THE TROMSØ HEART STUDY

POPULATION STUDIES OF CORONARY RISK FACTORS WITH SPECIAL EMPHASIS ON HIGH DENSITY LIPOPROTEIN AND THE FAMILY OCCURRENCE OF MYOCARDIAL INFARCTION

OLAV HELGE FØRDE   DAG STEINAR THELLE

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1. Bidrag til belysning av medisinske og sosiale for-
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    blant finskættede i Sør-Varanger kommune.
    Av Anders Forsdahl, 1976.

2. Sunnhetstilstanden, hygieniske og sosiale forhold
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    nalberetningene.
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3. Hjerte-karundersøkelsen i Finnmark - et eksempel på en
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T H E   T R O M S Ø   H E A R T   S T U D Y

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PREFACE

The University of Tromsø was founded for regional political reasons.
Research relevant to the problems in Northern Norway was given high
priority in the early plans for the University. One of the first
professors at the Medical School and Head of the Medical Department
at the University Hospital, Professor Arne Nordøy was early aware
of the high incidence of coronary heart disease and its impact as
a health problem in this part of the country. He therefore initiated
a population study in Tromsø, as an attempt to explore the problem
of coronary heart disease, and, if possible, to offer interventive
measures. This initiative was supported by the Municipal Health
Officer, Dr. Hans Anstad.

The organization structure of the Medical School in Tromsø, with
the close relationship between the institutes, made it natural to
plan the study as a collaborative project between the Institutes of
Clinical medicine, Community medicine and Medical Biology. The
practical work was performed by a working-group formally connected
to the Institute of Clinical Medicine.

ACKNOWLEDGEMENTS

Not being naturally honest, to reach a level of truthfulness
- above that afforded by chance - we have drawn on the stores of
Professor Knut Westlund.

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INTRODUCTION

The epidemiological approach to coronary heart disease (CHD) is
suggested by the sheer magnitude of the problem and the fact that
this highly lethal disease frequently attacks without warning.
Despite modern innovations in the management of the acute coronary
attack, the coronary care unit to safeguard the myocardial infarction
(MI) victim who reaches hospital alive, and the cardiac surgery to
revascularize and repair the ischaemic heart, there is no evidence
that coronary mortality has been substantially affected. Hope of
controlling this disease can only come from preventive measures
applicable to populations or population segments. Epidemiological
investigations form the basis on which preventive medicine depends.
They start with finding the facts about the population frequency
of the disease - prevalence and incidence - and if proper methods
and criteria are used they can reveal relationships between the
disease frequency and other characteristics of the population.
In other words, epidemiological studies should be able to provide
information relevant to the etiology of CHD.

In order to assess whether statistical associations are etiologically
important, the following criteria from the Report to the Surgeon
General on Smoking and Health (1) should be fulfilled:

1.   Strenght of association
2.   Graded nature of the association
3.   Temporal sequence, i.e., does the presumed etiologic factor
     precede the disease?
4.   Consistency of the finding, in study after study

5. Independence of each of the associations

6. Predictive capacity in other populations than the examined

7. Coherence of the findings -- in two senses, i.e. consistency
    of the epidemiological findings with those from other research
    methods (animal experimental, clinical and pathological
    investigation), and coherence in that reasonable pathogenetic
    mechanisms are known, indicating the pathways whereby the
    etiologic agents act to produce the disease.

Most of these criteria are analogous to those necessary to declare
causality in experimental biological settings. In contrast to these
settings, where experimental conditions may be controlled, the
epidemiological observations will inevitably be influenced by
confounding variables. This characteristic of epidemiological
studies requires emphasis on standardization, comparability and large
numbers as well as repetition in different populations.

The epidemiological studies can rarely produce final proof of a
causal sequence, particularly in CHD in which there is no single
cause. The pathological mechanisms and the biological explanations
are tasks for the basic medical sciences. This fact together with
the demands in criterion 7 - coherence with reasonable pathogenetic
mechanisms - implies close collaboration between epidemiological
investigators and more biologically oriented research groups.

