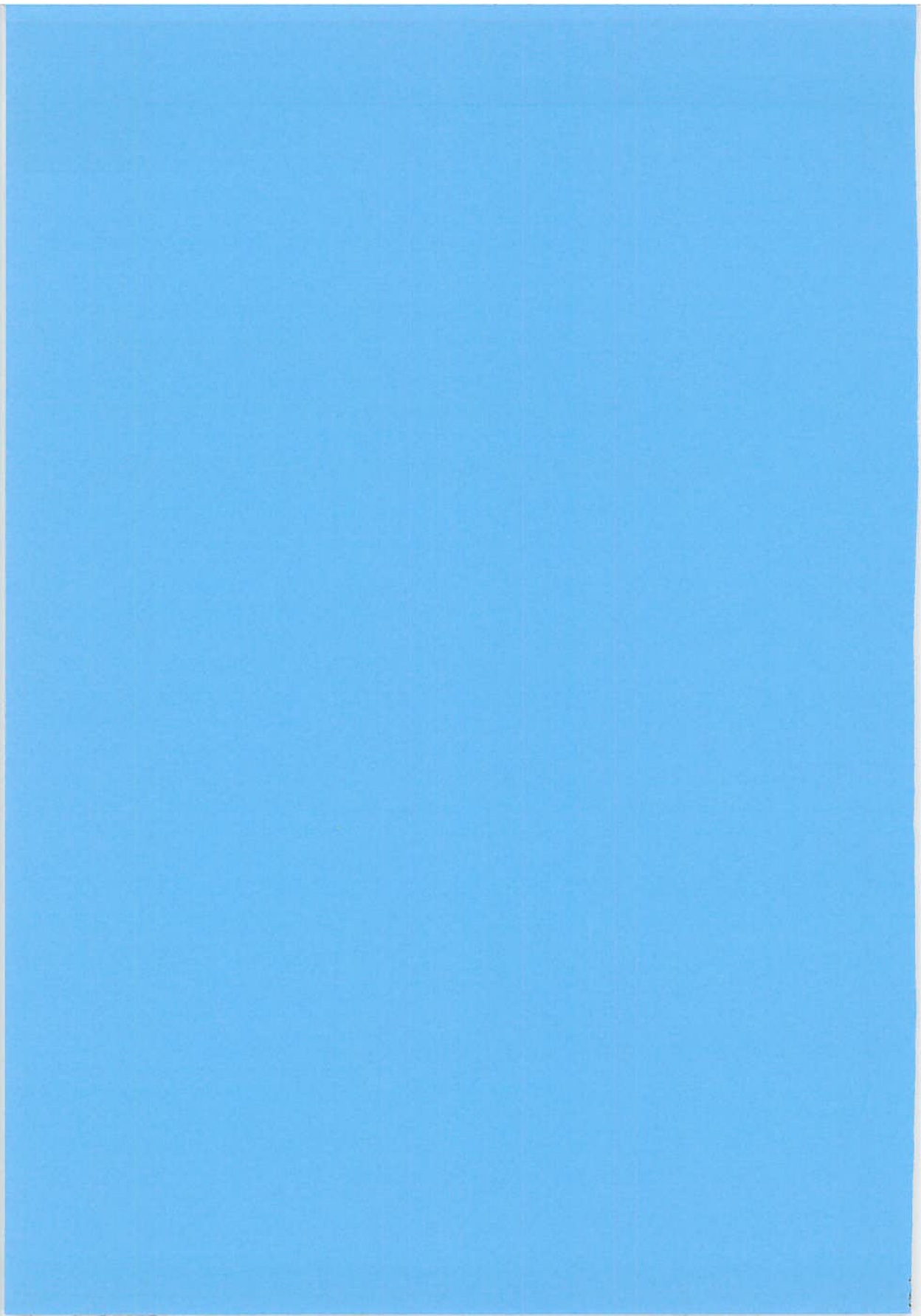
If as a result of this survey you need further medical examination, which general practitioner do you wish to be referred to ?
Write the doctor's name here:
.....

No particular doctor .....

APPENDIX E

Questionnaire I Tromsø Study 1994-1995

Original Norwegian version and English translation



Innbydelse til
HELSEUNDERSØKELSEN

Fødselsdato Personnr. Kommune Kretsnr.

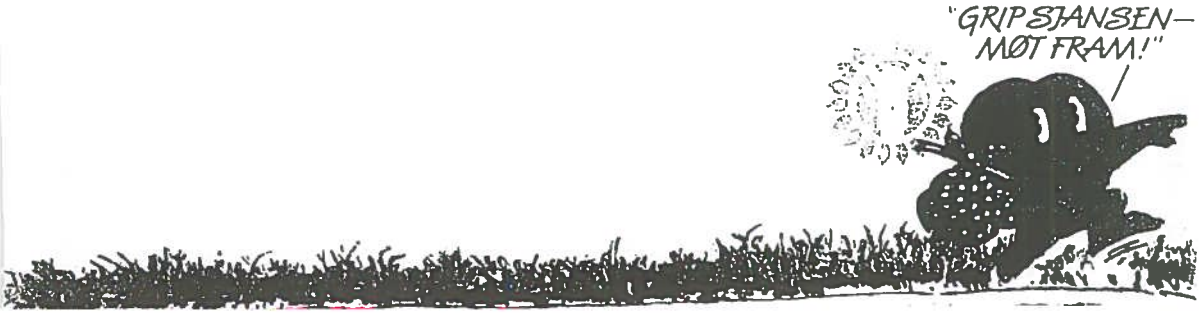
Velkommen til helseundersøkelsen i Tromsø!

Helseundersøkelsen kommer nå til Tromsø. Tid og sted for frammøte finner du nedenfor. Du finner også en orientering om undersøkelsen i den vedlagte brosjyren.

Vi ber deg fylle ut spørreskjemaet på baksiden og ta det med til undersøkelsen.

Undersøkelsen blir mest verdifull om frammøtet blir så fullstendig som mulig. Vi håper derfor at du har mulighet til å komme. Møt selv om du kjenner deg frisk, om du er under legebehandling, eller om du har fått målt kolesterol og blodtrykk i den senere tid.

Vennlig hilsen
Kommunehelsetjenesten
Fagområdet medisin, Universitetet i Tromsø
Statens helseundersøkelser



EGEN HELSE

Hvordan er helsen din nå? *Sett bare ett kryss.*

Dårlig	12	1
Ikke helt god		2
God		3
Svært god		4

Har du, eller har du hatt:

	JA	NEI	Alder første gang
Hjerteinfarkt 13			år
Angina pectoris (hjertekrampe) 16			år
Hjerneslag/hjerneblødning 19			år
Astma 22			år
Diabetes (sukkersyke) 25			år

Bruker du medisin mot høyt blodtrykk?

Nå 28		1
Før, men ikke nå		2
Aldri brukt		3

Har du i løpet av det siste året vært plaget med smerter og/eller stivhet i muskler og ledd som har vart i minst 3 måneder sammenhengende? 29 — JA / NEI

Har du de siste to ukene følt deg:

	Nei	Litt	En god del	Svært mye
Nervos og urolig? 30				
Plaget av angst? 31				
Trygg og rolig? 32				
Irritabel? 33				
Glad og optimistisk? 34				
Nedfor/deprimert? 35				
Ensom? 36				
	1	2	3	4

RØYKING

Røykte noen av de voksne hjemme da du vokste opp? 37 — JA / NEI

Bor du, eller har du bodd, sammen med noen dagligrøykere etter at du fylte 20 år? 38 — JA / NEI

Hvis "JA", hvor mange år tilsammen? 39 — Antall år

Hvor lenge er du vanligvis daglig tilstede i røykfylt rom? 41 — Antall timer
Sett 0 hvis du ikke oppholder deg i røykfylt rom.

Røyker du selv: — JA / NEI

Sigaretter daglig?	43
Sigarer/sigarillos daglig?	44
Pipe daglig?	45

Hvis du har røykt daglig tidligere, hvor lenge er det siden du sluttet? 46 — Antall år

Hvis du røyker daglig nå eller har røykt tidligere:

Hvor mange sigaretter røyker eller røykte du vanligvis daglig? 48 — Antall sigaretter

Hvor gammel var du da du begynte å røyke daglig? 52 — Alder år

Hvor mange år tilsammen har du røykt daglig? 54 — Antall år

MOSJON

Hvordan har din fysiske aktivitet i fritiden vært det siste året? *Tenk deg et ukentlig gjennomsnitt for året.*
Arbeidsvei regnes som fritid.

	Timer pr. uke: Ingen	Under 1	1-2	3 og mer
Lett aktivitet *(ikke svett/andpusten)* 56				
Hard fysisk aktivitet *(svett/andpusten)* 57				
	1	2	3	4

KAFFE

Hvor mange kopper kaffe drikker du daglig?
Sett 0 hvis du ikke drikker kaffe daglig.

Kokekaffe	58	Antall kopper
Annen kaffe	60	Antall kopper

ALKOHOL

Er du total avholdsmann/-kvinne? 62 — JA / NEI

Hvor mange ganger i måneden drikker du vanligvis alkohol? *Regn ikke med lettøl.*
Sett 0 hvis mindre enn 1 gang i mnd. 63 — Antall ganger

Hvor mange glass øl, vin eller brennevin drikker du vanligvis i løpet av to uker? 65
Regn ikke med lettøl.
Sett 0 hvis du ikke drikker alkohol.

Øl	Vin	Brennevin
glass	glass	glass

FETT

Hva slags margarin eller smør bruker du vanligvis på brødet? *Sett ett kryss.*

Bruker ikke smør/margarin	71	1
Meierismør		2
Hard margarin		3
Blot (soft) margarin		4
Smør/margarin blanding		5
Lettmargarin		6

UTDANNING/ARBEID

Hvilken utdanning er den høyeste du har fullført?

Grunnskole, 7-10 år, framhaldsskole, folkehøgskole	72	1
Realskole, middelskole, yrkesskole, 1-2-årig videregående skole		2
Artium, ok.gymnas, allmennfaglig retning i videregående skole		3
Høgskole/universitet, mindre enn 4 år		4
Høgskole/universitet, 4 år eller mer		5

Hva slags arbeidssituasjon har du nå?

Lønnet arbeid	73	
Hellids husarbeid	74	
Utdanning, militærtjeneste	75	
Arbeidsledig, permittert	76	

Hvor mange timer lønnet arbeid har du i uka? 77 — Antall timer

Mottar du nå noen av følgende ytelser?

Syketrygd (sykmeldt)	79	
Attføring	80	
Uførepensjon	81	
Alderspensjon	82	
Sosialstønad	83	
Arbeidsløshetstrygd	84	

SYKDOM I FAMILIEN

Har en eller flere av foreldre eller søsken hatt hjerteinfarkt (sår på hjertet) eller angina pectoris (hjertekrampe)? 85

JA	NEI	VET IKKE

English translation of invitation with the first questionnaire used in the health survey in Tromsø 1994/95

Translation based on translations by Kevin McCafferty and Anne Clancy

HEALTH SURVEY
INVITATION

"This is your chance"

Date of birth Social security No.

Municipality Electoral ward No.

Welcome to the Tromsø Health Survey!

The Health Survey is coming to Tromsø. This leaflet will tell you when and where. You will also find information about the survey in the enclosed brochure.

We would like you to fill in the form overleaf and take it with you to the examination.

The more people take part in the survey, the more valuable its results will be. We hope, therefore, that you will be able to come. Come along even if you feel healthy, if you are currently receiving medical treatment, or if you have had your cholesterol and blood pressure levels taken recently.

Yours sincerely,
Municipal Health Authorities
Faculty of Medicine - University of Tromsø
National Health Screening Service

"This is a real opportunity — Take it!"

Your own health

What is your current state of health?
Tick one box only.

- Poor ☐
- Not so good ☐
- Good ☐
- Very good ☐

Do you have, or have you ever had:

	YES	NO	Age first time
Myocardial infarction	☐	☐	_____ years
Angina pectoris	☐	☐	_____ years
Stroke/ brain haemorrhage	☐	☐	_____ years
Asthma	☐	☐	_____ years
Diabetes	☐	☐	_____ years

Do you take medicine for high blood pressure?

- At the moment ☐
- Used to, but not any longer ☐
- Never have ☐

Have you during the last year suffered from pains and/or stiffness in muscles and joints that have lasted continuously for at least 3 months?
YES ☐ NO ☐

Have you in the last two weeks felt:

	No	A little	A lot	Very much
Nervous or worried?	☐	☐	☐	☐
Anxious?	☐	☐	☐	☐
Secure and calm?	☐	☐	☐	☐
Irritable?	☐	☐	☐	☐
Happy and optimistic?	☐	☐	☐	☐
Down/depressed?	☐	☐	☐	☐
Lonely?	☐	☐	☐	☐

Smoking

Did any of the adults at home smoke while you were growing up? YES ☐ NO ☐

Do you now, or have you previously, lived with daily smokers after your 20th birthday?
YES ☐ NO ☐

If "YES", for how many years in all? ____Years

How many hours a day do you normally spend in smoke-filled rooms? ____Hours
Put 0 if you do not spend time in smoke-filled rooms.

Do you yourself smoke:	YES	NO
Cigarettes daily?	☐	☐
Cigars/cigarillos daily?	☐	☐
Pipe daily ?	☐	☐

If you previously smoked daily, how long is it since you stopped? _____ Years

If you smoke daily at the moment, or have smoked before:

How many cigarettes do you smoke/did you smoke per day? _____ Cigarettes

How old were you when you began smoking daily? Age _____ Years

How many years in all have you smoked daily? _____ Years

Exercise

How has your physical activity in leisure time been during this last year? *Think of your weekly average for the year. Time spent going to work counts as leisure time.*

	Hours pr. week None	Less than 1	1-2	3 or more
Light activity (*not sweating or out of breath*)	☐	☐	☐	☐
Hard activity (*sweating/ out of breath*)	☐	☐	☐	☐

Coffee

How many cups of coffee do you drink daily? *Put 0 if you do not drink coffee daily.* Cups

Boiled coffee ☐☐☐
(i.e., grind boiled and allowed to draw)
Other coffee ☐☐☐

Alcohol

Are you a teetotaler? YES ☐ NO ☐

How many times a month do you normally drink alcohol? *Do not count low-alcohol beer. Put 0 if less than once a month.* ____ Times

How many glasses of beer, wine or spirits do you normally drink in a fortnight? *Do not count low-alcohol beer. Put 0 if less than once a month.*

Beer Glasses	Wine Glasses	Spirits Glasses
☐☐	☐☐	☐☐

Fat

What kind of margarine or butter do you normally use on bread? *Tick one box only.*

Don't use butter/margarine	☐
Creamery butter	☐
Hard margarine	☐
Soft margarine	☐
Butter/margarine blend	☐
Light margarine	☐

Education/work

What is the highest level of education you have completed?

7-10 years primary/secondary school, modern secondary school, folk high school	☐
Technical school, middle school, vocational.. school, 1-2 years' senior high school	☐
A-levels/High school diploma, (3-4 years)	☐
College/university, less than 4 years	☐
College/university, 4 or more years	☐

What is your current work situation?

Paid work	☐
Full-time housework	☐
Education, military service	☐
Unemployed, redundant	☐

How many hours of paid work do you have pr. week? _____ Hours

Do you receive any of the following benefits?

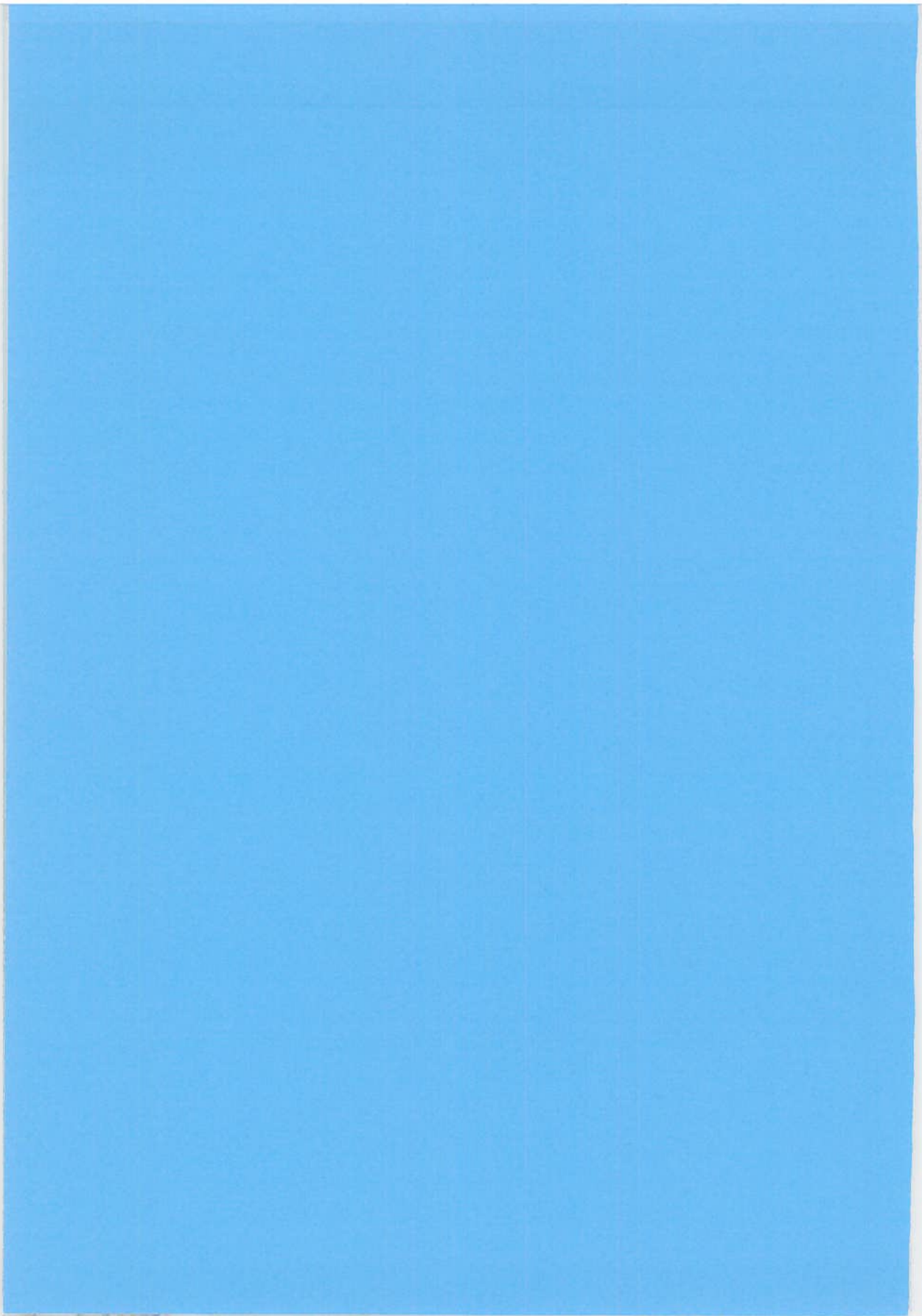
Sickness benefit (sick leave)	☐
Rehabilitation benefit	☐
Disability pension	☐
Old-age pension	☐
Social welfare benefits	☐
Unemployment benefit	☐

Illness in the family

Have one or more of your parents or siblings had a heart attack or had angina (heart cramp)?

YES	NO	DON'T KNOW
☐	☐	☐

PAPER I



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Tracking of blood pressure in adult men: the Tromsø Study 1974–1986

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Background Elevated blood pressure is a major risk factor for cardiovascular diseases. The object of this study was to assess the degree of blood pressure tracking among adult men in Tromsø, Northern Norway.

Methods A cohort of 4183 men 20–49 years old participated in three consecutive examinations (1974, 1979 and 1986). Tracking was assessed within each 5 year age group by three different methods: Pearson's correlation coefficient, Foulkes and Davis' tracking index and the proportion of men whose blood pressure at the subsequent examinations had changed from one of six baseline sixtile groups. Variations in each individual's blood pressure (intrasubject variation) over the three examinations were also computed.

Results All age groups displayed a statistically significant degree of tracking ($p < 0.0001$), where the youngest individuals had the least and those aged 35–39 years (in 1974) the largest degree of tracking for all three applied methods. Both pressures displayed a similar pattern across the age groups and tracking coefficients in general were lower for diastolic than for systolic blood pressure. The intrasubject variation pattern showed that individuals with blood pressure readings in the upper or lower tails at the baseline examination had a larger degree of variation than those who had values in between.

Conclusions This analysis suggests that individuals tend to retain their relative blood pressure level in a population throughout early adulthood and adult life.

Keywords blood pressure, tracking, longitudinal, men, intrasubject variation.

Introduction

Blood pressure is a biological variable with a tendency to vary during the day and during the year. Values are particularly likely to change in situations of stress, such as during a medical examination. It has also been documented that blood pressure values tend to increase with age[1–3]. Despite these instabilities an elevated level of blood pressure has been well-established as a major risk factor for cardiovascular disease[4–10]. In Norway it is recommended that individuals with mild hypertension are closely followed in order, if necessary, to start intervention with drug treatment or lifestyle changes. A lot of people with mild hypertension are not registered by the health care system. It would be easier to identify these people if one can establish a dependency of blood pressure values from early adulthood through mid-life. A longitudinal investigation of blood pressure variation is therefore of importance.

Tracking of the measured characteristic has been defined as maintenance of the same level over time, relative to other subjects. Most previous investigations of blood pressure tracking have been examined during childhood[11–14], or from adolescence into adulthood[15,16]. Studies on tracking among adult individuals[17,18] have been scarce. Most studies have focused on selected groups of individuals and reports based on the general population have been lacking. We had an opportunity to investigate blood pressure tracking in a population-based study, which has followed 4138 men, aged 20–49 years, in three consecutive examinations, in 1974, 1979 and 1986.

Methods

The study population

In 1974 the entire population of men in the municipality of Tromsø, aged 20–49 years, was invited to participate in the Tromsø Study. The same men were also invited for consecutive examinations in 1979 and 1986. The attendance rate at the baseline examination was 74%. 76% of the men who participated in 1974 also attended the second examination and in 1986 the attendance rate was 84%.

The examination methods used have been described in detail elsewhere[19–21]. The University of Tromsø and local health authorities have been responsible for the study and the examinations in 1979 and 1986 were carried out in co-operation with the National Health Screening Service.

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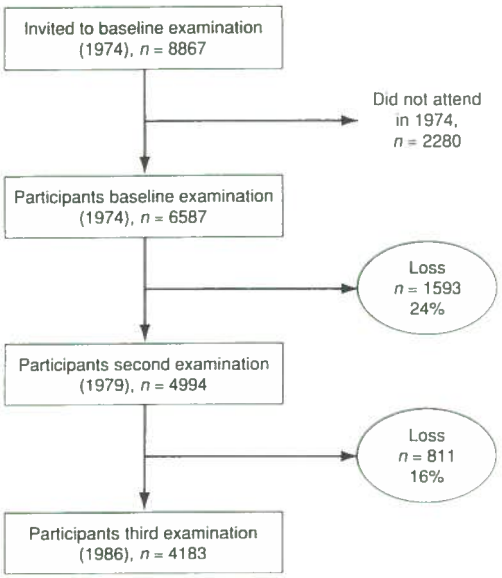

Fig. 1 Flowchart of male participants; the Tromsø Study 1974–1986.

Figure 1 shows a flow-chart of the study participants at the three examinations. This longitudinal study focuses on the 4183 individuals who participated in all three examinations. No individuals were excluded, not even those who were on anti-hypertensive drug treatment in 1974 or started drug treatment during the study period. The cohort were divided into six 5 year age groups according to age in 1974.

Blood pressure measurements

In 1974[19] the blood pressure was read to the nearest even number of mmHg. After 4 min of rest, two readings were taken at 4–5 min intervals using a mercury sphygmomanometer on the left upper arm, with the subject in a sitting position. Systolic blood pressure was measured when the first Korotkoff sound appeared (Phase 1) and 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. In 1979[20] blood pressure was measured using the same standards as in 1974. However, this time the right upper arm was used and after 2 min of rest the two readings were taken with a 1 min interval. In all three examinations blood pressure was measured by personnel trained according to tape recordings produced by the London School of Hygiene and Tropical Medicine. However, in 1986[21] the blood pressure was recorded with an automatic device (Dinamap Vital Signs Monitor 1846, Critikon Inc, Tampa, FL). After the participants had been seated for 2 min, three recordings were made on the upper right arm at 2 min intervals. The lowest blood pressure values in all three examinations were used in this report.

Data analysis

The word 'tracking' has been used to describe at least two different situations. It may reflect either the ability to predict subsequent observations from earlier measurements[22], or the maintenance of relative or percentile rank within a population over time[23,24]. In this paper, the latter definition has been used. We have used three methods to classify tracking of blood pressure. All calculations were performed within each 5 year age group, as well as for all men as a total. The first measure is Pearson's correlation coefficient. Although it does not fit fully into either of the tracking definitions, it is still the most commonly used measure of tracking found in the literature. The coefficient can only be used as a measure of tracking between two measurements per individual. We had three sets of data and consequently needed a more flexible method. Foulkes and Davis[23] have developed a tracking coefficient for studies with two or more examinations. The coefficient (or index), labelled as γ, is based on whether or not the relative positions of the observations from each pair of individuals are changed over time (often referred to as 'crossing of growth curves'). In instances where there are observations from two points of time, the growth curve is given as a linear function of time and, correspondingly, with three observations the function is polynomial of second degree. We calculated the tracking index using data from all three studies and the tracking indices for the three possible combinations of two measurements. The third method we applied was to split the data into sixtile groups for each 5 year age group and at the following examinations determine the number of individuals whose blood pressure remained in the same sixtile group and the number who changed to another group. These numbers were compared with the values expected had the individuals at each measurement been assigned randomly to the different sixtile groups.

We also examined how each individual's three blood pressure values varied (intrasubject variation) in terms of the standard deviation. After transforming the raw blood pressure data into normal scores derived from each age group, we calculated the standard deviation over the three examinations for each individual.

All processing of data was done using the SAS software package[25].

Results

Table 1 presents different baseline characteristics of all men according to whether or not they attended all three

Table 1 Age-adjusted descriptive measures of different characteristics taken at the baseline examination in 1974: the Tromsø Study 1974–1986

	Participants in all three examinations	
	Yes $n = 4183$ Mean (SD)	No $n = 2403$ Mean (SD)
Systolic blood pressure, mmHg	126.5 (14.9)	126.5 (15.0)
Diastolic blood pressure, mmHg	77.8 (11.4)	78.0 (11.5)
Total cholesterol, mmol l^{-1}	6.6 (1.3)	6.6 (1.4)
Triglycerides, mmol l^{-1}	1.4 (0.8)	1.5 (0.8)
Body height, cm	176.8 (6.7)	177.1 (6.7)
Body weight, kg	75.0 (10.1)	75.1 (10.1)
Body mass index, kg m^{-2}	24.0 (2.7)	24.0 (2.7)
Current smoker, %	58	63
Physical activity at leisure, regular or hard training, %	24	23

examinations. A comparison of the means showed no significant differences between the two groups (p values ranged from 0.83 to 0.12). However, the prevalence of current smokers was significant smaller ($p < 0.005$) in the group who attended all three examinations. Furthermore, the men who did not attend all three examinations were younger than the men who did attend all three (mean age 31.83 years compared with 34.82 years).

Table 2 gives a presentation of the sample sizes and the means and standard deviations for each of the three blood pressure examinations according to age. As expected, given that individuals were 5 years older, there was an increase in systolic and diastolic blood pressure means from 1974 to 1979. However, there was almost no increase in the systolic means and even a decrease in the diastolic means from 1979 to 1986. This is due to methodological differences: in the first two examinations blood pressure was measured manually, whereas in 1986 it was measured using an automatic device.

The age-specific blood pressure correlations between the various examinations are shown in Table 3. For systolic blood pressure, the age-specific correlations ranged from 0.409 to 0.623. The corresponding values for the diastolic pressure ranged from 0.327 to 0.575. The highest coefficients were recorded between the second and third examination and the lowest ones between the first and third examination. With a single exception, the systolic blood pressure showed a consistently higher corre-

Table 2 Descriptive measures of systolic and diastolic blood pressure in men examined three times: the Tromsø Study 1974–1986

		1974		1979		1986	
Age (years) in 1974	n	SBP[a] Mean (SD)	DBP[b] Mean (SD)	SBP Mean (SD)	DBP Mean (SD)	SBP Mean (SD)	DPB Mean (SD)
20–24	502	124.5 (13.3)	73.8 (11.3)	128.8 (11.6)	78.8 (10.2)	127.3 (12.9)	74.4 (10.0)
25–29	790	125.5 (13.4)	75.9 (10.1)	129.3 (12.1)	81.6 (9.2)	128.3 (12.1)	77.5 (9.6)
30–34	820	125.8 (13.3)	76.9 (10.5)	129.1 (12.6)	82.7 (9.6)	129.2 (13.4)	78.8 (10.0)
35–39	702	127.7 (14.5)	79.4 (11.1)	130.8 (13.9)	84.7 (10.2)	131.4 (15.2)	81.2 (10.4)
40–44	688	127.7 (16.6)	80.4 (11.5)	131.6 (14.7)	85.2 (10.5)	134.0 (17.0)	82.4 (10.7)
45–49	681	129.2 (16.6)	82.1 (11.6)	135.1 (17.3)	87.2 (10.5)	138.7 (18.7)	83.8 (11.0)
Total	4183	126.8 (14.8)	78.2 (11.4)	130.8 (14.0)	83.5 (10.3)	131.5 (15.5)	79.8 (10.7)

[a]SBP = systolic blood pressure.
[b]DBP = diastolic blood pressure.

Table 3 Pearson's correlation coefficients for paired combinations of the blood pressure examinations: the Tromsø Study 1974–1986

Age (years) in 1974	Systolic blood pressure			Diastolic blood pressure		
	I[a], II[b]	II, III[c]	I, III	I, II	II, III	I, III
20–24	0.430	0.483	0.409	0.349	0.506	0.332
25–29	0.567	0.602	0.507	0.402	0.483	0.369
30–34	0.520	0.579	0.456	0.429	0.547	0.347
35–39	0.594	0.623	0.460	0.534	0.575	0.418
40–44	0.558	0.593	0.476	0.463	0.513	0.379
45–49	0.577	0.587	0.409	0.509	0.523	0.327
Total	0.556	0.598	0.460	0.485	0.557	0.403

[a]I = baseline examination, 1974.
[b]II = second examination, 1979.
[c]III = third examination, 1986.

lation than the diastolic pressure and the smallest correlations appeared in the youngest age group for both. There was no other clear trend between correlation and age: however, most of the largest correlations were in the 35–39 year age group.

The correlation analysis was also performed with adjustment for time since last meal and anti-hypertensive drug treatment (data not given). These variables had a small impact, or no impact on the correlations. In addition, a calculation of the correlation coefficients excluding men on anti-hypertensive drug treatment (n = 288) displayed only small differences from the coefficients of the full data set; there were no clear differences between the younger and older age groups. A comparison with the correlations from the last row in Table 3 showed slightly smaller coefficients in the reduced data set (absolute values of 0.005, 0.008, 0.003, 0.033, 0.022 and 0.024, respectively).

From the group of men who did not participate in all three examinations and are therefore excluded from the present analysis, 811 men participated in 1974 (mean systolic and diastolic pressures 127.2 and 78.5 mmHg) and 1979 (mean systolic and diastolic pressures 132.1 and 84.6 mmHg), and 449 men participated in 1974 (mean systolic and diastolic pressures 126.0 and 75.6 mmHg) and 1986 (mean systolic and diastolic pressures 130.8 and 79.3 mmHg). A correlation analysis on these men did not show any trend towards lower or higher coefficients according to age compared with the numbers presented in Table 3.

Table 4 shows Foulkes and Davis' tracking coefficient for the blood pressure observations in each pair of

Table 4 Foulkes and Davis' tracking coefficients for various combinations of the blood pressure examinations: the Tromsø Study 1974–1986

Age (years) in 1974	Systolic blood pressure				Diastolic blood pressure			
	I[a], II[b]	II, III[c]	I, III	I, II, III	I, II	II, III	I, III	I, II, III
20–24	0.692	0.707	0.674	0.514	0.677	0.704	0.653	0.491
25–29	0.738	0.749	0.703	0.574	0.688	0.712	0.663	0.505
30–34	0.722	0.737	0.697	0.558	0.702	0.724	0.658	0.515
35–39	0.752	0.747	0.698	0.581	0.738	0.741	0.682	0.556
40–44	0.736	0.740	0.687	0.563	0.718	0.722	0.659	0.526
45–49	0.741	0.733	0.688	0.565	0.724	0.732	0.666	0.537
Total	0.733	0.738	0.693	0.563	0.717	0.735	0.678	0.541

[a]I = baseline examination, 1974.
[b]II = second examination, 1979.
[c]III = third examination, 1986.

Table 5 The proportion of sixtile group changes between the three blood pressure examinations: the Tromsø Study 1974–1986

Age (years) in 1974	Number of sixtile groups changed from baseline examination[a]									
	Systolic blood pressure					Diastolic blood pressure				
	0	1	2	3+4+5	0+1+2	0	1	2	3+4+5	0+1+2
20 – 24	0.090	0.239	0.311	0.361	0.639	0.088	0.247	0.271	0.394	0.606
25 – 29	0.134	0.291	0.305	0.270	0.730	0.090	0.257	0.273	0.380	0.620
30 – 34	0.101	0.310	0.290	0.299	0.701	0.098	0.241	0.291	0.370	0.630
35 – 39	0.108	0.348	0.295	0.249	0.751	0.108	0.302	0.289	0.301	0.699
40 – 44	0.118	0.301	0.311	0.270	0.730	0.108	0.278	0.251	0.363	0.637
45 – 49	0.117	0.328	0.275	0.280	0.720	0.110	0.253	0.319	0.318	0.682
Total	0.119	0.316	0.272	0.293	0.707	0.099	0.278	0.304	0.319	0.681
Expected[b]	0.028	0.139	0.222	0.611	0.389	0.028	0.139	0.222	0.611	0.389

[a]0 = no changes (results in the same sixtile group in all examinations), 1–5 = the number of sixtile groups change from the baseline examination.
[b]Result expected had there been no degree of tracking among examinations.

examinations, as well as for all three measurements jointly. Indices for both blood pressures were slightly smaller for the youngest age group than for the others and the diastolic blood pressure indices were all smaller than those for the systolic pressure. The data shows tracking in instances where the index is > 0.5 and all computed indices for two blood pressure measurements were significantly ($p < 0.0001$) greater than 0.5.

The last column of systolic blood pressure and the last of diastolic blood pressure in Table 4 give indices for the situation where all three measurements per individual are considered. For systolic blood pressure all coefficients were significantly greater than 0.5, even though they ranged from 0.514 to 0.581. Interestingly, for diastolic blood pressure, the youngest men exhibited a tracking coefficient < 0.5, thus indicating no degree of tracking.

Table 5 shows the proportion of men who remained in the same sixtile group, or moved into another group. All individuals were classified to one of the six possible change categories (0–5), given as the number of sixtile groups change from the baseline group. Thus, an individual who, during the three examinations, was observed in sixtile Group 2, 1 and 2, was classified to Change Category 1, an individual observed in Groups 1, 3 and 2 was classified to Change Category 2, and, finally, and individual in Groups 1, 3 and 5 was classified to Change Category 4. As seen, 63.9–75.1% of men, varying with subject age, moved a maximum of two steps away from the baseline sixtile group. These percentages are much higher than the expected 38.9% had the three blood pressure measurements been uncorrelated. The corresponding values observed for diastolic blood pressure ranged from 60.6 to 69.9%. Consequently, the numbers were slightly smaller than for the systolic pressure.

Figures 2 and 3 show the patterns of intrasubject variation for each age group across the sixtile groups. The absolute values of the intrasubject variation, as measured by standard deviation (SD) between three z-scores, is in itself of little interest; what is important is the relative degree of systolic and diastolic blood pressure variation across the age and sixtile groups. For systolic blood pressure the intrasubject variation followed the same trend across the sixtile groups in every age group. The intrasubject variation was relatively high in the first sixtile group, then it decreased to an almost constant level in Groups 2, 3 and 4, and increased again

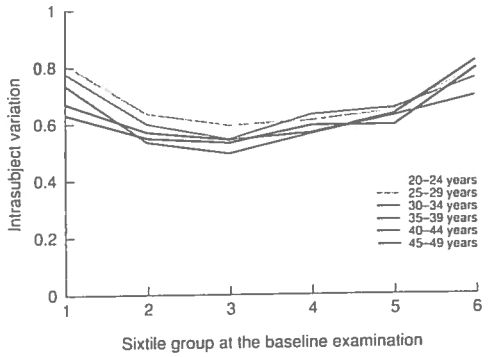

Fig. 2 Means (adjusted for high blood pressure treatment) of the SD of the normal scores of systolic blood pressure from three examinations by sixtile groups for each 5 year age group. The Tromsø Study 1974–1986.

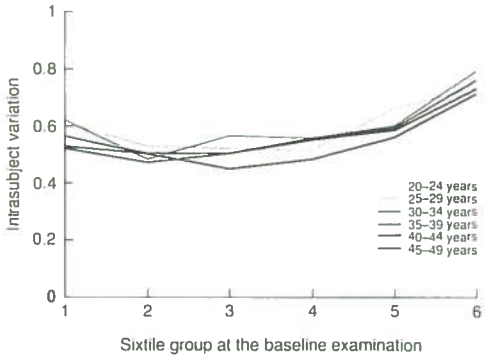

Fig. 3 Means (adjusted for high blood pressure treatment) of the SD of the normal scores of diastolic blood pressure from three examinations by sixtile groups for each 5 year age group. The Tromsø Study 1974–1986.

in the last two groups. There was no much variation across the age groups, but it is worth noting the larger intrasubject variation in the youngest age group.

A similar picture was present for diastolic blood pressure (Figure 3). However, the intrasubject variation patter showed a reversed J shape and there were larger differences between the age groups in the first part of the diastolic blood pressure distribution than in the last part.

Discussion

A significant degree of blood pressure tracking was observed in all age groups. Except for the youngest age group and the 35–39 year group, tracking was not very different. Thus, individuals with baseline ages 25–34 and 40–49 years were equally likely to keep their blood pressure rank position over time. However, the data showed that the strength of tracking decreased with time between examinations. The British Hypertension Society (BHS) has issued guidelines suggesting that, where possible, diastolic blood pressure should be brought to below 90 mmHg and systolic blood pressure should be below 160 mmHg[26]. Men who have blood pressures below the BHS's fixed cut-off points at a young age may still be at risk of crossing these cut-off points later in life. Knowledge of tracking may be helpful in identifying individuals at risk of developing hypertension.

An advantage of the present study may relate to certain data-set characteristics. Firstly, the cohort is based on a general population and not on a selected group of individuals. Secondly, the cohort is relatively large compared with the total population in the considered age group. In fact, 47% of the population of men in Tromsø, aged 20–49 years in 1974, were followed over a time period of 12 years. Finally, the cohort consists of a homogeneous group of individuals: few ethnic differences (race and/or religion) are present.

Some people dropped out due to missing one or both of the last two examinations. A concern may be what would have happened to the tracking coefficients had they attended. Table 1 shows that there were no major differences in baseline characteristics between the men who did and those who did not attend all three examinations. This indicates that there are no differences in tracking between the two groups. This assumption is further strengthened by the fact that the correlations calculated from the drop-out group (not presented in a table) showed no trend of difference compared with the correlations in the present study.

Although the three applied tracking methods are not directly comparable, they all showed the same trend of tracking in the six different age groups. However, as seen in the last column of Table 4, Foulkes and Davis' tracking index for three measurements per individual indicated that there was no tracking present in the two youngest age groups. This unexpected result contradicts the other coefficients presented in this report and may relate to the fact that our fitted growth curve (a second degree polynomial) is not optimal for each individual. There are a few other tracking methods that apply to situations with more than two measurements per individual[27]. Foulkes and Davis' method was chosen because it is easy to interpret and it also handles situations when there are only two measurements.

We noticed that tracking was slightly smaller for the diastolic than the systolic blood pressure. This is similar to most other findings[17,18,28]. The explanation may be that the measurement error for diastolic blood pressure may be greater than for systolic blood pressure. It is also known that the diastolic blood pressure has a tendency to decrease with time elapsed since last meal[29–31] and, because our examinations were non-fasting, the correlations may be under-estimated. When we brought the 'time since last meal' variable in for adjustment purposes, the recalculated correlations were not changed.

The finding that tracking was smallest for the youngest age group is consistent with other reports[17,18,32]. The reason for the weak tracking in young individuals may relate to the considerable changes of lifestyle knowing to take place during early adulthood. This period of life is characterised by moving out of the childhood residence, rapid shifts between school and work, irregular income and leisure-time activities.

Most tracking coefficients were highest for the 35–39 age group. However, if we follow this group as a birth cohort we find that it has the highest tracking coefficients, both for the observations between 1974 and 1979 and between 1979 and 1986. The University of Manitoba Follow-up Study covered a wider age range than

ours[28]. The strongest evidence of tracking was observed for men in the 45–55 age group. The study sample, however, was restricted to men who were found fit for pilot training in World War II.

The methods used in this paper do not consider potential confounding factors. Several variables are well-known to be related to blood pressure variability; changes in physical activity, smoking habits, alcohol intake and other dietary habits may certainly influence the blood pressure level. Changes in potential confounding variables may also be caused by the fact that participants in a longitudinal study change their behaviour after an examination because they are informed about their results. Obviously there is a strong possibility that subjects with hypertension undergo a treatment and/or change their dietary habits in order to reduce particularly high blood pressure values. Tracking coefficients may be under-estimated because of this possible change in confounding variables. However, when we removed results from the men who were on anti-hypertensive drug treatment, there were no important differences in the degree of tracking.

The switch from a standard sphygmomanometer to an automatic blood pressure measurement device (Dinamap) is a change of procedures that should be noted. A study[33] comparing these two methods concluded that the systolic blood pressure readings were about the same and that Dinamap showed slightly lower diastolic values. The difference diminished at a higher measurement level (diastolic pressures 95 mmHg). This result is compatible with the present mean decrease (Table 2). The study[33] also suggested that there is a linear relationship between readings from the two methods. Correlation analysis showed coefficients just below 0.90 for systolic blood pressure and coefficients just below 0.80 for diastolic blood pressure. The tracking methods used in this paper are independent of linear transformations which indicates that the switch to Dinamap does not lead to an under-estimation of the blood pressure tracking coefficients. Furthermore, if we compare the correlations from the first and second examination with the correlations from the second and third examination (where Dinamap is used) we notice that the latter displays the highest coefficients (for both systolic and diastolic pressures). A hypothesis that Dinamap under-estimates the tracking coefficients is not supported by this result.

Our analysis of the SD of the normal scores for each individual showed larger variability for the first and last, than the other sixtile group. This may be explained by the effect of the regression to the mean. The reason why the intrasubject variation was slightly larger in the right than the left tail of the systolic blood pressure distribution may relate to the fact that blood pressure, as other biologic characteristics, has a distribution skewed to the right. In addition, we believe that individuals with high blood pressure are particularly likely to try to reduce their blood pressure level.