The major part of to days knowledge of the etiology and prevention
of CHD stems from epidemiological studies which started in the USA
in the 1950s and later spread throughout the industrialized world.
The main finding from these studies was the establishment of serum

cholesterol, blood pressure, and cigarette smoking as major risk factors for CHD in middle-aged men. The criteria for the etiologically important association between these factors and CHD were fullfilled. Still, questions concerning both etiology and prevention of CHD remained unanswered. These questions to a great extent influenced the design of the epidemiological studies in Norway in the 1970s:

1. Which social and behavioural factors determine the variation of the coronary risk factors?
2. Do the risk factors of middle-aged men operate with similar impact in all populations or subgroups of the populations, i.e. sex, age, geographical, and social groups?
3. Can we find new factors which could increase our predictability of CHD?
4. Can intervention towards high-risk individuals reduce:
   a. The risk factor level?
   b. The subsequent incidence of CHD?

Population studies of CHD in Norway

It was shown in 1964 by Jervell et al (2) that there was a considerable difference in the incidence of CHD in different areas in Norway. This difference could to a large extent be explained by differences in the serum cholesterol level. A later prospective study comprising 6,886 men drawn from twenty industrial physicians in Oslo was carried out by Westlund and Nicolaysen (3). This study established serum cholesterol as a major risk factor for CHD in middle-aged urban men in Norway. The necessity of a further exploration of coronary risk factors in men aged 20-49 years and the demand for controlled

intervention trials initiated the Oslo Study in 1972 (4). The
methods of the cross-sectional part of this study was later
adapted by the Cardiovascular Disease Studies in Norwegian Counties
and the Tromsø Heart Study, both started in 1974 (5). The simi-
larities in the methods reflect to some extent the fact that the
planning committees for the studies had some members in common.
Future comparability was a main objective. This resulted in the
use of an almost identical main postal questionnaire, the same
methods for blood pressure measurements and the use of non-fasting
blood samples for lipid analyses. The Oslo Study and the County
Studies had their blood samples analysed in the same laboratory
at the Ullevål Hospital, Oslo, whereas the blood samples from the
Tromsø Heart Study were analysed in Tromsø. Parallel samples were
analysed to insure comparability in the two laboratories. In the
Oslo Study and the County Studies blood glucose was determined,
whereas hemoglobin was measured in the Tromsø Heart Study. The
re-examination of the Finnmark population took place in 1977-78,
and at this time HDL-cholesterol was analysed in all subjects.
The main differences in study populations and subprojects of the
three studies are shown in table 1.

Table 1

STUDY POPULATIONS AND MAJOR SUBPROJECTS OF THE OSLO STUDY, THE CARDIOVASCULAR DISEASE STUDY IN NORWEGIAN COUNTIES AND THE TROMSØ HEART STUDY

Study (geographical area)	Age	% invited	Number of subjects attending		Major subprojects
			Men	Women	
The Oslo Study (the municipality of Oslo)	20-39	7%	1,763	0	Randomized controlled trials of intervention on hypertension, serum cholesterol and smoking
	40-49	100%	16,202	0	
The Cardiovascular Disease Study in Norwegian Counties (the counties of Finnmark, * Sogn og Fjordane and Oppland)	20-34	10%	4,034	4,075	Investigation of impact of family occurrence of CHD *
					Investigation of the prevalence of peptic ulcur and pepsinogen determination *
	35-49	100%	25,163	24,556	Uncontrolled intervention on hypertension, hyperlipemia and smoking. Dietary investigation in subsamples
The Tromsø Heart Study (The municipality of Tromsø)	20-49	100%	6,595	0	Investigation of impact of family occurrence of CHD. Uncontrolled intervention on hyperlipemia and hypertension

* In four municipalities all subjects aged 20-49 years were invited.
The family history study, as well as the peptic ulcer study, were conducted in the same four municipalities

Recall frequency and intervention procedures after the Tromsø screening

Subjects satisfying the recall criteria for more than one group were re-examined according to the priority given in the following table.