It is not easy to explain why the intrasubject variation was slightly different between the two blood pressures. One may speculate that the reason can be found in the inherent differences in the two blood pressure distributions. For example, the fact that the systolic blood pressure distribution has a heavier right side tail may provide one answer to why the intrasubject variation in the last two sixtiles is larger for systolic blood pressure.

In conclusion, the findings in this longitudinal study show that adult men, to a certain extent, keep their blood pressure rank position within the population over time. Thus, a value registered in early adulthood seems to be a good predictor of later life blood pressure level, but the likelihood to stay in the same position within a population gets smaller over time.

Acknowledgments

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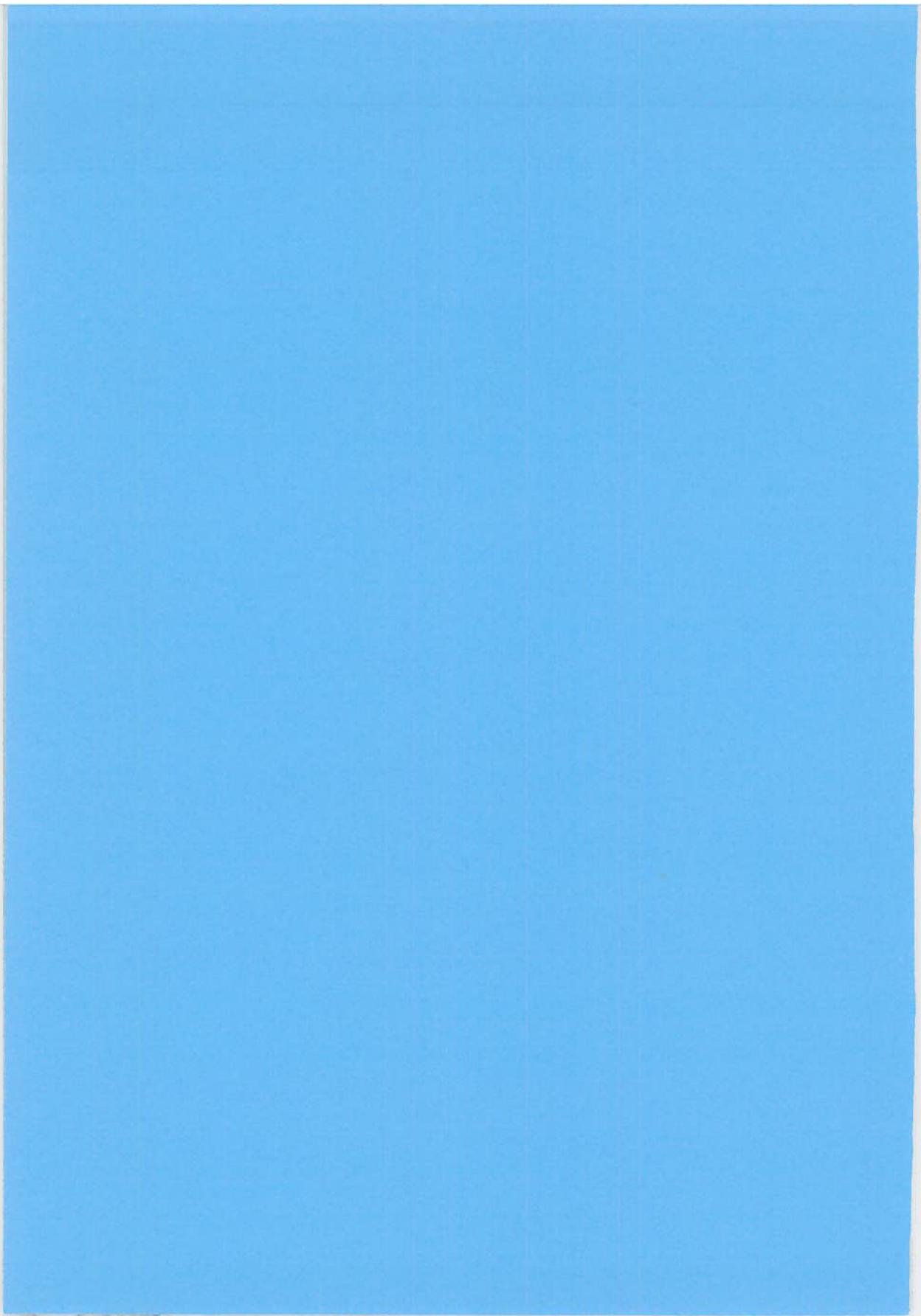
References

1 Kotchen JM, McKean HE, Kotchen TA. Blood pressure trends with aging. *Hypertension* 1982;4(III):128–34.
2 Flynn MA, Nolph GB, Baker AS *et al.* Aging in humans: a continuous 20 year study of physiologic and dietary parameters. *J Am Coll Nutr* 1992;11:660–72.
3 Weinberger MH, Fineberg NS. Sodium and volume sensitivity of blood pressure. Age and pressure change over time. *Hypertension* 1991;18:67–71.
4 Njølstad I, Arnesen E, Lund-Larsen PG. Smoking, serum lipids, blood pressure, and sex differences in myocardial infarction. A 12 year follow-up of the Finnmark Study. *Circulation* 1996;93:450–6.
5 Tverdal A. Systolic and diastolic blood pressures as predictors of coronary heart disease in middle-aged Norwegian men. *Br Med J Clin Res Ed* 1987;294:671–3.
6 Selmer R. Blood pressure and 20 year mortality in the city of Bergen, Norway. *Am J Epidemiol* 1992;136:428–40.
7 Rabkin SW, Mathewson AL, Tate RB. Predicting risk of ischemic heart disease and cerebrovascular disease from systolic and diastolic blood pressures. *Ann Intern Med* 1978; 88:342–5.
8 Salky N. Hypertension as a risk factor for the development of coronary heart disease. *J Tenn Dent Assoc* 1978;58:11–12.
9 Kannel WB. Mild hypertension as a cardiovascular risk factor. *Compr Ther* 1981;7:7–14.
10 Stokes JI, Kannel WB, Wolf PA *et al.* Blood pressure as a risk factor for cardiovascular disease: the Framingham Study — 30 years of follow-up. *Hypertension* 1989;13 (1):13–18.
11 Clarke WR, Schrott HG, Leaverton PE *et al.* Tracking of blood lipids and blood pressures in school age children: the Muscatine Study. *Circulation* 1978;58:626–34.

12 Palti H, Gofin R, Adler B *et al*. Tracking of blood pressure over an 8 year period in Jerusalem school children. *J Clin Epidemiol* 1988;41:731–5.
13 Webber LS, Cresanta JL, Voors AW *et al*. Tracking of cardiovascular disease risk factor variables in school-age children. *J Chron Dis* 1983;36:647–60.
14 Suh I, Nam CM, Lee ES *et al*. Blood pressure tracking in Korean schoolchildren. *Int J Epidemiol* 1994;23:710–15.
15 Yong LC, Kuller LH. Tracking of blood pressure from adolescence to middle age: the Dormont High School Study. *Prev Med* 1994;23:418–26.
16 Beckett LA, Rosner B, Roche AF *et al*. Serial changes in blood pressure from adolescence into adulthood. *Am J Epidemiol* 1992;135:1166–77.
17 Tate RB, Manfreda J, Krahn AD *et al*. Tracking of blood pressure over a 40 year period in the University of Manitoba Follow-up Study, 1948–1988. *Am J Epidemiol* 1995; 142:946–54.
18 Rabkin SW, Mathewson FA, Tate RB. Relationship of blood pressure in 20–39 year old men to subsequent blood pressure and incidence of hypertension over a 30 year observation period. *Circulation* 1982;65:291–300.
19 Thelle DS, Førde OH, Try K *et al*. The Tromsø heart study. Methods and main results of the cross-sectional study. *Acta Med Scand* 1976;200:107–18.
20 Bønaa KH, Thelle DS. Association between blood pressure and serum lipids in a population: the Tromø Study. *Circulation* 1991;83:1305–14.
21 Bønaa KH, Arnesen E. Association between heart rate and atherogenic blood lipid fractions in a population: the Tromsø Study. *Circulation* 1992;86:394–405.
22 Ware JH, Wu MC. Tracking: prediction of future values from serial measurements. *Biometrics* 1981;37:427–37.
23 Foulkes MA, Davis CE. An index of tracking for longitudinal data. *Biometrics* 1981; 37: 439–46.
24 McMahan CA. An index of tracking. *Biometrics* 1981; 37: 447–55.
25 SAS Institute Inc. *SAS/STAT User's Guide*. 4th ed. Cary, NC: SAS Institute Inc, 1989.
26 Sever P, Beevers G, Bulpitt C *et al*. Management guidelines in essential hypertension: report of the second working party of the British Hypertension Society. *Br Med J* 1993; 306:983–7.
27 Twisk JW, Kemper HC, Mellenbergh GJ. Mathematical and analytical aspects of tracking. *Epidemiol Rev* 1994;16:165–83.
28 Rosner B, Hennekens CH, Kass EH *et al*. Age-specific correlation analysis of longitudinal blood pressure data. *Am J Epidemiol* 1977;106:306–13.
29 de Mey C, Hansen Schmidt S, Enterling D. Postprandial haemodynamic changes: a source of bias in cardiovascular research affected by its own methodological bias. *Cardiovasc Res* 1988;22:703–7.
30 de Mey C, Enterling D, Brendel E *et al*. Postprandial changes in supine and erect heart rate, systemic blood pressure and plasma noradrenaline and renin activity in normal subjects. *Eur J Clin Pharmacol* 1987;32:471–6.
31 Muller AF, Fullwood L, Hawkins M *et al*. The integrated response of the cardiovascular system to food. *Digestion* 1992;52:184–93.
32 The National Health Screening Service, Oslo, Health Services of Finnmark, Sogn og Fjordane, and Oppland Counties, Ullevål Hospital, Central Laboratory, Oslo. *The cardiovascular disease study in Norwegian counties. Results from second screening*. Oslo, Norway: National Health Screening Service, 1988; 191.
33 Lund-Larsen PG. Blood pressure measured with a sphygmomanometer and with Dinamap under field conditions — a comparison. *Nor J Epidemiol* 1997;7:235–41.

PAPER II



Impact of Body Weight on Blood Pressure With a Focus on Sex Differences

The Tromsø Study, 1986-1995

Tom Wilsgaard, MSc; Henrik Schirmer, MD; Egil Arnesen, MD

Background: The prevalence of obesity and hypertension is increasing in Western societies. We examined the effects of initial body mass index ([BMI] weight in kilograms divided by height in meters squared) and change in BMI on change in blood pressure, and we assessed sex differences.

Methods: A general population in the municipality of Tromsø, northern Norway, was examined in 1986 and 1987 and again in 1994 and 1995. Altogether, 75% of the individuals, women aged 20 to 56 years and men aged 20 to 61 years, attended the baseline examination. A total of 15624 individuals (87% of all still living in the municipality) were examined twice.

Results: Mean BMI increased between the examinations, more for the younger than the older examinees, and also more among women than men ($P<.001$). Adjusted for several covariates, BMI change was associated with systolic and diastolic blood pressure change for both sexes (regression coefficients: 1.43 [95% confidence interval (CI), 1.23-1.64] and 0.90 [95% CI, 0.76-1.04], respectively, for men; and 1.24 [95% CI, 1.09-1.39] and 0.74 [95% CI, 0.63-0.84] for women). Baseline BMI was associated with systolic and diastolic blood pressure change for women only (regression coefficients: 0.38 [95% CI, 0.30-0.47] and 0.17 [95% CI, 0.11-0.23], respectively).

Conclusions: For women, both BMI at baseline and BMI change were independently associated with blood pressure change. For a given increase in BMI, obese women had a greater increase in blood pressure than lean women. This was not the case for men, for whom BMI change was the only significant predictor. Furthermore, a BMI increase for obese women induced a greater systolic blood pressure increase compared with men.

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INCREASED BLOOD pressure and hypertension are related to increased mortality and cardiovascular morbidity.[1-6] Blood pressure is well known to increase with age,[7-9] and age has been thought to be an independent cause of the increase.[10] Several studies, however, show that this hypothesis is only valid in populations with a high intake of salt and fatty acids or a large increase in body weight by age.[11-15] A number of reports have elucidated the association between different characteristics (age, leisure habits, levels of physical activity, serum cholesterol levels, etc) and blood pressure change.[16-22] The majority of these reports conclude that attained weight and weight change are the strongest predictors of absolute blood pressure level and blood pressure change. This causal association is supported by studies showing that weight reduction decreases blood pressure and consequences of hypertension such as left ventricle hypertrophy.[23-26] Furthermore, blood pressure change is reported to be associated with serum lipid levels, fatty acid levels, salt intake, and alcohol consumption.[12,16,27] Although most studies on cardiovascular risk factors have focused on men, sex differences have been shown in the effects of changes in weight and blood pressure on cardiovascular mortality.[28] Differences between the sexes are present for other cardiovascular disease risk factors as well.[2,29,30] However, to our knowledge, no study has focused on sex differences in the effects of initial body weight and weight change on blood pressure change. Nor has there been a focus on the interacting effects of initial body weight and weight change on blood pressure change. Does the effect of weight change vary by initial body weight? As health problems due to obesity increase, investigations on effects of obesity and weight change should be a high priority for cardiovascular research in the coming years.

In this report we had an opportunity to investigate a general population of more than 15000 men and women examined twice over an 8-year period. The aim was to examine the effects of initial body mass index (BMI [calculated as weight in kilograms divided by the square of height in meters]) and BMI change on blood pres-

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SUBJECTS AND METHODS

THE STUDY POPULATION

The study population consisted of men and women who participated in two population surveys carried out with an 8-year interval in Tromso, Norway. In the 1986-1987 survey, all men born between 1925 and 1966 and all women born between 1930 and 1966 were invited to participate. A total of 20602 individuals were examined, 75.1% of those invited. All men and women aged 25 years and over were invited to a second examination in 1994-1995. Eligible for the present study were 15624 individuals who participated in both surveys, 87.2% of all screened in 1986-1987 and still living in Tromsø. Individuals with missing information on blood pressure, serum lipid levels, age, smoking status, or BMI were excluded from the study (n=144). Women who had been pregnant at least once (n=335) were excluded as well. Hence, the present study group consisted of 7669 men aged 20 to 61 years and 7476 women aged 20 to 56 years at the end of 1986.

The University of Tromsø and local health authorities have been responsible for the study, and the examinations were carried out in cooperation with the National Health Screening Service.

MEASUREMENTS

The methods and questionnaires used in the 2 surveys are described in detail elsewhere.[11] Specially trained personnel using automatic devices such as the Dinamap Vital Signs Monitor 1846 (Critikon Inc, Tampa, Fla) recorded blood pressure. After the participants had been seated for 2 minutes, 3 recordings were made on the upper right arm at 2-minute intervals. The lowest blood pressure values in both examinations were used in this report. Height was measured to the nearest centimeter and weight to the nearest half kilogram with an electronic scale.

As a standardized method of classifying obesity, BMI was used. Serum lipid levels were measured in millimoles per liter. Variables used from the questionnaires included current smoker (yes/no), salt intake (3 categories on extra salt at dinner: rarely or never, sometimes or often, always or nearly always), 3 variables of alcohol consumption (beer, wine, and liquor; each with 5 categories according to amount of consumption: never or just a few times a year, once or twice a month, about once a week, 2-3 times a week, more or less daily), menopausal status, leisure-time physical activity (sedentary, moderate, regular, hard), and history of blood pressure treatment (yes/no).

STATISTICAL ANALYSIS

In order to investigate various variables' impact on blood pressure change, multiple linear regression analyses were used. Focus was on BMI and BMI change (ΔBMI), and additional variables resulting from the questionnaires and the physical examinations were included as covariates. Two-way interactions were modeled as the products of age and ΔBMI and of baseline BMI and ΔBMI.

In order to estimate the means of the dependent variables (systolic and diastolic blood pressure change) in subgroups adjusted for covariates, baseline BMI values were categorized into quartile and ΔBMI values were divided into 5 categories (ΔBMI cutpoints: 0, 1, 2, 3). Means were also estimated with stratification by age group.

Changes were the difference between the second and first examinations (ie, ΔBMI=BMI [1994-1995]−BMI [1986-1987]). All analyses were sex specific, and the data were processed using the SAS software package.[12]

sure change in each sex. Are these 2 variables independent predictors of blood pressure change? How do they interact with each other? Additional data on characteristics such as age, smoking habits, triglyceride levels, cholesterol levels, menopausal status, history of blood pressure treatment, intake of salt and alcohol, and leisure-time physical activity allowed us to make adjustments and to explore additional effects of the most common risk factors for cardiovascular disease.

RESULTS

A relatively small proportion (12.8%) of all individuals who attended the first survey and still lived in Tromsø in 1994-1995 did not attend the second survey. A comparison of baseline characteristics between the dropout group and the study group used in both analyses (individuals who did not drop out) is presented in **Table 1**. A comparison of mean values between the 2 groups shows that the largest difference observed was in the age variable. Both male and female participants at both examinations had significantly higher mean age ($P<.001$). Also worth noting was the higher prevalence of current smokers in the dropout group ($P<.001$).

Mean increases in systolic blood pressure, diastolic blood pressure, and BMI between 1986-1987 and 1994-1995 were shown for all age groups for both men and women (**Table 2**). At baseline, younger subjects had lower values than older subjects. The rate of increase in systolic but not diastolic blood pressure increased with age. The rate of increase in BMI decreased with age for men. Women belonging to the 3 youngest age groups had an equal mean increase in BMI. For systolic and diastolic blood pressure, no sex differences in SDs were observed. For BMI, however, a greater increase in variability was observed for women. Change in smoking status showed the opposite tendency compared with blood pressure and BMI. In all age groups and for both sexes, the relative number of current smokers dropped significantly between the 2 examinations. Furthermore, there was a tendency for younger individuals to smoke more frequently.

In all 5-year age groups, a mean BMI increase was registered (**Figure 1**). For men, a negative linear association between age and BMI increase was observed. The mean increases in BMI for the youngest and oldest age groups were 1.66 and 0.26, respectively. For women this trend was not as pronounced. A drop in mean BMI increase was not clearly observed until after age 40 years,

Table 1. Descriptive Characteristics of Subjects Who Participated in the Baseline Examination (1986-1987) but Not the Follow-up Examination (1994-1995) of the Tromsø Study*

	Men		Women	
	Participated in Follow-up (n = 7669)	Did Not Participate in Follow-up (n = 1315)	Participated in Follow-up (n = 7476)	Did Not Participate in Follow-up (n = 1011)
Age in 1986, y†	39.7 (10.8)	34.6 (10.6)	37.8 (9.5)	32.8 (9.1)
Systolic blood pressure, mm Hg†	129.5 (14.0)	129.8 (14.7)	119.8 (14.5)	121.2 (14.9)
Diastolic blood pressure, mm Hg†	76.3 (10.8)	75.5 (12.2)	72.7 (10.1)	72.8 (10.9)
Body mass index†	24.7 (3.0)	24.2 (3.2)	23.2 (3.5)	23.0 (3.8)
Total cholesterol†				
mmol/L	5.9 (1.2)	5.6 (1.3)	5.7 (1.2)	5.4 (1.1)
mg/dL	227.8 (46.3)	216.2 (50.2)	220.1 (46.3)	208.5 (42.5)
HDL cholesterol†				
mmol/L	1.36 (0.34)	1.37 (0.37)	1.64 (0.37)	1.62 (0.39)
mg/dL	52.1 (13.1)	52.9 (14.3)	63.3 (14.3)	62.5 (15.1)
Triglycerides†				
mmol/L	1.62 (0.97)	1.60 (1.12)	1.12 (0.62)	1.12 (0.73)
mg/dL	62.5 (37.5)	61.8 (43.2)	43.2 (23.9)	43.2 (28.2)
Current smoker, %	45.2	56.8	45.8	59.1
Leisure-time physical activity, %‡	27.4	28.3	9.6	12.4

*HDL indicates high-density lipoprotein.
†Values are mean (SD).
‡Regular or hard training.

Table 2. Blood Pressure, Body Mass Index, and Smoking Status by Sex and Age in the Tromsø Study

		Men			Women		
Characteristic	Age in 1986, y	No.	1986-1987	Change in 1994-1995*	No.	1986-1987	Change in 1994-1995*
Systolic blood pressure, mm Hg†	20-29	1518	127.7 (11.6)	1.6 (11.1)	1633	116.1 (9.9)	1.2 (10.3)
	30-39	2427	127.1 (12.0)	2.2 (11.4)	2620	116.1 (11.5)	5.1 (11.4)
	40-49	2088	129.3 (13.3)	4.6 (13.6)	2195	122.2 (15.2)	7.8 (13.9)
	50-61‡	1636	135.2 (17.5)	7.9 (17.0)	1028	130.1 (19.0)	9.6 (16.3)
Diastolic blood pressure, mm Hg†	20-29	1518	68.7 (8.8)	3.3 (8.8)	1633	67.7 (8.4)	0.5 (8.7)
	30-39	2427	74.3 (9.5)	2.7 (8.8)	2620	71.0 (8.8)	1.4 (8.4)
	40-49	2088	79.1 (9.9)	2.1 (9.6)	2195	75.6 (9.8)	1.3 (9.0)
	50-61‡	1636	82.5 (10.5)	0.9 (10.6)	1028	79.0 (11.1)	0.3 (10.2)
Body mass index†	20-29	1518	23.6 (2.9)	1.5 (1.7)	1633	22.1 (3.0)	1.6 (2.2)
	30-39	2427	24.4 (2.9)	1.1 (1.6)	2620	22.6 (3.0)	1.6 (1.9)
	40-49	2088	25.3 (2.8)	1.0 (1.5)	2195	24.0 (3.6)	1.6 (2.9)
	50-61‡	1636	25.4 (3.0)	0.6 (1.6)	1028	24.7 (3.7)	1.3 (2.1)
Current smoker, %	20-29	1518	44.1	−2.3	1633	54.4	−8.7
	30-39	2427	47.8	−8.3	2620	47.7	−4.0
	40-49	2088	42.8	−6.6	2195	41.0	−4.5
	50-61‡	1636	45.3	−10.9	1028	37.6	−5.8

*The 1994-1995 value minus the 1986-1987 value.
†Values are mean (SD).
‡For women, 50 to 56 years.

and there was a significant sex difference ($P<.001$). Women older than 24 years had significantly higher mean BMI increases compared with men.

Table 3 presents regression coefficients for ΔBMI, baseline BMI, age, and smoking status from 2 models. In addition to blood pressure treatment, the first model included all variables listed in the table. The second model was further adjusted for changes in triglyceride levels, total cholesterol level, high-density lipoprotein cholesterol level, menopause status, and baseline leisure-time physical activity. Change in BMI was a strong predictor for blood pressure change for both men and women. The *P* value for BMI change was lower than the *P* values for all other covariates in each model (except for age regressed on systolic blood pressure for men). Baseline BMI was significantly related to both blood pressures for women. For men, however, this relationship was not present ($P<.001$ and $P=.001$ for sex differences for systolic and diastolic blood pressure, respectively). Age at baseline was a strong predictor of change in systolic blood pressure, but not diastolic blood pressure. Change in smoking status was not an independent predictor of blood pressure change in men. For women, however, change in smoking status was significantly related to blood pres-

sure change. The estimated coefficients in the 2 models in Table 3 were quite similar, and there was no evidence that the adjustment variables confounded the variables of interest. Salt intake was nonsignificant in every analysis and thus was excluded as a covariate. Alcohol intake was significant in some analyses, but did not change the estimates of the variables of interest and was also excluded (there were 1016 missing observations).

To explore the possible effects of menopause, stratified multiple regression analyses were performed. The results for women of various ages (<40, 40-50, and >50 years) were consistent across the strata. With systolic blood pressure change as the dependent variable, regression coefficients for the age strata were 1.23, 1.28, and 1.18, respectively, for ΔBMI and 0.42, 0.39, and 0.47, respectively, for baseline BMI ($P<.001$ for all). Concordant results for diastolic blood pressure were also observed. Furthermore, analyses stratified by menopause at the second survey showed stratum-specific regression coefficients (menopause [yes/no[and systolic and diastolic blood pressure, respectively) of 1.28, 1.20, 0.75, and 0.74 for ΔBMI and 0.40, 0.35, 0.20, and 0.13 for baseline BMI. Tests of interactions between menopause and ΔBMI and between menopause and baseline BMI were insignificant.

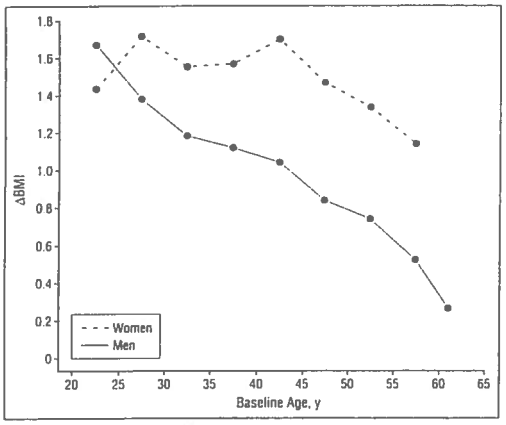

Figure 1. *Mean body mass index change (ΔBMI) by sex and age in the Tromsø Study, 1986-1987 and 1994-1995.*

The association between age and blood pressure change is presented in **Figure 2**. Whereas approximately horizontal lines were observed for diastolic blood pressure change, an increasing trend was observed for systolic blood pressure change. The blood pressure increases for men in the 3 youngest age groups were not significantly different and on the same level as for women aged 20 to 24 years.

Figure 3 and **Figure 4** further elucidate sex differences and the relationships between the independent variables from Table 3 for blood pressure change. Both figures show stratified means of blood pressure change adjusted for several covariates. The stratifications were 2-way cross-tabulations for ΔBMI × age groups (Figure 3) and for ΔBMI × baseline BMI in quartiles (Figure 4). Although the figures focus on the stratified results, all statistical tests, including interaction terms, were analyzed without the above groupings as results from multiple regression analyses controlling for all the main effects listed in Table 3. Consistent in both figures was a

Table 3. Multiple Linear Regression Analyses of Change in Systolic and Diastolic Blood Pressure in the Tromsø Study, 1986-1995*

	Men (n = 7669)		Women (n = 7476)		
	β†	β (95% CI)‡	β†	β (95% CI)‡	*P*
Systolic Blood Pressure					
ΔBMI	1.38	1.43 (1.23 to 1.64)	1.23	1.24 (1.09 to 1.39)	.14
BMI in 1986-1987	0.04	0.04 (−0.06 to 0.15)	0.36	0.38 (0.29 to 0.46)	<.001
Age in 1986-1987	0.26	0.27 (0.24 to 0.30)	0.27	0.30 (0.25 to 0.34)	.32
Smoking status					
Never smoker	Reference value				
Stopped smoking	−0.56	−0.98 (−1.97 to 0.00)	−1.11	−1.34 (−2.37 to −0.31)	.62
Started smoking	0.09	0.43 (−1.07 to 1.92)	−1.92	−1.79 (−3.32 to −0.25)	.04
Consistent smoker	0.28	0.19 (−0.47 to 0.86)	−0.32	−0.38 (−1.00 to 0.24)	.22
Model correlation coefficient (*R*)	0.23	0.27	0.31	0.34	
Diastolic Blood Pressure					
ΔBMI	0.95	0.90 (0.76 to 1.04)	0.73	0.74 (0.63 to 0.84)	.07
BMI in 1986-1987	−0.02	0.01 (−0.06 to 0.08)	0.15	0.17 (0.11 to 0.23)	.001
Age in 1986-1987	−0.03	−0.01 (−0.04 to 0.01)	−0.00	0.02 (−0.01 to 0.05)	.06
Smoking status					
Never smoker	Reference value				
Stopped smoking	−0.34	−0.34 (−1.03 to 0.35)	−0.85	−0.92 (−1.64 to −0.19)	.01
Started smoking	0.06	0.31 (−0.73 to 1.36)	−0.60	−0.48 (−1.56 to 0.60)	.83
Consistent smoker	−0.38	−0.33 (−0.79 to 0.14)	0.16	0.17 (−0.27 to 0.60)	.13
Model correlation coefficient (*R*)	0.21	0.27	0.18	0.24	

*ΔBMI indicates body mass index change.
†Model with ΔBMI, BMI at baseline, age, smoking status, and blood pressure treatment.
‡Model with additional adjustment for leisure-time physical activity in 1986-1987 and changes in total cholesterol, triglyceride, and high-density lipoprotein cholesterol levels and menopausal status.
§R represents the square root of the proportion of the variance of the response variable explained by the full model.

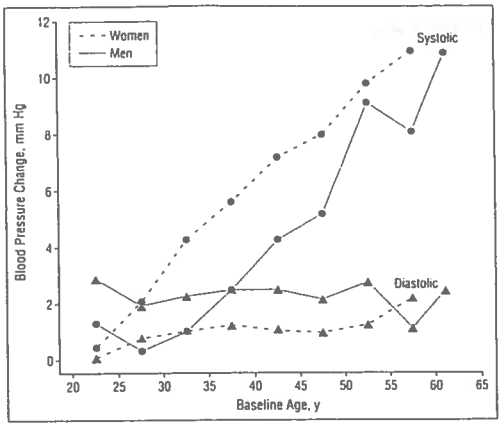

Figure 2. *Mean change of systolic and diastolic blood pressure by sex and age in the Tromsø Study, 1986-1987 and 1994-1995, adjusted for baseline body mass index and leisure-time physical activity and for changes in body mass index, total cholesterol, high-density lipoprotein cholesterol, triglycerides, smoking status, menopause status, and blood pressure treatment.*

positive linear relationship between ΔBMI and blood pressure change for both men and women.

Figure 3 shows that the relationships between systolic blood pressure change and ΔBMI differed across the age groups. Older men and women had a higher mean increase in systolic blood pressure than younger men and women. There was no significant interaction between age and ΔBMI ($P=.39$ and $P=.11$ for men and women, respectively). For diastolic blood pressure, no age pattern appeared.

For men, baseline BMI was nonsignificant as a predictor for systolic and diastolic blood pressure change (Figure 4). For women, however, a prediction of blood pressure increase is best modeled with stratification by baseline BMI. If 2 women have an equal increase in BMI but unequal baseline BMI, the woman with the higher baseline BMI is likely to have a greater increase in blood pressure. This association was observed for both systolic and diastolic blood pressure, although it was more pronounced for systolic blood pressure. Interactions between baseline BMI and ΔBMI were nonsignificant for women and men for diastolic blood pressure ($P>.42$ in all 3 models). The significant interaction for men for systolic blood pressure indicates that the linear association between ΔBMI and blood pressure change (the slope of the regression lines) varies with baseline BMI level. However, Figure 4 presents no obvious and clear distinctions between the estimated lines. Assessment of the interaction is not straightforward. Worth noting is that the largest difference in systolic blood pressure change across the baseline BMI quartiles was observed for ΔBMI between 2 and 3.

COMMENT

In the present study we have shown that in a general Norwegian population, both baseline BMI and ΔBMI were independent predictors of systolic and diastolic blood pressure change in women. For a given BMI increase, obese

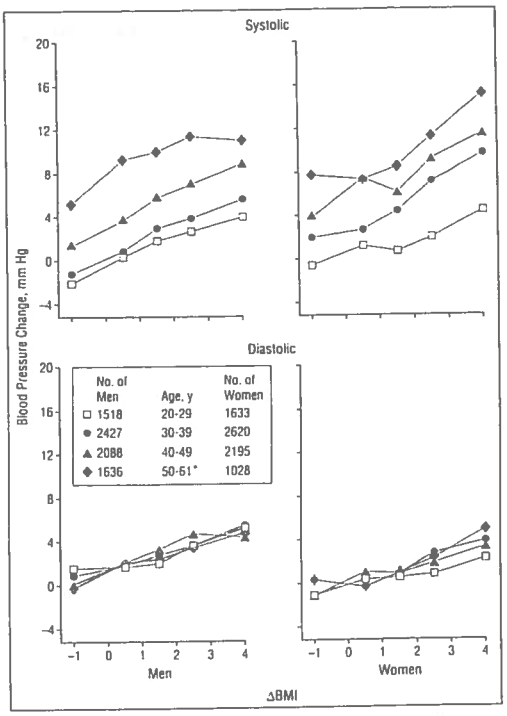

Figure 3. *Mean systolic and diastolic blood pressure change by age and body mass index (ΔBMI) in the Tromsø Study, 1986-1987 and 1994-1995, adjusted for baseline BMI and leisure-time physical activity and for changes in total cholesterol, high-density lipoprotein cholesterol, triglycerides, smoking status, menopause status, and blood pressure treatment. Asterisk indicates age 50 to 56 years for women.*

women had a greater systolic and diastolic blood pressure increase than lean women. In men, blood pressure change was associated with ΔBMI, but the blood pressure increase was independent of the BMI value at baseline. Another sex difference worth noting was that in obese women a given BMI increase induced a much greater systolic blood pressure increase than in obese men. For men and women with baseline BMI greater than 28 with a BMI increase between studies greater than 3, systolic blood pressure increased by 5.1 mm Hg and 13.3 mm Hg, respectively.

Even though this and other studies support a causal association between BMI increase and blood pressure increase, the underlying pathophysiological mechanism is not fully understood. Increased BMI is associated with increased blood pressure as well as with increased serum, glucose, insulin, aldosterone, and renin levels and with increased sympathetic tone.[33,34] All the latter factors are thought to increase blood pressure by increasing vascular volume or peripheral resistance. In a randomized trial, however, an analysis of heterogeneity of the effect of weight reduction in hypertensive obese patients showed that only 72% of the patients responded with a decrease in blood pressure despite successful weight reduction[34]; this finding casts doubts on a direct effect of increased BMI on blood pressure. In addition to be-

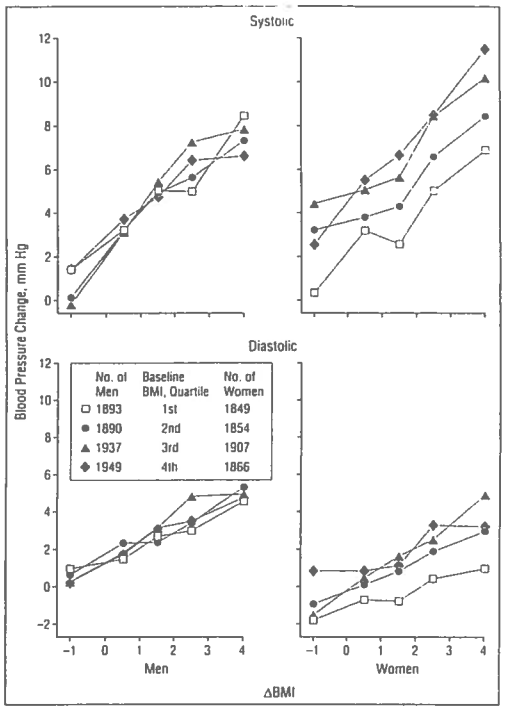

Figure 4. *Mean change of systolic and diastolic blood pressure change by baseline body mass index (BMI) quartiles and BMI change (ΔBMI) in the Tromsø Study, 1986-1987 and 1994-1995, adjusted for baseline age and leisure-time physical activity and for changes in total cholesterol, high-density lipoprotein cholesterol, triglycerides, smoking status, menopause status, and blood pressure treatment.*

ing associated with BMI, sympathetic tone is also associated with other factors that have an independent effect on blood pressure, such as psychological factors and physical activity.[35] In addition, BMI-induced change in sympathetic tone could, through adaptation as seen with baroreceptor response, lead to increased tone that does not respond to decreased BMI.

An assessment of why a sex difference is present in our data is far from easy. Noteworthy is the observed difference in ΔBMI development (Figure 1 and Table 2). The 8-year BMI increase was significantly greater for women than men. In addition, the BMI variation within each examination (1986-1987 and 1994-1995) was greater for women, as was the increase in BMI variation between the 2 examinations.

One should look at differences in other risk factors and determinants of cardiovascular disease as well. The majority of earlier studies have focused on cardiovascular risk factors for men. Until recently there have been few studies on women[36] and only a few studies have looked at sex differences in cardiovascular risk in the same study population. Some of the existing articles have shown that the age-specific incidence of cardiovascular disease is significantly higher for men than for women.[1,2,29,36] However, attempts to explain this difference by looking at a number of etiological variables have not given any answer.[1,2] A study examining risk factors for myocardial infarction showed that the relative risk asssociated with increases in variables such as blood pressure, total cholesterol, high-density lipoprotein cholesterol, and triglycerides did not display any sex differences.[2] An exception was that smoking had a much larger relative detrimental impact in women. This result is in accordance with the findings of other studies.[37,38]

A hypothesis that the observed sex differences in this article may be related to possible effects of menopause is contradicted by the stratified multivariate regression analyses. The consistent results across the age and the menopause (yes/no) strata are a good indication that there is no interaction between ΔBMI and baseline BMI associated with menopause. These results also provided further evidence that there were no interactions between ΔBMI and baseline BMI associated with age. Furthermore, menopause status and change of menopause status were used as categorical variables for adjustment purposes in all multiple analyses in this study. Although these variables contributed a significant independent effect on diastolic blood pressure change ($P=.007$), they did not confound the observed effects of ΔBMI or baseline BMI.

One potential source of bias was that a significant number of subjects with diseases may have influenced BMI and blood pressure measurements. In fact, 14.8% of the men and 10.4% of the women reported that they had a history of asthma, angina, heart attack, diabetes, or stroke. Excluding these subjects from the analyses did not change the presented results or trends.

Individuals who reported a history of antihypertensive drug treatment ($n=1117$) were not excluded. A secondary analysis excluding these individuals did not change the results. Furthermore, coefficients estimated from a multiple regression analysis restricted to individuals with a history of drug treatment displayed estimates quite similar to those in Table 3. The regression coefficients for ΔBMI for men and women for systolic and diastolic blood pressure were 1.49, 1.31, 0.84, and 1.02, respectively. For baseline BMI, the estimates were 0.01, 0.20, −0.28 and 0.14, respectively. Even though a negative value was displayed (diastolic blood pressure for men), the effect was not significant ($P=.07$).

Some men and women who participated in the first survey never participated in the second survey, and these dropouts might have contributed to another interpretation of our analyses. Table 1 shows the baseline characteristics for the dropouts compared with those who attended both examinations. No major differences were detected, although the dropout group was clearly younger than the study group. Plausible explanations for this age difference are that younger individuals are more likely to move and that younger individuals are known to participate less often in health surveys.

Other studies have shown a positive association between baseline BMI and ΔBMI for blood pressure change. In the Framingham offspring, a consistent association between ΔBMI and blood pressure change was shown.[16] However, the focus was not on sex differences or on the association with baseline BMI. The baseline age of the

Framingham participants was 20 to 29 years; when we restricted our analyses to this age group, our coefficients for ΔBMI were remarkably similar to those in the Framingham study.

A study in the biracial population of Evans County[39] presented results consistent with those in our study. Change in BMI was positively correlated with blood pressure change. For white women, baseline BMI showed an association as well (although it had only borderline significance for systolic blood pressure [$P=.055$]). The Evans County study did not address the association between baseline BMI and ΔBMI.

Another study that addressed the same questions as our study was the Normative Aging Study.[22] The study included only men and was not population based. Men with systolic blood pressure greater than 140 mm Hg or diastolic blood pressure greater than 90 mm Hg were excluded. In contrast to our results, the study showed that, in a multiple regression analysis, baseline weight, in addition to the percentage weight change, was a significant predictor of systolic and diastolic blood pressure change. The study did not address the question of interaction between the 2 variables. The exclusion criteria of the Normative Aging Study would have excluded 26% of our subjects older than 40 years, which would have left us with a biased and healthier study population than a normal, general population.

In conclusion, independent of ΔBMI, baseline BMI was found to be a predictor of systolic and diastolic blood pressure change in women but not in men. In both sexes, ΔBMI was also a significant predictor of blood pressure change. The implication is that obese women are more likely than lean women to have increases in blood pressure with increasing BMI, and a BMI increase in obese women induces a greater systolic blood pressure increase than in obese men. To counter this effect, it seems to be more important for women with a high baseline BMI not to increase their weight compared with women with lower baseline BMI values.