Recall group	Recall criteria *	Number of persons satisfying the recall criteria			Total
		Age group			
		20-29	30-39	40-49	
Hemoglobin (g/dl)	<12.5 or > 17.5	27	18	29	74
Chest pain	"Rose formula"	65	55	92	212
Leg pain	"Rose formula"	63	56	61	180
Serum cholesterol (mg/dl)	20-29 $\gtrless$ 300	179			
	30-39 $\gtrless$ 350		152		
	40-49 $\gtrless$ 380			89	
					420
Blood pressure	DBP SBP 20-29>100 or >160	51			
	30-39>105 or >170		47		
	40-49>110 or >180			36	
					134
Serum triglycerides (mmol/l)	$\gtrless$ 4.5	20	55	35	110
Total		405	383	342	1,130
Number of men screened		2,387	2,344	1,864	6,595

* Not recalled:
  Subjects who reported to have or have had diabetes mellitus, myocardial infarction, angina pectoris, treated hypertension, or other atherosclerotic disorder

Hemoglobin

Of the 74 men called for re-examination, 59 actually turned up.
At the reexamination 46 proved to have hemoglobin values within
the recall limits. Ten men had hemoglobin below 12.5 g/dl, but
the majority of these were aware of their anaemic state.

Chest pain

207 men were re-examined. Of these 13 were found to have angina
pectoris according to common clinical criteria.

Leg pain

101 men were re-examined. Of these two were found to have athero-
sclerotic obliterative disease. One was previously diagnosed
(but not reported as a known disease by the subject at the primary
examination).

Serum cholesterol

390 men out of 420 met at the first re-examination, which consisted
of a single fasting blood sample for lipid analysis.
The 152 men who at this examination had serum cholesterol below
the recall limits were not further examined, only given a brochure
with dietary advice. 238 men were invited to take part in a die-
tary intervention trial, including interview and instruction by
a dietician. 175 of these men were followed for twelve weeks,
with serum cholesterol determination every six weeks. The results

from this intervention will be described when the long-term
effect is available from the new study planned for 1979-80 in
Tromsø.

61 subjects who did not respond satisfactorily to the dietary
intervention were included in a randomized double blind cross-over
study with clofibrate and placebo. Only 34 of these men kept up
with the trial throughout the planned six months. This high
drop-out rate reflects to some extent side-effects, which young
asymptomatic men find intolerable, but also our own attitude to-
wards persuading these men to continue to take two pills of partly
unknown effect four times a day.

Figure 1 summarizes the results of the trial. In spite of the
small numbers the cholesterol lowering effect of clofibrate was
significant. None of the men continued with clofibrate medication
after the trial.

Serum triglycerides

23 men had fasting serum triglycerides above 2.5 mmol/l at the
first re-examination. They were recommended dietary changes like
reduction of carbohydrate and caloric intake.

Blood pressure

The procedure and results of the intervention on high blood pres-
sure are published elsewhere (10) and will only be summarized
here. Subjects who exceeded the blood pressure limits only were

directly referred to one of six general practitioners. Those
who also satisfied other recall criteria were first examined at
the out-patient clinic, and thereafter, if blood pressure medi-
cation was considered, referred to their general practitioner.
Of the 134 men who at the screening exceeded the recall limits,
95 men were referred*. The general practitioners found indication
for medical treatment in twelve men, 34 were recommended further
observation and eight were declared normotensive.

Fig. 1
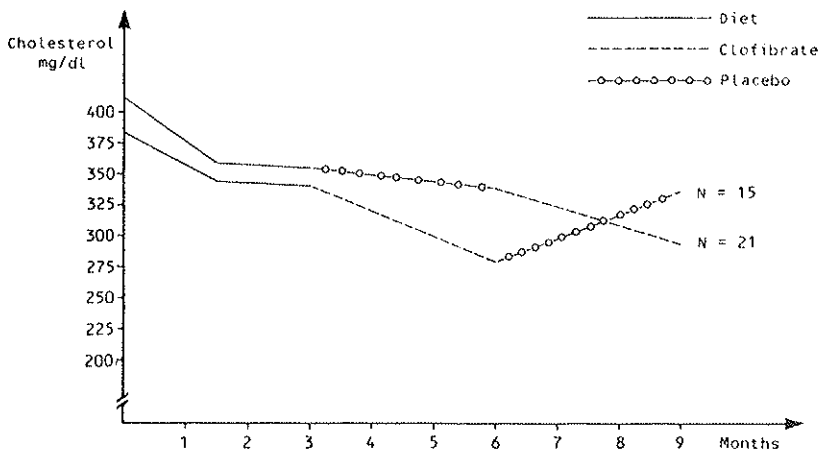
A double-blind randomized controlled trial with placebo and clofibrate in
36 men aged 20-49 years