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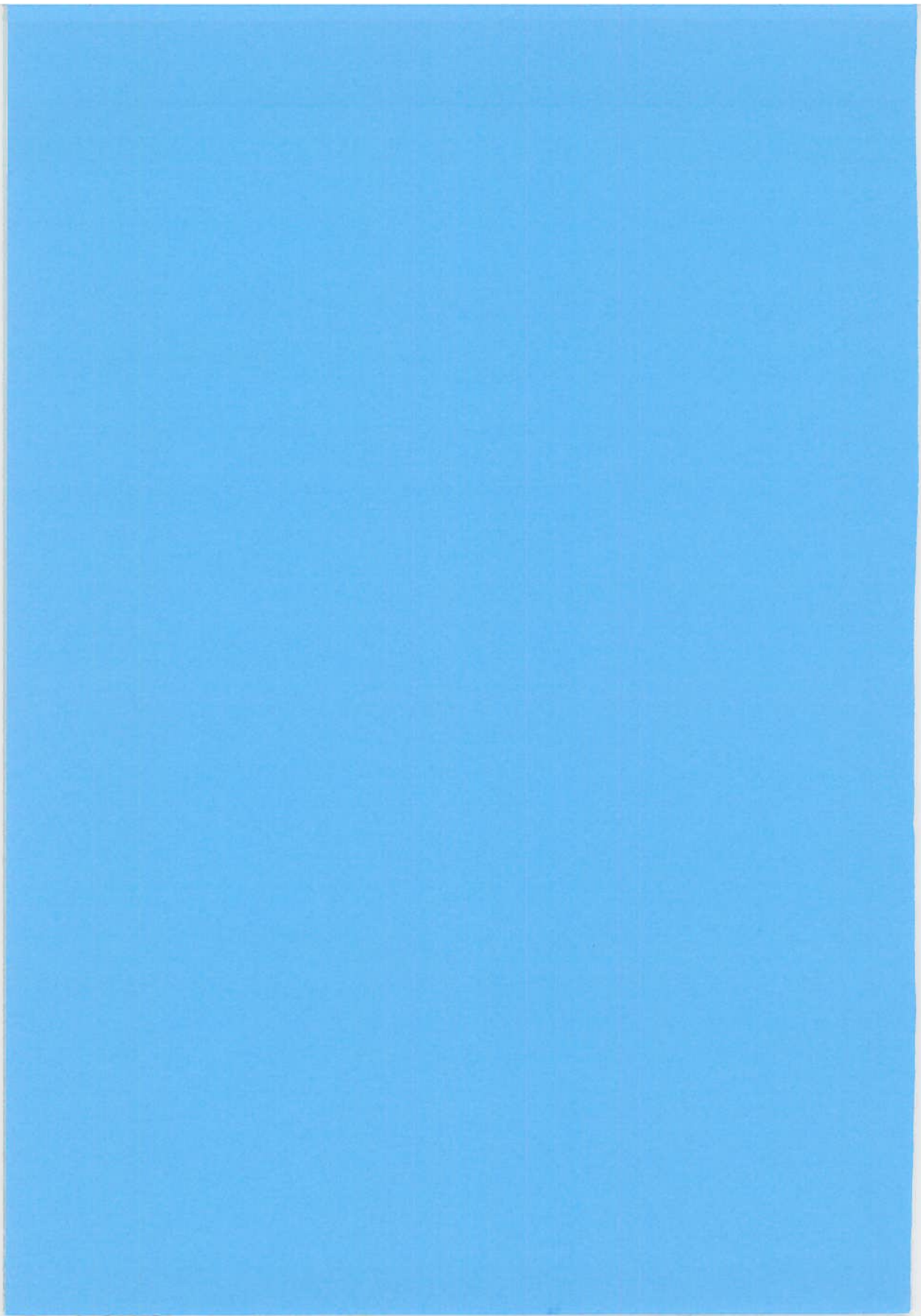
REFERENCES

1. Selmer R. Blood pressure and twenty-year mortality in the city of Bergen, Norway. *Am J Epidemiol.* 1992;136:428-440.
2. Njølstad I, Arnesen E, Lund-Larsen PG. Smoking, serum lipids, blood pressure, and sex differences in myocardial infarction: a 12-year follow-up of the Finnmark Study. *Circulation.* 1996;93:450-456.
3. Tverdal A. Systolic and diastolic blood pressures as predictors of coronary heart disease in middle aged Norwegian men. *BMJ.* 1987;294:671-673.
4. Rabkin SW, Mathewson AL, Tate RB. Predicting risk of ischemic heart disease and cerebrovascular disease from systolic and diastolic blood pressures. *Ann Intern Med.* 1978;88:342-345.
5. Kannel WB. Mild hypertension as a cardiovascular risk factor. *Compr Ther.* 1981; 7:7-14.
6. Stokes J III, Kannel WB, Wolf PA, D'Agostino RB, Cupples LA. Blood pressure as a risk factor for cardiovascular disease: the Framingham Study—30 years of follow-up. *Hypertension.* 1989;13(5 suppl):I13-I18.
7. Kotchen JM, McKean HE, Kotchen TA. Blood pressure trends with aging [review]. *Hypertension.* 1982;4(5, pt 2):III28-III34.
8. Flynn MA, Nolph GB, Baker AS, Krause G. Aging in humans: a continuous 20-year study of physiologic and dietary parameters. *J Am Coll Nutr.* 1992;11:660-672.
9. Weinberger MH, Fineberg NS. Sodium and volume sensitivity of blood pressure: age and pressure change over time. *Hypertension.* 1991;18:67-71.
10. Lakatta EG. Arterial pressure and aging [review]. *Int J Cardiol.* 1989;25(suppl 1) S81-S89.
11. Appel LJ, Moore TJ, Obarzanek E, et al, for the DASH Collaborative Research Group. A clinical trial of the effects of dietary patterns on blood pressure. *N Engl J Med.* 1997;336:1117-1124.
12. Elliott P, Stamler J, Nichols R, et al, for the Intersalt Cooperative Research Group. Intersalt revisited: further analyses of 24 hour sodium excretion and blood pressure within and across populations. *BMJ.* 1996;312:1249-1253.
13. Poulter NR, Khaw KT, Mugambi M, Peart WS, Rose G, Sever P. Blood pressure patterns in relation to age, weight and urinary electrolytes in three Kenyan communities. *Trans R Soc Trop Med Hyg.* 1985;79:389-392.
14. Huang Z, Willett WC, Manson JE, et al. Body weight, weight change, and risk for hypertension in women. *Ann Intern Med.* 1998;128:81-88.
15. Pavan L, Casiglia E, Pauletto P, et al. Blood pressure, serum cholesterol and nutritional state in Tanzania and in the Amazon: comparison with an Italian population. *J Hypertens.* 1997;15:1083-1090.
16. Hubert HB, Eaker ED, Garrison RJ, Castelli WP. Life-style correlates of risk factor change in young adults: an eight-year study of coronary heart disease risk factors in the Framingham offspring. *Am J Epidemiol.* 1987;125:812-831.
17. Sparrow D, Garvey AJ, Rosner B, Thomas HE Jr. Factors in predicting blood pressure change. *Circulation.* 1982;65:789-794.
18. Svärdsudd K, Wedel H, Wilhelmsen L. Factors associated with the initial blood pressure level and with the subsequent blood pressure increase in a longitudinal population study: the study of men born in 1913. *Eur Heart J.* 1980;1:345-354.
19. Sonne Holm S, Sørensen TI, Jensen G, Schnohr P. Independent effects of weight change and attained body weight on prevalence of arterial hypertension in obese and non-obese men. *BMJ.* 1989;299:767-770.
20. Meltzer AA, Mueller WH, Annegers JF, Grimes B, Albright DL. Weight history and hypertension. *J Clin Epidemiol.* 1988;41:867-874.
21. Sedgwick AW, Davidson AH, Taplin RE, Thomas DW. Relationships between weight change and changes in blood pressure and serum lipids in men and women. *Int J Obes.* 1984;8:343-353.
22. Borkan GA, Sparrow D, Wisniewski C, Vokonas PS. Body weight and coronary disease risk: patterns of risk factor change associated with long-term weight change: the Normative Aging Study. *Am J Epidemiol.* 1986;124:410-419.
23. Tuck ML, Sowers J, Dornfeld L, Kledzik G, Maxwell M. The effect of weight reduction on blood pressure, plasma renin activity, and plasma aldosterone levels in obese patients. *N Engl J Med.* 1981;304:930-933.
24. Jones DW. Body weight and blood pressure: effects of weight reduction on hypertension. *Am J Hypertens.* 1996;9:50s-54s.
25. MacMahon SW, Wilcken DE, Macdonald GJ. The effect of weight reduction on left ventricular mass: a randomized controlled trial in young, overweight hypertensive patients. *N Engl J Med.* 1986;314:334-339.
26. Neaton JD, Grimm RH Jr, Prineas RJ, et al, for the Treatment of Mild Hypertension Study Research Group. Treatment of Mild Hypertension Study: final results. *JAMA* 1993;270:713-724.
27. Bønaa KH, Thelle DS. Association between blood pressure and serum lipids in a population: the Tromsø Study. *Circulation.* 1991;83:1305-1314.
28. Selmer R, Tverdal A. Body mass index and cardiovascular mortality at different levels of blood pressure: a prospective study of Norwegian men and women. *J Epidemiol Community Health* 1995;49:265-270.
29. Njølstad I, Arnesen E, Lund-Larsen PG. Body height, cardiovascular risk factors, and risk of stroke in middle-aged men and women: a 14-year follow-up of the Finnmark Study. *Circulation.* 1996;94:2877-2882.
30. Johansson S, Bergstrand R, Ulvenstam G, et al. Sex differences in preinfarction characteristics and longterm survival among patients with myocardial infarction. *Am J Epidemiol.* 1984;119:610-623.
31. Bønaa KH, Bjerve KS, Straume B, Gram IT, Thelle D. Effect of eicosapentaenoic and docosahexaenoic acids on blood pressure in hypertension: a population-based intervention trial from the Tromsø study. *N Engl J Med.* 1990;322:795-801.
32. SAS Institute Inc. *SAS/STAT User's Guide.* Cary, NC: SAS Institute Inc; 1989.
33. Rosenbaum M, Leibel RL, Hirsch J. Obesity [review]. *N Engl J Med.* 1997;337: 396-407.
34. Berchtold P, Jorgens V, Kemmer FW, Berger M. Obesity and hypertension: cardiovascular response of weight reduction [review]. *Hypertension.* 1982;4(5, pt 2):III50-III55.
35. Rostrup M, Ekeberg O. Awareness of high blood pressure influences on psychological and sympathetic responses. *J Psychosom Res.* 1992;36:117-123.
36. Lerner DJ, Kannel WB. Patterns of coronary heart disease morbidity and mortality in the sexes: a 26-year follow-up of the Framingham population. *Am Heart J.* 1986;111:383-390.
37. Tverdal A, Thelle D, Stensvold I, Leren P, Bjartveit K. Mortality in relation to smoking history: 13 years' follow-up of 68,000 Norwegian men and women 35-49 years. *J Clin Epidemiol.* 1993;46:475-487.
38. Nyboe J, Jensen G, Appleyard M, Schnohr P. Smoking and the risk of first acute myocardial infarction. *Am Heart J.* 1991;122:438-447.
39. Daniels SR, Heiss G, Davis CE, Hames CG, Tyroler HA. Race and sex differences in the correlates of blood pressure change. *Hypertension.* 1988;11:249-255.

PAPER III



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Tracking of Cardiovascular Risk Factors

The Tromsø Study, 1979–1995

Tom Wilsgaard, Bjarne K. Jacobsen, Henrik Schirmer, Inger Thune, Maja-Lisa Løchen, Inger Njølstad, and Egil Arnesen

Tracking of cardiovascular risk factors (blood pressure, body mass index (BMI), and serum lipids) has not been studied much in a general, adult population. No known study has compared tracking of these factors for both sexes. In the present study, 17,710 men and women aged 20–61 years at baseline attended two or three population-based health surveys in Tromsø, Norway, over 16 years (between 1979–1980 and 1994–1995). Tracking coefficients were estimated by using different methods, and possible predictors of tracking were found. There was a high degree of tracking for BMI (overall tracking coefficients: 0.85 for men, 0.80 for women). Relatively high (or moderate) tracking was found for systolic blood pressure (respective sex-specific coefficients: 0.52, 0.54), diastolic blood pressure (0.48, 0.48), high density lipoprotein cholesterol (0.55, 0.64), and total cholesterol (0.77, 0.65). The lowest coefficients were for triglycerides (0.43, 0.39). Analysis of tracking in the upper sextile confirmed these results. Although some baseline predictors were associated with tracking, the effects were relatively weak. When predictors for tracking in the upper sextile were assessed, significant associations were found with relatively strong effects. No major sex differences were observed in tracking. However, women were more likely than men to remain in the upper sextile of systolic and diastolic blood pressures and of BMI. *Am J Epidemiol* 2001;154:418–26.

blood pressure; body mass index; cohort studies; lipids

Biologic and lifestyle variables such as serum lipids, blood pressure, smoking habits, and body weight are all risk factors for cardiovascular diseases (1–4). If one assessment was representative of the long-term level of these risk factors, this measurement could predict disease occurrence. Tracking of a characteristic has been defined as either the stability of a certain variable over time (e.g., maintenance of a relative position within a distribution of values over time) or the predictability of later values from earlier measurements (5–7), and it is therefore of considerable interest. Most earlier studies have examined tracking of risk factor levels in childhood or adolescence into adulthood (8–13). The few existing papers concerning adults either did not assess sex differences (14, 15) or did not investigate a broad number of variables (12, 14, 15). Furthermore, few have analyzed large samples from a general population.

Tracking of cardiovascular risk factors may facilitate understanding of how a variable changes over time. Knowledge about tracking is important for several reasons, for example, to be able to identify in early adulthood persons at increased risk of cardiovascular disease. Assessment of sex differences in the stability of a certain variable over time may lead to a better understanding of sex differences in the incidence of cardiovascular diseases. Furthermore, knowledge of tracking of different characteristics provides the opportunity to investigate and compare the degree of tracking between different risk factors within a population.

The first purpose of this study was to address sex differences and degree of tracking of blood pressure, body mass index (BMI), and serum lipids in a general population of more than 18,000 persons examined two or three times over a period of 16 years. To quantify the tendency for subjects to maintain high levels of these variables over time, tracking was also assessed by focusing on the upper distributions of these risk factors. The second purpose was to investigate predictors of tracking (dichotomized), both in general and restricted to the upper distributions of risk factors.

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Abbreviations: BMI, body mass index; GEE, generalized estimating equations; HDL, high density lipoprotein.

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MATERIALS AND METHODS

Study population

The persons included in the study were men and women who participated in at least two of three population surveys carried out between 1979–1980 and 1994–1995 in the municipality of Tromsø, northern Norway (table 1). In 1979–1980, all men born between 1925 and 1959 and all

TABLE 1. Number (percentage) of participants, by examination year and sex, in the Tromsø Study, Tromsø, Norway, 1979–1995

	Men		Women		Total	
	Invited	Attended	Invited	Attended	Invited	Attended
Invited and attended						
In 1979–1980	11,483	8,478	9,957	8,142	21,440	16,620
In 1986–1987	14,537	10,413	12,879	10,189	27,416	20,602
In 1994–1995*	9,850	8,242	9,501	8,300	19,351	16,542
Subjects included in the study						
In 1979–1980 and 1986–1987 only		1,011 (10.9)		819 (9.0)		1,830 (9.9)
In 1979–1980 and 1994–1995 only		504 (5.5)		414 (4.5)		918 (5.0)
In 1986–1987 and 1994–1995 only		2,561 (27.7)		2,615 (28.7)		5,176 (28.2)
In all three examinations		5,177 (55.9)		5,271 (57.8)		10,448 (56.9)
All subjects		9,253 (100)		9,119 (100)		18,372 (100)

* Participants who attended at least one of the previous two examinations.

women born between 1930 and 1959 were invited to participate in a health survey. The total number examined was 16,621 (78 percent attendance rate). Men born between 1925 and 1966 and women born between 1930 and 1966 were again invited to participate in a second health survey in 1986–1987. The invited population consisted of 27,416 men and women (75 percent attendance rate). All men and women aged ≥25 years who lived in the area were invited to a third examination in 1994–1995. Of those persons who attended at least one of the previous two surveys, 19,351 were invited to this last survey; 16,542 were examined (85 percent attendance rate). The 18,372 men and women who had participated in at least two of the three surveys were eligible for the present study. Persons with missing measures of blood pressure, BMI, high density lipoprotein (HDL) cholesterol, total cholesterol, or triglycerides; with missing information about smoking habits; or with treatment for hypertension were excluded from the study ($n = 156$). Women who were pregnant at one of the examinations were also excluded ($n = 506$). Hence, data on 9,168 men and 8,542 women were included in the present analyses.

Measurements

At each survey, the weight, height, and blood pressure of all participants were measured. Blood samples were taken, and the subjects answered a questionnaire (variables of interest were "current smoker" (yes/no) and "treatment for hypertension" (yes/no)). The methods used at the three examinations were almost identical and are presented in detail elsewhere (16, 17). Height and weight were measured with subjects wearing light clothing and no shoes. BMI was calculated as weight in kilograms divided by the square of height in meters (kg/m^2).

Personnel trained by physicians and by listening to tape recordings of Korotkoff sounds, which were produced by the London School of Hygiene and Tropical Medicine (United Kingdom), measured blood pressure. In 1979–1980, after subjects rested for 4 minutes, two readings—separated by a 1-minute interval—were taken by using a standard stethoscope and mercury sphygmomanometer. The first and fifth Korotkoff phases represented systolic and diastolic blood pressures, respectively. In 1986–1987 and 1994–1995, blood pressure was recorded by using an automatic device (Dinamap Vital Signs Monitor 1846; Critikon Inc., Tampa, Florida). After participants rested for 2 minutes in a sitting position, three readings were taken on the upper right arm, separated by 2-minute intervals. In 1979–1980, the average of the two blood pressure readings was used whereas in 1986–1987 and 1994–1995, the average of the last two readings was used.

Blood pressures measured with the Dinamap device are slightly lower than those measured with a sphygmomanometer (Erkameter; ERKA, Bad Tölz, Germany), especially for diastolic blood pressure (18). However, there is a linear relation, with correlation coefficients of 0.9 for systolic blood pressure and 0.8 for diastolic blood pressure. Therefore, to adjust for the change in method, we transformed our Dinamap measurements into predicted values of Erkameter measurements.

The nonfasting blood samples were analyzed at the Department of Clinical Chemistry, University Hospital of Tromsø. The laboratory was standardized against the World Health Organization's Lipid Reference Laboratory in Prague (Czech Republic). In 1979–1980, total cholesterol was measured directly by using the enzymatic oxidase method and a commercially available kit (Boehringer-Mannheim, Mannheim, Germany). Triglyceride levels were enzymatically determined as glycerol (Boehringer 15725; Boehringer-Mannheim). In 1986–1987 and 1994–1995, total cholesterol and triglycerides were analyzed by using colorimetric methods and commercially available kits (CHOD-PAP for cholesterol, GPO-PAP for triglycerides; Boehringer-Mannheim). HDL levels were measured after precipitation of lower-density lipoproteins with heparin and manganese chloride.

Analyses

Tracking indices may be calculated by using different methods. In our study, we used two methods. The first was

introduced by Twisk et al. (19) and is a multivariate linear regression model, as follows:

$$Y_{it} = \beta_0 + \beta_1 Y_{it_1} + \beta_2 t_1 + \beta_3 t + \sum_j \beta_{4j} X_{ijt} + \sum_k \beta_{5k} Z_{ik} + \varepsilon_{it} \quad (1)$$

- Y_{it} is the dependent variable (which, in the present study, may be blood pressure, BMI, HDL cholesterol, total cholesterol, or triglycerides) for subject i at time t_2 or t_3, and the baseline examination of each subject is modeled as time t_1 (either 1979–1980 or 1986–1987).
- $t = t_2$ is the second examination (either 1986–1987 or 1994–1995), and $t = t_3$ is the third examination (if any in 1994–1995).
- β_0 is the intercept.
- β_1 is the standardized regression coefficient used as the tracking index, and Y_{it_1} is the initial value of the dependent variable for subject i at time t_1.
- β_2 is the regression coefficient of time at the baseline examination.
- β_3 is the regression coefficient of time, and t is time of examination of the dependent variable (t_2 or t_3).
- β_{4j} is the regression coefficient of the time-dependent covariate j, and X_{ijt} is the time-dependent covariate j for subject i.
- β_{5k} is the regression coefficient of the time-independent covariate k, and Z_{ik} is the time-independent covariate k for subject i.
- ε_{it} is the measurement error for subject i.

The tracking coefficient β_1 may be interpreted as the prediction of the dependent variable's initial value when the dependent variable changes at time t_2 and t_3.

The present model has several advantages compared with other tracking models. It handled missing values of the dependent variable, so a balanced data set was not required. All of the available longitudinal data could be used to calculate the tracking indices. Use of covariates, both time dependent and time independent, allowed us to adjust for possible confounders. The statistical technique used, which controls for dependencies between repeated observations in the same subject, is called generalized estimating equations (GEE) (20).

The second method presented the proportion of subjects who remained in the same sextile throughout the different examinations. We also classified the number of sextiles changed relative to the subject's initial examination. All proportions were compared with the proportions expected if all subjects were classified randomly to a sextile group at each examination. If the changes from one examination to the next had been random, we would have expected 38.9 percent of the subjects to have changed fewer than three sextiles. Comparisons between observed and expected proportions would have been valid only if the observed numbers were restricted to subjects who attended all three examinations. Hence, the number of participants included in these calculations was reduced to 5,014 men and 4,917 women.

To assess the tendency to maintain a high level of a certain risk factor over time, we used a method comparable to an ordinary multivariate logistic regression analysis. However, the difference was that GEE were used to control for dependencies between repeated observations of the same participant. Participants were dichotomized to a binary variable according to whether they belonged to the upper sextile of the specified risk factor. Tracking coefficients were given as odds ratios for participants belonging to the upper sextile at the initial examination who maintained this position at later examinations.

The same models—interpreted as an ordinary logistic regression analysis—were also used to investigate the predictors of tracking (dichotomized). Tracking was defined by two classification methods: first, tracking was present whenever participants maintained their baseline position in a sextile; second, tracking was present whenever subjects maintained their position in the upper sextile.

Two-sided p values of less than 0.05 were considered statistically significant. All statistical analyses were carried out by using the SAS software system (21).

RESULTS

Overall means and standard deviations, and means according to sextile groups of baseline characteristics, are presented in table 2. In every sextile, women had lower mean values of systolic and diastolic blood pressures, BMI, total cholesterol, and triglycerides than men did. Men had lower mean values of HDL cholesterol.

Table 3 shows the standardized regression coefficients that were interpreted as tracking coefficients according to age for blood pressure, BMI, and serum lipids. The coefficients were adjusted for age, blood pressure treatment, time of baseline examination (1979–1980 or 1986–1987), and time of follow-up examination (1986–1987 and/or 1994–1995). For systolic and diastolic blood pressures, and for BMI in women, the tracking coefficients tended to increase with age. The tracking coefficients for BMI were higher than for all other risk factors, and the ones for triglycerides were the lowest. There was no sex difference for systolic blood pressure, diastolic blood pressure, and triglycerides. Overall, the observed coefficients for systolic blood pressure, diastolic blood pressure, BMI, HDL cholesterol, total cholesterol, and triglycerides were 0.52, 0.48, 0.85, 0.55, 0.77, and 0.43 for men and 0.54, 0.48, 0.80, 0.64, 0.65, and 0.39 for women, respectively.

To study the influence of smoking habits, we stratified for smoking (never smoker, stopped smoking, started smoking, consistent smoker) in a separate set of analyses. The coefficients for subjects who changed their smoking habits tended to be lower than those for subjects who were either consistent smokers or never smokers, although the differences did not reach significance (results not shown in tables).