* In the published abstract it was erroneously stated that 61 men
  were referred for hypertension, this is however the number of
  available reports from the general practitioners.

SUMMARY AND MAIN CONCLUSIONS OF THE PAPERS

The present papers are, with the exception of paper IV, based on
The Tromsø Heart Study. Paper IV describes a subproject of the
Cardiovascular Disease Study in Finnmark.
The papers deal with three main topics:

A.   The occurrence and the level of coronary risk factors and their
     relation to physical and social variables, (Papers I and II).

B.   The relationship between the occurrence of myocardial infarction
     (MI) among first degree relatives and the subsequent risk for MI,
     (Papers III, IV, and V).

C.   HDL-cholesterol as a risk factor for coronary heart disease,
     (Papers VI, VII, VIII, IX).

A.   The occurrence and the level of coronary risk factors and their
relation to physical and social variables

The first paper describes the methods and some of the cross-sectional
results. The high level of serum cholesterol and its rapid increase
with age were not unexpected considering the high mortality rate of
CHD observed in Troms County. The cigarette consumption was a
little higher than for the country as a whole. The blood pressure
level in Tromsø was lower than in The Oslo Study. The observation
in paper I that some social characteristics were related to coronary
risk factors, was further explored by multiple regression technique
presented in paper II.

Even if the impact of several variables was reduced to some extent
by this technique, it was confirmed that characteristics related
to lower social groups i.e. low height, heavy physical work, and
residence in rural areas, were associated with a higher coronary
risk factor level. Similar observations have also been made in
The Oslo Study (6). In the future CHD will therefore probably occur
predominantly in the lower social classes.

B. The relationship between the occurrence of myocardial infarction (MI) among first degree relatives and the subsequent risk for MI

First degree relatives of MI cases have been reported to have a
significantly higher MI risk compared to subjects without MI
relatives (7). In paper III and IV this risk elevation could only
to a small extent be explained by higher levels of blood pressure,
blood lipids, and cigarette consumption. On this basis we therefore
concluded that the occurrence of MI among first degree relatives
must be considered an independent risk factor for later MI. The
methodological problems in assessing the occurrence of MI among
relatives in population studies, and in the use of this
variable in the risk analysis, are large. These problems are
discussed in paper V and enlarged upon in the general discussion.
A model is suggested for estimating a continuous variable containing
the family-associated risk. Our intention with this variable is to
use it in addition to other coronary risk factors in order to improve
the predictability of MI. The real value of this variable can first
be evaluated in a prospective material.

C. HDL cholesterol as a risk factor for CHD

In 1975 Miller and Miller (8) put forward the hypothesis that lower HDL cholesterol was associated with an increased risk for CHD. Already six months earlier contact between O. Mjøs and N. Miller lead to the inclusion of HDL cholesterol analysis in a family study which was part of the Tromsø Heart Study (paper VI). This family study did not reveal any difference in the HDL cholesterol level in subjects with and without MI among their relatives. However, in this comparison the family histories were not verified. The HDL cholesterol level in males aged 30-49 years was lower than in females. Stored serum samples from the 1974 survey permitted testing of the HDL hypothesis in a small prospective case-control study, (Paper VII). This analysis established HDL cholesterol as a strong discriminant variable between cases and controls, an observation which has been confirmed in a larger prospective study from Framingham (9). In paper VIII it was examined if the observed difference in HDL cholesterol between cases and controls in this material reflected a corresponding difference in apoprotein AI level. A difference was observed but less than for HDL cholesterol, and as the material was accidentally reduced, the conclusions are only tentative. The promising findings from the prospective studies encouraged us to try to clear up differences in CHD incidence which could not be explained by conventional risk factors. The differences in CHD incidence between the three ethnic groups in Tromsø, however, could not be explained by differences in HDL cholesterol (Paper IX).