A higher-than-expected proportion of subjects did not change sextile over the three examinations (table 4). Changes of one (or two) sextile(s) represented participants who moved one (or two) sextile(s) away from the baseline sextile in at least one of the two examinations that followed the baseline examination. These proportions may be com-

TABLE 2. Means of baseline characteristics, by sextile group and sex, the Tromsø Study, Tromsø, Norway, 1979–1995

Baseline predictor*	Means (SD†)	Sextile					
		1	2	3	4	5	6
Men (n = 9,168)							
Systolic BP† (mmHg)	132.2 (13.4)	114.3	122.5	128.4	133.6	140.0	154.3
Diastolic BP (mmHg)	82.5 (10.0)	68.4	76.0	80.0	84.0	88.9	98.3
Body mass index (kg/m²)	24.3 (2.9)	20.5	22.3	23.4	24.6	25.9	29.0
HDL† cholesterol (mmol/liter)	1.42 (0.42)	0.95	1.16	1.30	1.44	1.61	2.08
Total cholesterol (mmol/liter)	5.88 (1.29)	4.14	4.94	5.50	6.05	6.70	7.96
Triglycerides (mmol/liter)	1.62 (0.97)	0.67	0.97	1.24	1.55	1.99	3.30
Age (years)	35.2 (9.6)	22.1	27.0	32.0	36.4	42.3	51.0
Women (n = 8,542)							
Systolic BP (mmHg)	122.6 (13.3)	106.1	113.7	118.6	123.0	129.2	144.8
Diastolic BP (mmHg)	79.0 (9.0)	66.6	72.8	76.7	80.0	84.2	93.6
Body mass index (kg/m²)	22.6 (3.3)	18.9	20.5	21.6	22.6	24.1	28.2
HDL cholesterol (mmol/liter)	1.70 (0.40)	1.17	1.42	1.58	1.74	1.95	2.35
Total cholesterol (mmol/liter)	5.58 (1.18)	4.06	4.75	5.20	5.68	6.28	7.52
Triglycerides (mmol/liter)	1.08 (0.59)	0.52	0.71	0.86	1.04	1.30	2.06
Age (years)	32.9 (8.2)	22.1	26.4	30.6	34.4	38.9	45.8

* For each baseline predictor, each sextile represents a different set of subjects; the predictor was measured in either 1979–1980 or 1986–1987.

† SD, standard deviation; BP, blood pressure; HDL, high density lipoprotein.

pared with what is expected given that each subject was randomly assigned to a sextile at each examination. For all risk factors, a significantly higher proportion of participants changed fewer than three sextiles, clearly indicating the presence of tracking. No major sex difference was observed, although tracking seemed to be higher for women than for men. BMI was an exception. The rank order of the risk factors, from highest to lowest, for which both men and women changed fewer than three sextiles was as follows: BMI, total cholesterol, HDL cholesterol, systolic blood pressure, diastolic blood pressure, and triglycerides. To more easily assess the stability of each risk factor over time and to use all available data, we calculated the proportions of participants who remained in the same sextile between two examinations. We found that 32.1, 31.6, 49.9, 36.2, 39.9, and 27.1 percent of the men remained in the same sextile of systolic blood pressure, diastolic blood pressure, BMI, HDL cholesterol, total cholesterol, and triglycerides, respectively. The corresponding estimates for women were 33.7, 32.1, 47.5, 36.3, 40.7, and 28.0.

There were no strong baseline predictors for tracking in the same sextile for blood pressure, BMI, and serum lipids, although some were statistically significant (results not shown). A few sex differences were found, however. Tracking of BMI was significantly associated with age, HDL cholesterol, total cholesterol, triglycerides, and current smoking. For men, only triglycerides contributed statistically significantly. In addition, BMI at baseline had a significant association with tracking of systolic and diastolic blood pressures in women, but not in men.

Table 5 shows the tracking coefficients expressed as odds ratio estimates for participants in the upper sextile (for HDL, the lowest sextile) at baseline, relative to all other subjects, remaining in the upper sextile (lowest sextile for HDL) at later examinations. The coefficients for the youngest subjects (aged 20–24 years) tended to be the lowest, but no other age trend was observed. Consequently, the results were presented without any age stratification. The odds ratio for the BMI coefficient is notable because it is much higher than the odds ratios for the other coefficients. Participants in the upper sextile of baseline BMI had more than 30 times higher odds of remaining in this sextile at later examinations compared with participants in the other five sextiles. There was no significant sex difference in the odds ratio estimates for serum lipids. For blood pressures and BMI, the estimates for women were significantly higher ($p \leq 0.003$). The proportion of participants who remained in the high-risk group (upper sextile) varied from 40 to 75 percent.

For cardiovascular risk factors, participants who maintained their position in the upper sextile (lower sextile for HDL cholesterol) at later examinations were categorized as tracking in the upper (lower) sextile. Table 6 shows the association between tracking and baseline variables. All baseline risk factors (except HDL cholesterol and, for women, current smoker) were significantly associated with tracking of systolic and diastolic blood pressures in the upper sextile.

TABLE 3. Tracking coefficients* (SE†) for cardiovascular risk factors, by age at baseline and sex, the Tromsø Study, Tromsø, Norway, 1979–1995

Sextile of baseline age (years)	No.	Systolic BP†	Diastolic BP	Body mass index	HDL† cholesterol	Total cholesterol	Triglycerides
				Men (n = 9,168)			
20–24	1,366	0.50 (0.02)	0.38 (0.03)	0.80 (0.02)	0.53 (0.09)	0.70 (0.02)	0.30 (0.03)
25–29	1,600	0.51 (0.03)	0.46 (0.03)	0.84 (0.01)	0.52 (0.08)	0.74 (0.02)	0.41 (0.03)
30–34	1,765	0.57 (0.02)	0.47 (0.02)	0.83 (0.02)	0.52 (0.08)	0.72 (0.02)	0.46 (0.03)
35–38	1,271	0.49 (0.02)	0.48 (0.02)	0.83 (0.02)	0.56 (0.09)	0.72 (0.02)	0.49 (0.04)
39–46	1,707	0.56 (0.02)	0.52 (0.02)	0.82 (0.01)	0.53 (0.07)	0.73 (0.02)	0.45 (0.03)
47–61	1,459	0.55 (0.02)	0.50 (0.02)	0.82 (0.02)	0.62 (0.08)	0.69 (0.03)	0.43 (0.03)
Overall	9,168	0.52 (0.01)	0.48 (0.01)	0.85 (0.01)	0.55 (0.03)	0.77 (0.01)	0.43 (0.01)
				Women (n = 8,542)			
20–24	1,531	0.50 (0.02)	0.43 (0.02)	0.73 (0.02)	0.51 (0.06)	0.62 (0.02)	0.33 (0.04)
25–29	1,748	0.53 (0.02)	0.45 (0.02)	0.76 (0.02)	0.66 (0.02)	0.68 (0.02)	0.35 (0.03)
30–34	1,852	0.56 (0.02)	0.45 (0.02)	0.79 (0.02)	0.66 (0.02)	0.69 (0.02)	0.39 (0.06)
35–38	1,175	0.55 (0.02)	0.52 (0.02)	0.79 (0.03)	0.62 (0.06)	0.65 (0.02)	0.37 (0.09)
39–46	1,608	0.59 (0.02)	0.55 (0.02)	0.82 (0.01)	0.69 (0.02)	0.66 (0.02)	0.45 (0.06)
47–56	628	0.61 (0.04)	0.55 (0.03)	0.82 (0.04)	0.66 (0.04)	0.65 (0.05)	0.51 (0.05)
Overall	8,542	0.54 (0.01)	0.48 (0.01)	0.80 (0.01)	0.64 (0.02)	0.65 (0.01)	0.39 (0.02)

* Standardized regression coefficients with the baseline measurement as the independent variable and later measurements as dependent variables; all coefficients adjusted for age, treatment for hypertension, time of baseline examination (1979–1980 or 1986–1987), and time of follow-up examination (1986–1987 and/or 1994–1995).

† SE, standard error; BP, blood pressure; HDL, high density lipoprotein.

For tracking of BMI in the upper sextile, all variables listed in table 6 were significant predictors ($p < 0.01$). Significant predictors for tracking of HDL cholesterol in the lower sextile were BMI, triglycerides, current smoker, and age (and systolic blood pressure in women only). Systolic blood pressure in men and HDL cholesterol in women were not significant as baseline predictors for tracking in the upper sextile of total cholesterol. Except for age in men, all listed variables were significant predictors for tracking of triglycerides in the upper sextile. For most of the independent variables considered, direct relations were observed between the variable and the odds of remaining in the upper sextile. For some variables, an inverse relation was found, however. Current smokers had decreased odds for tracking of systolic blood pressure, diastolic blood pressure (in men), and BMI. Higher values of HDL cholesterol were associated with decreased odds for tracking of BMI and triglycerides.

DISCUSSION

In this paper, we have presented tracking coefficients and predictors for tracking of systolic blood pressure, diastolic blood pressure, BMI, HDL cholesterol, total cholesterol, and triglycerides in a population-based cohort study over a period of 16 years. For both men and women, significant tracking coefficients were found for all six cardiovascular risk factors. However, when the degree of tracking is evaluated, the magnitude rather than the significance of the coefficients should be used. Nonfasting triglycerides, for which our tracking coefficients were close to 0.30 in the youngest age groups, are hardly stable over time. Systolic and diastolic blood pressures and HDL cholesterol in men, for which the overall coefficients were at or just below 0.50, showed a moderate degree of tracking. For total cholesterol, HDL cholesterol in women, and BMI, the tracking coefficients were more than 0.50, indicating relatively high stability over time.

Tracking was strongest for BMI in both men and women, and there was no significant sex difference for tracking of blood pressure and triglycerides. For tracking in the upper sextile, a similar picture was observed; BMI had the highest level of tracking and triglycerides the lowest. Compared with men, women had a significantly higher level of tracking of systolic and diastolic blood pressures and of BMI in the upper sextile. Otherwise, there were no sex differences.

To understand the implications of the odd ratios presented in table 5, we compared them with the corresponding percentages of remaining in the upper sextile calculated from 2 × 2 tables (predictive values of the baseline measurement). An odds ratio of 38.3 (BMI in women) translates into a predictive value of 71 percent, whereas odds ratios of 10 and 5 correspond to predictive values of approximately 52 and 41 percent, respectively. These percentages indicate that, although the difference between odds ratios of 38 and 10 (BMI and cholesterol in women) is rather high, the differ-

TABLE 4. Estimated probabilities of changing sextile group in a 16-year follow-up,* the Tromsø Study, Tromsø, Norway, 1979–1995

	No. of sextile groups changed relative to the baseline examination†				
	0	1	2	0 + 1 + 2	3 + 4 + 5
	Men (n = 5,014)				
Systolic BP‡	0.134	0.320	0.295	0.749	0.251
Diastolic BP	0.130	0.306	0.299	0.735	0.265
Body mass index	0.294	0.445	0.193	0.932	0.068
HDL‡ cholesterol	0.185	0.359	0.268	0.812	0.188
Total cholesterol	0.205	0.397	0.261	0.863	0.137
Triglycerides	0.102	0.254	0.293	0.649	0.351
Expected§	0.028	0.139	0.222	0.389	0.611
	Women (n = 4,917)				
Systolic BP	0.158	0.341	0.290	0.789	0.211
Diastolic BP	0.130	0.319	0.292	0.741	0.259
Body mass index	0.278	0.441	0.206	0.925	0.075
HDL cholesterol	0.182	0.371	0.261	0.815	0.185
Total cholesterol	0.211	0.400	0.261	0.872	0.128
Triglycerides	0.104	0.276	0.280	0.660	0.340
Expected§	0.028	0.139	0.222	0.389	0.611

* Unadjusted results.
† 0, no changes (in the same sextile group in all examinations); 1–5, number of sextile groups changed relative to the baseline examination.
‡ BP, blood pressure; HDL, high density lipoprotein.
§ The expected distribution if no tracking took place (the subjects were randomly assigned to a sextile group at each examination).

ence between the corresponding predictive values (71 and 52 percent) is more moderate. Note that predictive values calculated from the odds ratios do not necessarily coincide with the percentages shown in table 5. The odds ratios were adjusted for dependencies between repeated observations and for covariates, whereas the predictive values in table 5 are unadjusted results. However, if we consider a predictive value of 51.3 percent (HDL cholesterol in women), the corresponding unadjusted odds ratio would be 9.8, almost equal to the odds ratio given in table 5. It is not straightforward to

TABLE 5. Percentage of subjects who remained in the upper sextile and odds ratio estimates for subjects in the upper sextile (relative to subjects in the other five sextiles) of being in the upper sextile at later examinations,* the Tromsø Study, Tromsø, Norway, 1979–1995

Baseline upper sextile† of	Men (*n* = 9,168)			Women (*n* = 8,542)			*p* value for sex difference
	%‡	OR§	95% CI§	%‡	OR	95% CI	
Systolic BP§	50.6	6.5	5.8, 7.4	59.5	8.7	7.6, 9.9	0.0007
Diastolic BP	49.4	4 9	4.3, 5.6	54.0	6.1	5.4, 6.9	0.0002
Body mass index	71.0	32 4	28.3, 37.1	75.2	38.3	33.1, 44.2	0.003
HDL cholesterol	50.2	9.4	8.4, 10.5	51.3	10.2	9.1, 11.4	0.4
Total cholesterol	61.5	12.9	11.4, 14.5	63.7	10.6	9.3, 12.2	0.3
Triglycerides	40.2	4.7	4.2, 5.3	41.3	4.8	4.3, 5.3	0.5

* In each of the six models, the coefficient was adjusted for age, treatment for hypertension, time of baseline examination (1979–1980 or 1986–1987), and time of follow-up examination (1986–1987 and/or 1994–1995).
† For high density lipoprotein (HDL) cholesterol, odds ratios were estimated for subjects classified in the lower sextile.
‡ Percentage of subjects who remained in the upper sextile.
§ OR, odds ratio; CI, confidence interval; BP, blood pressure.

TABLE 6. Sex-specific odds ratio estimates of baseline predictors of remaining in the upper sextile relative to the baseline examination,† the Tromsø Study, Tromsø, Norway, 1979–1995

Baseline predictor	Remained in the upper (lower for HDL‡ cholesterol) sextile at later examinations for					
	Systolic BP‡	Diastolic BP	Body mass index	HDL cholesterol	Total cholesterol	Triglycerides
			Men (n = 9,168)			
Age (10 years)	2.09***	2.12***	1.39***		2.16***	
Systolic BP (15 mmHg)	—§	—§	1.38***			1.33***
Body mass index (3 kg/m²)	1.34***	1.52***	—§	1.66***	1.26***	1.91***
HDL cholesterol (1 mmol/liter)			0.30***	—§	1.28***	0.28***
Total cholesterol (1 mmol/liter)	1.14***	1.17***	1.38***		—§	1.87***
Triglycerides (1 mmol/liter)	1.18***	1.27***	1.61***	1.67	1.55***	—§
Current smoker (yes/no)	0.84*	0.85*	0.84**	1.30***	1.28***	1.20*
			Women (n = 8,542)			
Age (10 years)	3.24***	2.76***	1.90***	0.79***	3.66***	1.65***
Systolic BP (15 mmHg)	—§	—§	1.62***	1.10*	1.21***	1.43***
Body mass index (3 kg/m²)	1.47***	1.48***	—§	1.41***	1.30***	1.65***
HDL cholesterol (1 mmol/liter)			0.36***	—§		0.12***
Total cholesterol (1 mmol/liter)	1.17***	1.24***	1.37***		—§	1.87***
Triglycerides (1 mmol/liter)	1.29***	1.30***	1.79***	2.20***	2.06***	—§
Current smoker (yes/no)	0.70***		0.74***	2.42***	1.48***	1.66***

* $p < 0.05$; ** $p < 0.01$; *** $p < 0.001$.

† All coefficients adjusted for age, treatment for hypertension, time of baseline examination (1979–1980 or 1986–1987), and time of follow-up examination (1986–1987 and/or 1994–1995); only significant coefficients are presented.

‡ HDL, high density lipoprotein; BP, blood pressure.

§ Variable not included.

set a cutoff point for the level of the predictive value to classify tracking. In a general population, predictive values of about 50 percent may be moderate, however, although they are still important markers for later classification in high-risk groups, depending on the variable in question. In this study, HDL cholesterol and total cholesterol showed odds ratios of about 10, with corresponding predictive values of about 50 percent, whereas the predictive values for systolic blood pressure, diastolic blood pressure, and triglycerides ranged between 40 and 50 percent.

For tracking of the risk factors in the upper sextile (table 6), most of the baseline predictors had significant and relatively large effects. There were no clear sex differences, although the odds ratios for the baseline predictors tended to be stronger for women than for men.

Although the distributions of many of the variables examined in this study were quite different between men and women, a lack of sex difference in tracking was observed for some variables. This finding may be remarkable; however, a sex difference in baseline distribution does not necessarily imply that the stability of a variable over time should differ as well.

Comparisons of the tracking coefficients found in this study with those of other studies were hampered because both the methods used and the time span considered differed. To our knowledge, the Amsterdam Growth and Health Study (11), which introduced the GEE tracking coefficients, is the only one that has used a directly comparable method. However, that study had a mean baseline age of 13 years and included only 181 subjects. The tracking coefficients for systolic blood pressure, diastolic blood pressure, and total cholesterol were considered not to differ between the sexes and were estimated to be 0.43, 0.34 and 0.71, respectively. For HDL cholesterol, the coefficients were 0.51 and 0.65 for men and women, respectively. These results may be relevant to the results obtained for our youngest age group.

The correlation coefficient is the most frequently used measure of tracking. The advantage of the GEE tracking coefficient, which also ranges between −1 and 1, is that the GEE method uses all available data; allows for adjustment of covariates, both time dependent and independent; and accounts for the correlation among the repeated observations for a given subject. The GEE also handle missing values.

In a comparison with the traditional method, a correlation analysis between the first and the last surveys showed coefficients of 0.52, 0.46, 0.79, 0.50, 0.66, and 0.39 for systolic blood pressure, diastolic blood pressure, BMI, HDL cholesterol, total cholesterol, and triglycerides in men, respectively. For women, the respective coefficients were 0.60, 0.49, 0.80, 0.61, 0.68, and 0.38. These coeffi-

cients tended to be lower than the GEE tracking coefficients. In an earlier paper from the Tromsø Study (22), we found correlation coefficients of blood pressure lower but also still comparable to the present results. A total of 4,183 men aged 20–49 years at baseline were examined in 1974, 1979–1980, and 1986–1987, and the correlation coefficients between the first and last examinations were 0.46 and 0.40 for systolic and diastolic blood pressures, respectively. The Cardiovascular Risk in Young Finns study (13) presented tracking of serum lipids in subjects with an initial age of 18 years. The 12-year Spearman's correlation coefficients were 0.54, 0.73, and 0.49 for HDL cholesterol, total cholesterol, and triglycerides in men and 0.56, 0.51, and 0.37 in women, respectively. These estimates were somewhat higher than those found in our youngest age group. However, considering the small sample size—65 men and 51 women—the general impression is comparable to the Tromsø Study. The findings in the Framingham Study (23), which included 1,605 men and women aged 49–82 years, agree with those from the oldest age group in the Tromsø Study. The 8-year correlation coefficients for HDL cholesterol and total cholesterol were 0.68 and 0.69 for men and 0.60 and 0.61 for women, respectively. In the Dormont High School Study (24), tracking was assessed for systolic blood pressure, diastolic blood pressure, and weight. The mean baseline age was 34 years, and the respective 12-year correlation coefficients for 202 subjects were 0.38, 0.44, and 0.88 for men and 0.54, 0.54, and 0.81 for women.

Classification of the change in sextile group relative to the baseline examination (table 4) provided further and unadjusted information about the stability of the tracking variables (compared with the GEE method). Although the methods address the same questions, the interpretation is somewhat different, because the results shown in table 4 reflect exactly the proportions of movement between the sextile groups.

Several studies have shown results of tracking in the upper part of the distribution of risk factors (8, 11, 13, 14). However, it is difficult to compare these findings with the present results. Most studies show the frequency of subjects who remain (or the relative likelihood of remaining) in a high position between two examinations. In the Amsterdam Growth and Health Study (11), the odds ratios for subjects who were at risk at the age of 13 years to still be at risk 15 years later were 4.0, 4.8, 14.1, and 10.4 for systolic blood pressure, diastolic blood pressure, HDL cholesterol, and total cholesterol, respectively. No significant sex differences were found.

Although some studies have used baseline measurements as predictors for later values (13, 19, 25), to our knowledge no study has classified subjects who maintain their relative position over time (subjects who track) and then assessed predictors for tracking. Consequently, our results could not be compared with other studies.

There were some sources of bias in this study. People who were treated for hypertension in at least one of the examinations were not excluded from the analyses. However, in a separate set of analyses, we did exclude subjects with a history of treatment for hypertension. None of the results presented was altered significantly, and all conclusions remained unchanged. If we had excluded subjects who had a history of blood pressure treatment (1,339 men and women), we would have missed 16.5 percent of our cohort with a baseline age of more than 39 years.

The problem of measurement error may have had an impact on tracking. Single values of blood pressure and serum lipids may not reflect a person's true level as well as a single value of BMI, which may lead to underestimation of tracking, especially for systolic and diastolic blood pressures and for triglycerides. Since this study was nonfasting, it could have influenced the values of some of the variables. Measurements of diastolic blood pressure and triglycerides, in particular, may be associated with "time since last meal." However, including this variable in our models did not change the results.

Clinical implications for cardiovascular disease may be drawn from the present results. The stability of BMI over time indicates that we can, with a relatively high degree of certainty, identify participants who maintain their high BMI value. To improve the general health profile of persons later in life, a focus on physical activity and change in food habits during adolescence and young adulthood is therefore advocated. Although the predictability of initial values of blood pressure and serum lipids was lower than that of BMI, the implication of maintaining a high level should not be overlooked. Several studies have shown that a reduction in total cholesterol or an increase in HDL cholesterol predicts a reduction in cardiovascular disease (26, 27). Identification of subjects in the upper part of the total cholesterol distribution (lower part for HDL cholesterol) is therefore of clinical importance in preventive medicine. The same can be said for systolic and diastolic blood pressures, for which, in this study, the odds ratios were slightly lower than the odds ratio for cholesterol.

In conclusion, over a period of 16 years, we found a high degree of tracking of BMI for young and middle-aged men and women, in either the general BMI distribution or the upper part of the distribution. The stability of blood pressure, HDL cholesterol, total cholesterol, and triglycerides over time was more moderate, but still not negligible. Values from other baseline variables had a relatively low predictability of the overall tracking of a specified risk factor, whereas baseline predictors contributed a relatively strong association to tracking in the upper sextile. With the exception that women were more likely to stay in the upper sextile of systolic and diastolic blood pressures, no major sex differences were detected in this study.

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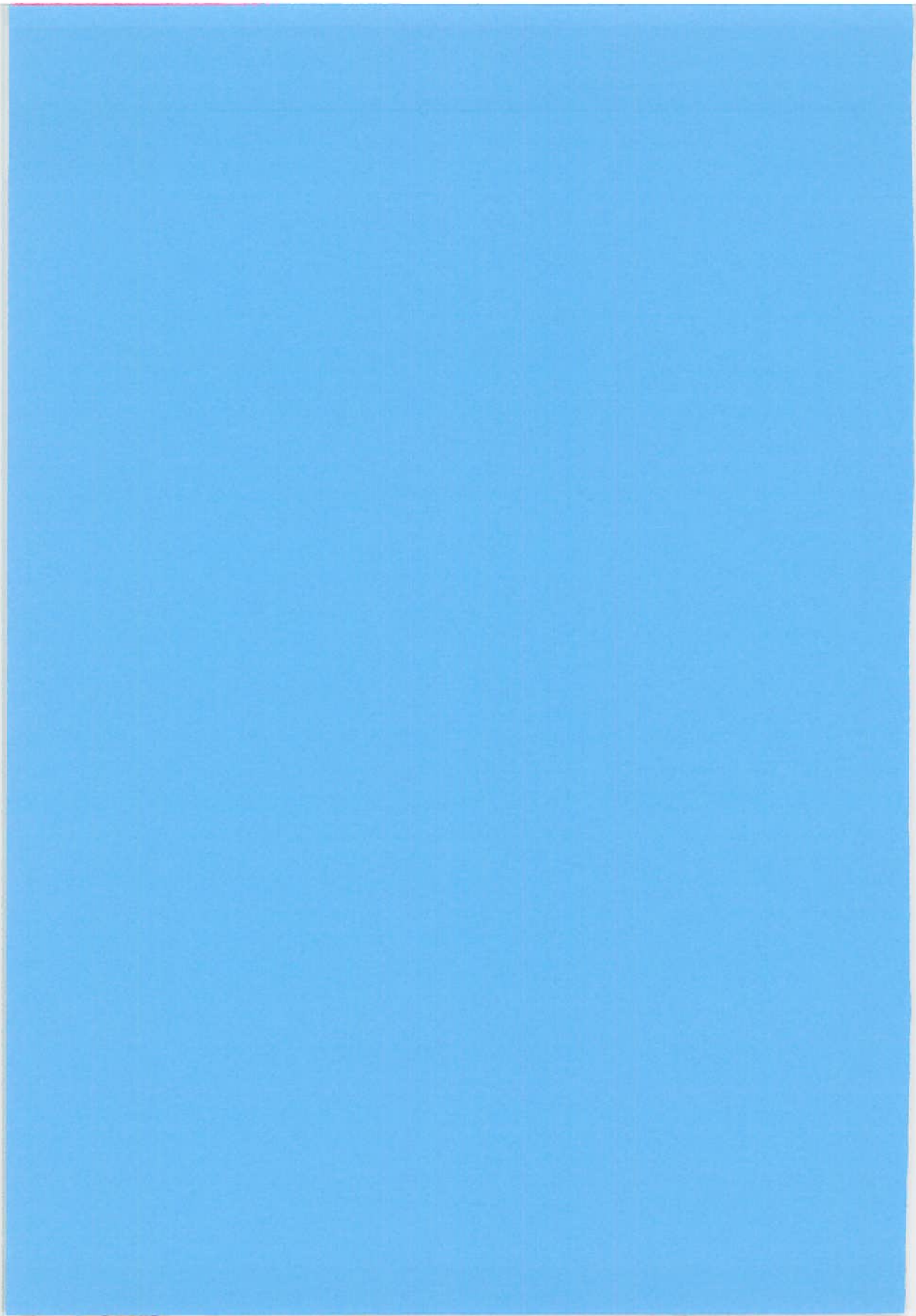
REFERENCES

1. Njølstad I, Arnesen E, Lund Larsen PG. Smoking, serum lipids, blood pressure, and sex differences in myocardial infarction. A 12-year follow-up of the Finnmark Study. Circulation 1996;93:450–6.
2. Stokes JI, Kannel WB, Wolf PA, et al. Blood pressure as a risk factor for cardiovascular disease. The Framingham Study—30 years of follow-up. Hypertension 1989;13(suppl):II3–18.
3. Selmer R, Tverdal A. Body mass index and cardiovascular mortality at different levels of blood pressure: a prospective study of Norwegian men and women. J Epidemiol Community Health 1995;49:265–70.
4. Hubert HB, Feinleib M, McNamara PM, et al. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation 1983;67:968–77.
5. Foulkes MA, Davis CE. An index of tracking for longitudinal data. Biometrics 1981;37:439–46.
6. McMahan CA. An index of tracking. Biometrics 1981;37: 447–55.
7. Ware JH, Wu MC. Tracking: prediction of future values from serial measurements. Biometrics 1981;37:427–37.
8. Clarke WR, Schrott HG, Leaverton PE, et al. Tracking of blood lipids and blood pressures in school age children: the Muscatine study. Circulation 1978;58:626–34.
9. Webber LS, Cresanta JL, Voors AW, et al. Tracking of cardiovascular disease risk factor variables in school-age children. J Chronic Dis 1983;36:647–60.
10. Andersen LB, Haraldsdottir J. Tracking of cardiovascular disease risk factors including maximal oxygen uptake and physical activity from late teenage to adulthood. An 8-year follow-up study. J Intern Med 1993;234:309–15.
11. Twisk JW, Kemper HC, van Mechelen W, et al. Tracking of risk factors for coronary heart disease over a 14-year period: a comparison between lifestyle and biologic risk factors with data from the Amsterdam Growth and Health Study. Am J Epidemiol 1997;145:888–98.
12. Iribarren C, Jacobs DR Jr, Slattery ML, et al. Epidemiology of low total plasma cholesterol concentration among young adults: the CARDIA study. Coronary Artery Risk Development in Young Adults. Prev Med 1997;26:495–507.
13. Porkka KV, Viikari JS, Taimela S, et al. Tracking and predictiveness of serum lipid and lipoprotein measurements in childhood: a 12-year follow-up. The Cardiovascular Risk in Young Finns study. Am J Epidemiol 1994;140:1096–110.
14. Tate RB, Manfreda J, Krahn AD, et al. Tracking of blood pressure over a 40-year period in the University of Manitoba Follow-up Study, 1948–1988. Am J Epidemiol 1995;142:946–54.
15. Rabkin SW, Mathewson FA, Tate RB. Relationship of blood pressure in 20–39-year-old men to subsequent blood pressure and incidence of hypertension over a 30-year observation period. Circulation 1982;65:291–300.
16. Bønaa KH, Thelle DS. Association between blood pressure and serum lipids in a population. The Tromsø Study. Circulation 1991;83:1305–14.
17. Bønaa KH, Arnesen E. Association between heart rate and atherogenic blood lipid fractions in a population. The Tromsø Study. Circulation 1992;86:394–405.
18. Lund Larsen PG. Blood pressure measured with a sphygmomanometer and with Dinamap under field conditions—a comparison. Nor J Epidemiol 1997;7:235–41.
19. Twisk JW, Kemper HC, Mellenbergh DJ, et al. Factors influencing tracking of cholesterol and high-density lipoprotein: the Amsterdam Growth and Health Study. Prev Med 1996;25: 355–64.
20. Zeger SL, Liang KY. Longitudinal data analysis for discrete and continuous outcomes. Biometrics 1986;42:121–30.
21. SAS Institute, Inc. SAS/STAT user's guide, version 6, 4th ed. Cary, NC: SAS Institute, Inc, 1989.
22. Wilsgaard T, Brenn T, Arnesen E. Tracking of blood pressure in adult men: the Tromsø Study 1974–1986. J Epidemiol Biostat 1998;3:269–76.
23. Castelli WP, Garrison RJ, Wilson PW, et al. Incidence of coronary heart disease and lipoprotein cholesterol levels. The Framingham Study. JAMA 1986;256:2835–8.
24. Yong LC, Kuller LH. Tracking of blood pressure from adolescence to middle age: the Dormont High School Study. Prev Med 1994;23:418–26.
25. Twisk JW, Kemper HC, Mellenbergh GJ, et al. Relation between the longitudinal development of lipoprotein levels and biological parameters during adolescence and young adulthood in Amsterdam, the Netherlands. J Epidemiol Community Health 1996;50:505–11.
26. Gordon DJ, Probstfield JL, Garrison RJ, et al. High-density lipoprotein cholesterol and cardiovascular disease. Four prospective American studies. Circulation 1989;79:8–15.
27. Rifkind BM. Lipid Research Clinics Coronary Primary Prevention Trial: results and implications. Am J Cardiol 1984; 54:30C–34C.

PAPER IV



Change of serum lipids and body mass index by age, sex, and smoking status. The Tromsø Study 1986 – 1995

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FOOTNOTES PAGE

Abbrevations

BMI, Body Mass Index; HDL, High Density Lipoprotein

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ABSTRACT

The steady increase in body weight is currently considered to develop into a major health problem in western societies. How body weight increase influence upon established disease risk factors, thus has become an important task to investigate. We assessed the association between eight-year change of body weight and serum lipids in a population-based study comprising 15,624 men and women aged 20 – 61 years at baseline in 1986. Comparisons between different strata of age, sex, initial weight and categories of smoking status were also addressed. Significant associations between body mass index (BMI) change and change of high density lipoprotein (HDL) cholesterol, total cholesterol and triglycerides were observed in all 10-year age groups both in men and women. The weakest associations were observed in persons older than 50 years of age and the associations were also weaker in women than in men. Different associations were observed in the quartiles of baseline BMI. For the heaviest persons, HDL and total cholesterol changes were less pronounced than in persons with middle or low baseline BMI. The association between BMI change and serum lipid change was stronger for persons who were consistent smokers or non-smokers at the surveys compared to persons who changed their smoking status. We conclude that an increase in body weight has been shown to have an adverse effect upon major disease risk factors.

Keywords: cohort studies; body weight; lipids; association

High density lipoprotein (HDL) cholesterol, total cholesterol, triglycerides and body weight are all considered to be risk factors for cardiovascular diseases(1-4). Changes in each of these risk factors have also been associated with cardiovascular morbidity and mortality(5-13). Although some of the studies have analysed data from longitudinal cohort studies randomised from a general population most of the conclusions have been drawn from selected groups, clinical trials or cross sectional studies. Cohort studies, which address the association between change of body weight and change of serum lipids, are also presented(14-23). Many of these are hampered with small sample sizes(15, 16, 19, 20, 22), selected age groups(16, 20) or do not include both men and women(14, 20, 22, 23). To our knowledge, no study has simultaneously assessed the association between change of body weight on change of HDL cholesterol, total cholesterol and triglycerides in both men and women. Furthermore, no study has focused on these associations in different strata of age, baseline weight and categories of smoking status change. We had the opportunity to assess these associations in a population-based cohort study of more than 15,000 men and women examined in 1986-87 and again in 1994-95.

MATERIALS AND METHODS

Study population

The persons in the study were men and women who participated in two population surveys carried out in 1986-87 and 1994-95 in the municipality of Tromsø, northern Norway. In 1986-87 all men (n = 14,537) born between 1925 and 1966 and all women (n = 12,879) born between 1930 and 1966 were invited to participate. The attendance rates were 71.6 percent and 79.1 percent, respectively. In 1994-95, 17,915 persons were still living in the municipality and they were all invited to the follow-up survey. Eligible for the present study were those who participated in both surveys, which comprised 15,624 men and women (87.2 percent of

those who participated in 1986-87 and who still were living in the municipality in 1994-95). Persons with missing information on age, serum lipids, body mass index (BMI; kg/m^2), or smoking status were excluded from the study (n = 162). So were all those 335 women who where pregnant in at least one of the examinations. If a person increased his/her body height with more than five centimetres between the 1986-87 and the 1994-95 survey, the variable was considered as miscoded in one of the surveys. A total number of 32 miscoding were found. However, in 23 cases we found and imputed the correct body height from one of the previous surveys conducted in 1974 or 1979-80. The nine persons with no previous record of height were considered as missing. Hence, the present analyses comprised 7,660 men aged 20 – 61 years and 7,458 women aged 20 – 56 years at the end of 1986.

Measurements

In both surveys the participants attended a physical examination. Non-fasting blood samples were taken and weight, height, and blood pressure were measured. The participants returned a one-page questionnaire and were asked to complete a second questionnaire at home. The methods and questionnaires used in both surveys were almost identical and are described in detail elsewhere(24). Height and weight were measured with participants wearing light clothing and no shoes. Height was measured to the nearest centimetre and weight to the nearest half-kilogram on regularly calibrated scales. As a measure of obesity, we used the body mass index. Serum total cholesterol and triglycerides were analysed by enzymatic colorimetric methods with commercial kits (CHOD-PAP for cholesterol and GPO-PAP for triglycerides; Boehringer-Mannheim, Mannheim, Germany). Serum HDL cholesterol was measured after the precipitation of lower density lipoproteins with heparin and manganese chloride. The non-fasting blood samples were analysed at the Department of Clinical

Chemistry, University Hospital of Tromsø. The laboratory was standardised against the World Health Organisation's Lipid Reference Laboratory in Prague (Czech Republic).

Analyses

Analyses were sex specific and further grouped by age, change of smoking status, or quartiles of baseline BMI. Change of serum lipids and BMI was calculated as the difference between the 1994-95 value minus the 1986-87 value. Change of smoking status was coded into four categories (never smoker, stopped smoking, started smoking, consistent smokers) using changes in the variable current daily smoker (yes/no) from both surveys. The primary aim was to examine the association between change of serum lipids (HDL cholesterol, total cholesterol and triglycerides) and change of BMI. Multiple linear regression analyses were used with change of serum lipids as the dependent variable. The analyses were adjusted for baseline age, baseline BMI, a history of blood pressure treatment (yes/no), and change of smoking status. All analyses were carried out by using the SAS software system(25). All p-values less than or equal to 0.05 were considered as statistical significant.

RESULTS

In both sexes, an eight-year increase in total cholesterol, triglycerides and BMI was observed for all age groups, except for total cholesterol in 50 – 61 years old men (Table 1). For HDL cholesterol, only small mean changes were observed. The Table also shows age and sex specific levels of current smokers. The prevalence of female smoker was higher in the youngest age group and lower in the oldest age group compared to male smokers.

Table 2 shows the result of the multiple regression analyses. Significant associations between BMI change and serum lipid change are shown in all age groups both in men and women. The associations for men were all stronger than for women (10 out of 12 p-values for

sex difference were significant). Regression coefficients were lowest in the oldest age group except for HDL cholesterol in men. However, when we removed persons aged 50 years or more the association between BMI change and serum lipid change did not vary significantly across the age groups. For total cholesterol in women, however, the association decreased with age.

Table 3 shows a significant association between serum lipid change and BMI change in each quartile of baseline BMI both in men and women. However, the magnitude of the association differed between the quartiles. For HDL cholesterol and total cholesterol the strongest associations were observed in the first three quartiles of baseline BMI. Persons who increased their body weight and were in the fourth quartile had a more favourable decrease in HDL cholesterol and increase in total cholesterol than persons in the middle or lower part of the baseline BMI distribution. As in the previous table, significant sex differences were observed in this table.

Figure 1 further elucidates the association between BMI change and serum lipid change grouped by quartiles of baseline BMI. Regardless of baseline BMI, lipid profiles were more adverse the larger was the BMI increase (given in five strata according to units of change with cut points at 0, I, 2, 3). There was no apparent trend that any particular baseline BMI group came out better or worse than the other groups. However, for HDL cholesterol in men in the upper part of baseline BMI with an increase of BMI higher than 2 kg/m^2, a more favourable decrease was observed. Although a significant interaction between baseline BMI and BMI change were observed for HDL cholesterol in women ($p = 0.02$ in Table 3), a clear trend of difference between the lines were not observed in Figure 1. Furthermore, when we excluded persons who reported a history of angina, myocardial infarction or stroke, the interaction term became non significant ($p = 0.11$). For total cholesterol, a better profile was observed for persons in the fourth quartile of baseline BMI. The differences between the quartiles

increased with increase in BMI change. Men in the fourth quartile of baseline BMI with a BMI increase between 2 – 3 units (7.2 kg – 10.8 kg for a 1.80 meters tall person) registered a mean total cholesterol increase of 0.28 mmol/l compared to men in the second quartile of baseline BMI who registered a 0.57 mmol/l increase. Distinct differences between the different parts of baseline BMI were not observed for triglycerides.

BMI change for persons who either had started or stopped smoking between 1986-87 and 1994-95 was weaker associated with serum lipids compared to persons who either were consistent smokers or non-smokers (results not shown). Consequently, we coded the smoking variable into two categories; change or no change. A BMI increase for persons who changed their smoking status induced a significant lower decrease of HDL cholesterol and increase of triglycerides compared to persons who did not change their smoking status (Table 4). This trend was less apparent for total cholesterol.

DISCUSSION

The association between change of serum lipids and change of body mass index stratified for possible effect modifiers such as sex, age, baseline weight, and change in smoking status have been examined in a general Norwegian population over an eight-year period. A direct and significant association was present between BMI change and change of total cholesterol and triglycerides in all strata of sex, age, and smoking status. An inverse significant association was present when assessing HDL cholesterol. A BMI increase in the oldest individuals induced a more favourable change in total cholesterol and triglycerides compared to younger individuals. Women had better profiles than men and it was observed a stronger association in persons who did not change their smoking status compared to persons who changed their smoking status.

When we excluded persons aged 50 years or more no significant interaction between age and BMI change was observed, except for total cholesterol in women (Table 2). The weaker association in the oldest age group may be explained by a different change pattern in BMI and serum lipids. Total cholesterol, triglycerides, and BMI are known to increase with age. However, the risk factor levels have been observed to peak at late middle age and even decline in older ages(18, 26-28). This trend was confirmed in our analyses as well with weaker increases in the 50 – 61 year age group for BMI and total cholesterol in both sexes, and for triglycerides in men only.

The current study included questionnaire information of diseases such as angina, myocardial infarction or stroke. These factors may have confounded or biased the observed associations. A total of 557 men and 166 women did report a history of such diseases in at least one of the two surveys. We repeated the analyses after excluding these persons. The results in Table 2, 3 and 4 remained virtually unchanged. Worth noting was that the significant interaction terms (table 3) between baseline BMI and BMI change in women became non-significant for HDL cholesterol and triglycerides, $p > 0.10$.

Other sources of bias may be present in the study. A comparison between people lost to follow-up with the participants who attended both surveys did not give us any reason to suspect a selection bias(29). Although persons who did not participate in follow-up were younger, pronounced differences in cardiovascular risk factors such as systolic and diastolic blood pressure, BMI, and serum lipids were not observed. The high response rates, above 70% in 1986-87 and 87% at follow-up, further strengthen our confidence of no serious bias.

The observed difference between those that changed and did not change their smoking status could not easily be explained. However, in our population significant different mean levels of weight change were observed in the different categories of change of smoking status (ANOVA F-statistics > 90 both for men and women). This is also partly confirmed in the

literature where weight gain is strongly related to smoking cessation(30, 31). In our population this association is not equally strong for change of smoking status and serum lipids (all F-statistics < 10). Consequently, one may speculate that this difference in association could influence the association between BMI change and serum lipid change in such a way that the association is weaker for persons who change their smoking status.

In our analyses we easily could have used body weight and weight change instead of BMI and BMI change. Because body height remains stable over time in the age range considered, results would obviously be quite similar. Especially when focusing on change between two surveys the observed change of weight could be just as good as a predictor for serum lipid change as the observed change of BMI. However, a 1kg change of body weight does not necessarily induce equal change in serum lipids between persons of different heights. Thus, we believe that BMI change is a better measure of obesity change. In a separate set of analyses we did, however, use weight and weight change as independent variables. The results and conclusions remained for the most part unchanged.

Although no study has, to our knowledge, presented strata specific results directly comparable to our study, the present results may still be compared to other papers. The Nijmegen Cohort Study(21) showed a significant association between weight gain and change of total cholesterol in 2,335 men and women. The study did not focus on sex differences. However, a higher correlation coefficient was seen for men, which is in agreement with our observation that a BMI increase for men induces a higher total cholesterol increase than for women. Data from the Framingham Study revealed that an increase in BMI is associated with an increase in total cholesterol and a decrease in HDL cholesterol among 4,435 men and women up through the 50 – 64 year age group(18). As in our study and in the Nijmegen Cohort Study there seemed to be a stronger association between weight increase and total cholesterol increase in men than in women. However, the Framingham Study did not register

a sex difference for HDL cholesterol. The Framingham Offspring Study has also demonstrated significant associations between BMI change and serum lipid change in an eight-year follow up period(16). The study included 397 men and 497 women aged 20 – 29 years. As the other studies have shown, the regression coefficients for men were higher than for women.