GENERAL DISCUSSION

Causality and prediction

Assuming that preventive measures are effective, the incidence
of CHD can be reduced by changing detrimental living habits in
the population. But even in an improved environment there will
remain in the foreseeable future high risk individuals who may
benefit from personally adapted intervention. Such intervention
must be based on the ability to identify the high risk subjects
through predictive tests. Much knowledge has been gained on pre-
disposing factors for CHD, and our ability to predict future CHD
victims is higher than for any other chronic lethal disease.
Still, a combined risk function of serum cholesterol, blood pressure
and cigarette smoking can only place 50 per cent of the future
MI cases in the upper quintile of risk (11, 12, 13). This finding
is consistent in most population studies, disregarding differences
in incidence of CHD in the populations. The MI cases found in
the lower four quintiles of risk, the so-called "unexplained"
cases, are a recurrent source of controversy. Their existence
has been used as an argument against the causal role of the major
risk factors. Such inference is based on the misconception of
a one to one relationship between pathogenic agent and disease,
- relationships which are extremely rare in medicine. The fact
that a majority of cases occurs at risk levels below the upper
10 or 20 per cent is of course irrelevant for the assessment of
causation. As the risk is continuously increasing without any
threshold which distinguishes between those with and without risk,

a certain number of cases has to occur below the upper quintile.
Such cases might therefore more properly be called unpredicted
than "unexplained". This lack of predictive power to some extent
reflects the methodological difficulties in assessing the true
level of the risk factors. The assessment of individual risk in
most longitudinal studies is based on a single measurement, which
to a great extent is influenced by intra-individual variation and
analytical errors, and which leads to misclassification of subjects.
The errors involved are well-documented for serum cholesterol and
blood pressure (14, 15, 16, 17), and are of such magnitude that
they have to confound prediction of risk in individuals (3). The
assessment of smoking habits is also encumbered by considerable
methodological difficulties. If we therefore want to avoid the
extra, and mostly non-applicable effort of multiple measurements
in the same individual, we have to develop methods which to a
large extent measure the true level of the risk factors. The
methods for measurements of the major risk factors and the errors
involved are in fact principally the same today as they were thirty
years ago. Thus more promising alternatives would probably be
to examine subfractions of the risk factors - possibly closer to
the biological mechanism - and assessed with greater accuracy,
or to include other factors in the risk function to increase the
predictive power.

Improvement of prediction is an important objective - and may
also improve our insight into the web of causation. Future re-
search will probably reveal specific agents which will increase
our knowledge of the pathological mechanisms of CHD, but they are
unlikely to be sufficient causes of CHD anymore than the bacillus

is for tuberculosis. Retrospectively, it is admissable to say
that the drastic reduction of tuberculosis as cause of death in
the industrialized world did not depend on the recognition of the
bacillus.

The role of high density lipoprotein in lipid transport

The high predictive power of HDL cholesterol compared to total
cholesterol (paper VIII, 9, 18) may depend on either a higher
reliability of the HDL cholesterol measurements, or that HDL chole-
sterol plays an independent part in the atherogenesis. Recent
data indicates that within-subject variation and the analytical
error do not differ considerably in HDL cholesterol and total
cholesterol measurements (19). Thus the higher predicitive power
of HDL cholesterol if it proves to be a general phenomenon - is
probably explained by this variable being closer to the athero-
genic process. The advantage of the HDL hypothesis is that it
fits into an already existing theory of lipid transport without
conflicting with the consistent epidemiological observations of
the association between total serum cholesterol and CHD. A large
fraction of the low density lipoproteins (LDL) which carries most
of the lipids accumulating in atherosclerotic lesions, is degraded
in peripheral cells. The cholesterol moiety, however, can only
be degraded in the liver. Thus cholesterol brought into the cell
by the LDL or synthetized intracellularly must be transported back
to the liver for degradation. The LDL uptake in the cell, and
thereby the cholesterol uptake, is primarily determined by recep-
tors on the cell membrane (20). Any interference with the LDL