Similar results have also been presented from the MONICA Augsburg Cohort(17). A feature common for the above-mentioned studies is the lack of analyses in strata of initial weight and also in strata of smoking status change. Although the studies did include both men and women, significance tests for sex difference were not performed. We are not aware of population-based studies for men and women, which also include serum triglycerides. A few smaller studies do exist. The Adelaide 1000 comprised 382 men and 273 women who volunteered for a fitness programme. It was found that changes in weight and lipids were significantly related and the relationship was stronger for men than for women(32). The San Antonio Family Heart Study(15) and a paper by Noppa(14) also confirmed some of the present results. Although the above mentioned studies collected blood samples after a specified period of fast, they are comparable to our non-fasting results. We had the opportunity to adjust for the variable "time-since-last meal". However, despite that the variable in itself was significant in our models, it did not change the variables of interest and were thus not considered to be a confounder.

The strong association between weight increase and serum lipid increase may have profound public health implications. In western countries the prevalence of obesity is increasing(33, 34), which may be a paradox with respect to the fact of a decreasing trend in the mortality of coronary heart diseases(35-37). However, improvements in medical surveillance and primary and secondary medical intervention could explain much of the decline. Other factors that could support a decreasing mortality trend are dietary intake. A

significant association between individual fatty acids and cholesterol have been established(38). Different effects between serum lipids and saturated, monounsaturated and polyunsaturated fatty acids are also observed. It is clear that saturated fatty acids are hypercholesterolemic and that unsaturated fatty acids elicit a hypocholesterolemic effect compared with saturated fatty acids(39).

If the use of polyunsaturated fatty acids increases in western countries it could have a positive influence on serum lipids levels. Furthermore, diets high in mono- or polyunsaturated fatty acids have a positive influence on blood coagulation and appear to improve morbidity and mortality by modifying the disease process. Despite a possible improvement in the use of fatty acids, there are no indications that the obesity epidemic is not harmful to health. The significant association between weight increase and unfavourable changes in serum lipids may result in unfavourable coronary heart disease outcomes in the coming years.

In conclusion, significant and strong associations were found between BMI increase and serum lipid increase (decrease for HDL cholesterol) in a general adult population. The associations were significantly stronger for men than for women, generally weaker for older persons, and weaker for persons in the upper quartile of baseline BMI for HDL and total cholesterol. Persons who changed their smoking status had better profiles compared to persons who either were consistent smokers or non-smokers at both surveys. The well-known body weight increase in western societies may thus be associated with an adverse serum lipid profile and an increased risk of serious disease.

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REFERENCES

1. Njølstad I, Arnesen E, Lund Larsen PG. Smoking, serum lipids, blood pressure, and sex differences in myocardial infarction. A 12-year follow-up of the Finnmark Study. Circulation 1996;93:450-6.
2. Selmer R, Tverdal A. Body mass index and cardiovascular mortality at different levels of blood pressure: a prospective study of Norwegian men and women. J Epidemiol Community Health 1995;49:265-70.
3. Hubert HB, Feinleib M, McNamara PM, et al. Obesity as an independent risk factor for cardiovascular disease: a 26-year follow-up of participants in the Framingham Heart Study. Circulation 1983;67:968-77.
4. Cholesterol consensus: a trans-Atlantic perspective. Amsterdam, The Netherlands, 31-October-1 November 1991. Int J Cardiol 1992;37 Suppl 1:S1-37.
5. Peters ET, Seidell JC, Menotti A, et al. Changes in body weight in relation to mortality in 6441 European middle-aged men: the Seven Countries Study. Int J Obes Relat Metab Disord 1995;19:862-8.
6. Rosengren A, Wedel H, Wilhelmsen L. Body weight and weight gain during adult life in men in relation to coronary heart disease and mortality. A prospective population study. Eur Heart J 1999;20:269-77.
7. Tervahauta M, Pekkanen J, Enlund H, et al. Change in blood pressure and 5-year risk of coronary heart disease among elderly men: the Finnish cohorts of the Seven Countries Study. J Hypertens 1994;12:1183-9.
8. Galanis DJ, Harris T, Sharp DS, et al. Relative weight, weight change, and risk of coronary heart disease in the Honolulu Heart Program. Am J Epidemiol 1998;147:379-86.

9. Willett WC, Manson JE, Stampfer MJ, et al. Weight, weight change, and coronary heart disease in women. Risk within the 'normal' weight range. JAMA 1995;273:461-5.

10. Wannamethee G, Shaper AG. Weight change in middle-aged British men: implications for health. Eur J Clin Nutr 1990;44:133-42.

11. Walker M, Wannamethee G, Whincup PH, et al. Weight change and risk of heart attack in middle-aged British men. Int J Epidemiol 1995;24:694-703.

12. Selmer R, Tverdal A. Changes in blood pressure as a predictor of coronary heart disease and stroke mortality: a 27-year follow-up of 15518 men and women in the City of Bergen, Norway. Journal of Epidemiology and Biostatistics 1996;1:41-50.

13. Pekkanen J, Nissinen A, Vartiainen E, et al. Changes in serum cholesterol level and mortality: a 30-year follow-up. The Finnish cohorts of the seven countries study. Am J Epidemiol 1994;139:155-65.

14. Noppa H. Body weight change in relation to incidence of ischemic heart disease and change in risk factors for ischemic heart disease. Am J Epidemiol 1980;111:693-704.

15. Rainwater DL, Mitchell BD, Comuzzie AG, et al. Association among 5-year changes in weight, physical activity, and cardiovascular disease risk factors in Mexican Americans. Am J Epidemiol 2000;152:974-82.

16. Hubert HB, Eaker ED, Garrison RJ, et al. Life-style correlates of risk factor change in young adults: an eight-year study of coronary heart disease risk factors in the Framingham offspring. Am J Epidemiol 1987;125:812-31.

17. Eberle E, Doering A, Keil U. Weight change and change of total cholesterol and high-density-lipoprotein cholesterol. Results of the MONICA Augsburg cohort study. Ann Epidemiol 1991;1:487-92.

18. Wilson PW, Anderson KM, Harris T, et al. Determinants of change in total cholesterol and HDL-C with age: the Framingham Study. J Gerontol 1994;49:M252-7.

19. Criqui MH, Frankville DD, Barrett-Connor E, et al. Change and correlates of change in high and low density lipoprotein cholesterol after six years: a prospective study. Am J Epidemiol 1983;118:52-9.

20. Berns MA, de Vries JH, Katan MB. Increase in body fatness as a major determinant of changes in serum total cholesterol and high density lipoprotein cholesterol in young men over a 10-year period. Am J Epidemiol 1989;130:1109-22.

21. Bakx JC, van den Hoogen HJ, Deurenberg P, et al. Changes in serum total cholesterol levels over 18 years in a cohort of men and women: The Nijmegen Cohort Study. Prev Med 2000;30:138-45.

22. Bonithon Kopp C, Raison J, Courbon D, et al. Relationships between 3-y longitudinal changes in body mass index, waist-to-hip ratio, and metabolic variables in an active French female population. Am J Clin Nutr 1992;56:475-82.

23. Borkan GA, Sparrow D, Wisniewski C, et al. Body weight and coronary disease risk: patterns of risk factor change associated with long-term weight change. The Normative Aging Study. Am J Epidemiol 1986;124:410-19.

24. Bønaa KH, Arnesen E. Association between heart rate and atherogenic blood lipid fractions in a population. The Tromsø Study. Circulation 1992;86:394-405.

25. SAS Institute Inc. SAS/STAT User's Guide. Cary, NC: SAS Institute Inc., 1989.

26. Anderson KM, Wilson PW, Garrison RJ, et al. Longitudinal and secular trends in lipoprotein cholesterol measurements in a general population sample. The Framingham Offspring Study. Atherosclerosis 1987;68:59-66.

27. Ferrara A, Barrett-Connor E, Shan J. Total, LDL, and HDL cholesterol decrease with age in older men and women. The Rancho Bernardo Study 1984-1994. Circulation 1997;96:37-43.

28. Weijenberg MP, Feskens EJ, Kromhout D. Age-related changes in total and high-density-lipoprotein cholesterol in elderly Dutch men. Am J Public Health 1996;86:798-803.

29. Wilsgaard T, Schirmer H, Arnesen E. Impact of body weight on blood pressure with a focus on sex differences: the Tromsø Study, 1986-1995. Arch Intern Med 2000;160:2847-53.

30. Williamson DF, Madans J, Anda RF, et al. Smoking cessation and severity of weight gain in a national cohort. N Engl J Med 1991;324:739-745.

31. Caan B, Coates A, Schaefer C, et al. Women gain weight 1 year after smoking cessation while dietary intake temporarily increases. J Am Diet Assoc 1996;96:1150-5.

32. Sedgwick AW, Thomas DW, Davies M, et al. Relationships between weight change and blood lipids in men and women: 'the Adelaide 1000'. Int J Obes 1990;14:439-50.

33. Jacobsen BK, Njølstad I, Thune I, et al. Increase in weight in all birth cohorts in a general population: The Tromsø Study, 1974-1994. Arch Intern Med 2001;161:466-72.

34. Hill JO, Peters JC. Environmental contributions to the obesity epidemic. Science 1998;280:1371-74.

35. Rosamond WD, Chambless LE, Folsom AR, et al. Trends in the incidence of myocardial infarction and in mortality due to coronary heart disease, 1987 to 1994 [see comments]. N Engl J Med 1998;339:861-7.

36. Kuulasmaa K, Tunstall PH, Dobson A, et al. Estimation of contribution of changes in classic risk factors to trends in coronary-event rates across the WHO MONICA Project populations. Lancet 2000;355:675-87.

37. Hunink MG, Goldman L, Tosteson AN, et al. The recent decline in mortality from coronary heart disease, 1980-1990. The effect of secular trends in risk factors and treatment. JAMA 1997;277:535-42.

38. Grimsgaard S, Bønaa KH, Bjerve KS. Fatty acid chain length and degree of unsaturation are inversely associated with serum triglycerides. Lipids 2000;35:1185-93.

39. Kris-Etherton PM, Yu S. Individual fatty acid effects on plasma lipids and lipoproteins: human studies. Am J Clin Nutr 1997;65:1628S-44S.

Table 1. Serum lipids, body mass index, and smoking status by sex and age. The Tromsø Study 1986 - 1995.

	Men			Women		
Age in 1986	No.	1986-87	Change in 1994-95*	No.	1986-87	Change in 1994-95*
HDL Cholesterol†						
20 – 29 years	1518	1.32 (0.28)	-0.03 (0.26)	1627	1.55 (0.33)	-0.00 (0.30)
30 – 39 years	2422	1.35 (0.33)	0.00 (0.27)	2613	1.62 (0.36)	0.03 (0.29)
40 – 49 years	2084	1.38 (0.35)	0.02 (0.28)	2191	1.69 (0.39)	0.01 (0.32)
50 – 61 years‡	1636	1.42 (0.37)	0.01 (0.29)	1027	1.73 (0.41)	-0.05 (0.31)
Total Cholesterol†						
20 – 29 years	1518	5.00 (0.97)	0.59 (0.75)	1627	4.95 (0.91)	0.35 (0.78)
30 – 39 years	2422	5.72 (1.11)	0.38 (0.83)	2613	5.32 (0.99)	0.40 (0.73)
40 – 49 years	2084	6.27 (1.19)	0.18 (0.86)	2191	6.01 (1.15)	0.53 (0.93)
50 – 61 years‡	1636	6.53 (1.16)	-0.00 (0.90)	1027	6.92 (1.31)	0.10 (1.03)
Triglycerides†						
20 – 29 years	1518	1.46 (0.88)	0.32 (1.13)	1627	1.06 (0.53)	0.11 (0.67)
30 – 39 years	2422	1.61 (0.97)	0.22 (1.10)	2613	1.04 (0.56)	0.14 (0.65)
40 – 49 years	2084	1.69 (1.06)	0.12 (1.07)	2191	1.17 (0.69)	0.23 (0.71)
50 – 61 years‡	1636	1.68 (0.91)	0.03 (0.96)	1027	1.35 (0.71)	0.18 (0.73)
Body mass index†						
20 – 29 years	1518	23.6 (2.9)	1.5 (1.7)	1627	22.1 (3.0)	1.6 (2.2)
30 – 39 years	2422	24.4 (2.9)	1.1 (1.5)	2613	22.6 (3.0)	1.6 (1.9)
40 – 49 years	2084	25.3 (2.8)	1.0 (1.5)	2191	24.0 (3.6)	1.6 (2.0)
50 – 61 years‡	1636	25.4 (3.0)	0.6 (1.6)	1027	24.7 (3.7)	1.3 (2.0)
Current smoker (%)						
20 – 29 years	1518	44.1	-2.2	1627	54.5	-8.7
30 – 39 years	2422	47.8	-8.2	2613	47.8	-4.0
40 – 49 years	2084	42.8	-6.6	2191	41.0	-4.4
50 – 61 years‡	1636	45.3	-10.8	1027	37.6	-5.8

*The 1994-95 value minus the 1986-87 value.

† Values are mean (SD); HDL, high density lipoprotein.

‡ For women, 50 – 56 years.

Table 2. Change of body mass index (ΔBMI) as a predictor for change of serum lipids by sex and age*. Multiple linear regression analyses. The Tromsø Study 1986 – 1995.

	Coefficient (β) with 95 % confidence interval (CI) for ΔBMI				
	Men		Women		P value for sex difference
	$\beta \times 10^2$	95%CI	$\beta \times 10^2$	95%CI	
Age strata	**ΔHDL† Cholesterol**				
20 – 29 years	-3.9	-4.7, -3.2	-2.8	-3.4, -2.1	0.01
30 – 39 years	-3.4	-4.1, -2.7	-3.3	-3.9, -2.7	0.73
40 – 49 years	-4.0	-4.8, -3.2	-2.7	-3.4, -2.0	0.01
50 – 61 years‡	-3.7	-4.6, -2.8	-2.0	-2.9, -1.0	0.008
P value, age×ΔBMI					
20 – 61 years‡	0.93		0.14		
20 – 49 years	0.52		0.79		
Age strata	**ΔTotal Cholesterol**				
20 – 29 years	12.8	10.7, 14.9	9.3	7.6, 10.9	0.008
30 – 39 years	14.0	11.9, 16.1	8.1	6.6, 9.5	<0.001
40 – 49 years	10.8	8.4, 13.3	7.0	5.0, 9.0	0.004
50 – 61 years‡	9.6	6.8, 12.4	6.6	3.5, 9.8	0.19
P value, age×ΔBMI					
20 – 61 years‡	0.01		0.14		
20 – 49 years	0.15		0.01		
Age strata	**ΔTriglycerides**				
20 – 29 years	19.8	16.6, 23.0	10.5	9.1, 11.9	<0.001
30 – 39 years	22.3	19.5, 25.1	9.6	8.3, 10.8	<0.001
40 – 49 years	20.5	17.5, 23.6	9.7	8.2, 11.1	<0.001
50 – 61 years‡	14.7	11.7, 17.6	7.4	5.2, 9.7	<0.001
P value, age×ΔBMI					
20 – 61 years‡	0.02		0.06		
20 – 49 years	0.80		0.16		

* Adjusted for baseline age, baseline BMI, smoking category and blood pressure treatment.

† HDL, high density lipoprotein.

‡ For women, 20 – 56 years.

Table 3. Change of body mass index (ΔBMI) as a predictor for change of serum lipids by sex and quartiles of baseline BMI*. Multiple linear regression analyses. The Tromsø Study 1986 – 1995.

	Coefficient (β) with 95 % confidence interval (CI) for ΔBMI				
	Men		Women		P value for sex difference
	$\beta \times 10^2$	95%CI	$\beta \times 10^2$	95%CI	
Baseline BMI	**ΔHDL† Cholesterol**				
1. quartile	-4.5	-5.4, -3.6	-2.5	-3.4, -1.6	0.001
2. quartile	-4.0	-4.9, -3.2	-3.6	-4.4, -2.8	0.34
3. quartile	-3.9	-4.8, -3.1	-2.7	-3.4, -2.0	0.03
4. quartile	-3.0	-3.6, -2.4	-2.3	-2.9, -1.8	0.07
P value, BMI×ΔBMI	0.002		0.02		
Baseline BMI	**ΔTotal Cholesterol**				
1. quartile	13.6	11.1, 16.1	11.3	9.1, 13.4	0.005
2. quartile	15.7	13.2, 18.2	9.5	7.3, 11.8	<0.001
3. quartile	13.5	11.1, 15.9	9.6	7.7, 11.5	0.001
4. quartile	8.4	6.2, 10.5	6.0	4.3, 7.6	0.03
P value, BMI×ΔBMI	<0.001		<0.001		
Baseline BMI	**ΔTriglycerides**				
1. quartile	19.1	16.3, 21.9	6.8	5.4, 8.3	<0.001
2. quartile	18.5	15.5, 21.5	10.2	8.7, 11.8	<0.001
3. quartile	21.1	18.0, 24.2	11.0	9.3, 12.6	<0.001
4. quartile	19.4	16.4, 22.5	9.4	8.0, 10.8	<0.001
P value, BMI×ΔBMI	0.08		0.02		

* Adjusted for baseline age, baseline BMI, smoking category and blood pressure treatment.

† HDL, high density lipoprotein.

Table 4. Change of body mass index (ΔBMI) as a predictor for change of serum lipids by sex and smoke category*. Multiple linear regression analyses. The Tromsø Study 1986 – 1995.

	Coefficient (β) with 95 % confidence interval (CI) for ΔBMI				
	Men		Women		P value for sex difference
	β×10²	95%CI	β×10²	95%CI	
Smoking status	**ΔHDL† Cholesterol**				
Changed	-1.3	-2.2, -0.4	-0.7	-1.5 to 0.1	0.25
Not changed	-4.0	-4.5, -3.6	-3.0	-3.4, -2.6	<0.001
P value, ΔBMI×smoke	<0.001		<0.001		
Smoking status	**ΔTotal Cholesterol**				
Changed	9.2	6.6, 11.8	6.9	4.6, 9.1	0.07
Not changed	12.4	11.1, 13.6	8.1	7.1, 9.2	<0.001
P value, ΔBMI×smoke	0.06		0.26		
Smoking status	**ΔTriglycerides**				
Changed	15.9	12.6, 19.3	6.3	4.5, 8.1	<0.001
Not changed	20.1	18.5, 21.7	10.0	9.1, 10.8	<0.001
P value, ΔBMI×smoke	0.03		<0.001		

* Adjusted for baseline age, baseline BMI and blood pressure treatment.

† HDL, high density lipoprotein.

LEGEND TO FIGURE

Figure 1. Mean change of high density lipoprotein (HDL), total cholesterol, and triglycerides by baseline body mass index (BMI) and BMI change (ΔBMI) in the Tromsø Study 1986-87 – 1994-95, adjusted for baseline age, smoke category, and blood pressure treatment.

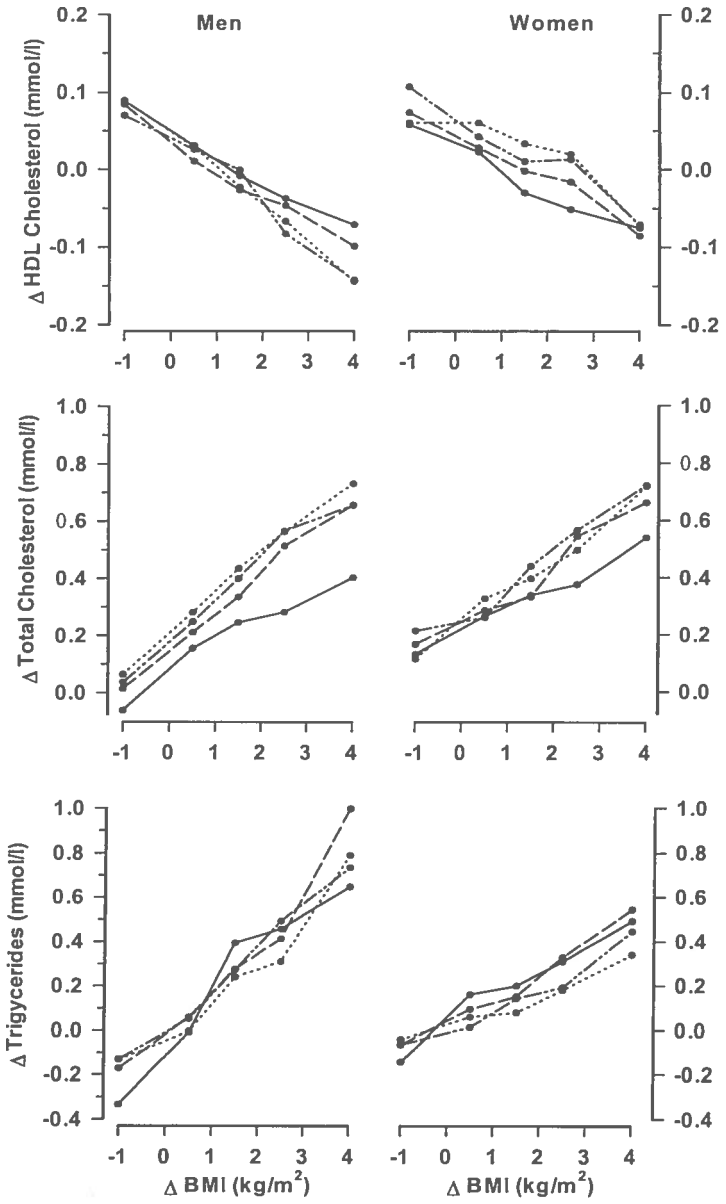
Baseline BMI

..... 1st quartile

–·–·– 2nd quartile

– – – – 3rd quartile

——— 4th quartile


Men
Women
Δ HDL Cholesterol (mmol/l)
Δ Total Cholesterol (mmol/l)
Δ Trigycerides (mmol/l)
Δ BMI (kg/m²)
Δ BMI (kg/m²)

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