uptake will slow atherogenesis by reducing the rate of cholesterol
delivered to the cell. HDL may interfere with this process either
by inhibition of the LDL uptake in the cells or through facili-
tating cholesterol transport back to the liver. The inhibition
of the LDL uptake may be effected through competition for the re-
ceptor sites. Recent studies have shown that subfractions of HDL,
apoprotein E, compete more effectively than unfractioned HDL with
LDL for the receptor sites (21). This finding may be indirectly
supported by the lack of increased predictive power of apoprotein
AI compared to HDL cholesterol reported in paper VIII. However,
the need for a larger body of quantitative data from epidemiological
studies, as well as further research on the control of the lipid
transport across the cell membrane are evident before the true
role of HDL as a risk factor for CHD can be defined.

Methodological problems in assessing the family occurrence of
CHD in population studies

Despite early recognition of the family history as a risk factor,
this variable has not been included in the risk function based on
the major risk factors. There are mainly two reasons for this:
firstly the widespread view that the family-associated risk ope-
rates through the major risk factors, a view which is not supported
by our data, and secondly the fact that "measurement" of the
family history also is associated with considerable methodological
difficulties.
A thirty-eight year old man who participated in one of our
screenings was interviewed on the family occurrence of MI. He
reported to have had MI one year earlier, but to the question

concerning MI among his first degree relatives, he was obviously in doubt. During the interview the following history was revealed. His father was healthy and aged sixty years. His mother, who was fifty-eight years old, had had angina pectoris for the last five years. Two of his mother's brothers had died from MI before the age of fifty, and his mother's youngest brother had a MI at the age of forty-four. His two sisters were healthy at the age of thirty-three and thirty-six respectively. This young man, who according to common clinical judgement had a heavy family pre- disposition for CHD, was recorded with a negative family history according to our criteria. The history illustrates the following methodological problems.

1.   Choice of endpoints, which to a large extent determines the reliability of the family history. (Generally the softer the end-points, the less reliable the data.) Angina pectoris, with its often imperceptible and undramatic natural history, is too soft an end-point in mass-interviews. Nevertheless, also angina pectoris may well confer risk on first degree relatives, especially when it occurs in young women. A harder end-point is age of death of the relatives. This end-point, however, requires - to be dis- criminating - a high age of relatives, which again implies high age of the survey population, or data on grand-parents. If the last alternative is chosen, the family history is extended to include:

2.   Data on second degree relatives, which inevitably would be less reliable than data on first degree relatives.

To our experience interviewees have more than enough difficulties in giving reliable information on morbidity in first degree re- latives. But we are well aware of the possible loss of information due to the exclusion of the second degree relatives from the family

histories. This loss of information may lead to:

3. Misclassification due to few and young first degree relatives.
This is a persisting problem when data is collected in young
subjects. Often the number of first degree relatives is small and
their age so low that the chance of finding a MI case among them
is very low. Thus, a negative family history in these subjects
has a low predictive value. A practical compromise for the fa-
mily history of CHD which would fulfil both the demands for re-
liability and for high predictive power might perhaps be to collect
information both on the occurrence of MI among first degree rela-
tives and longevity in grand-parents. It then remains to find a
practical and reliable method for collection of the family data;

4. Interview or self-administered questionnaire. Our choice of
interview together with a verification procedure was made with
the intention of optimizing reliability. The procedures, espe-
cially the verification, are, however, too laborious to be appli-
cable in routine screenings. The main questionnaire included a
question on the occurrence of MI or angina pectoris among first
degree relatives. This enables comparison of the two methods,
the interviews and the self-administered questionnaire. The answers
from the interviews and the questionnaires are cross-tabulated in
table 2. The higher number of positive responses to the question-
naire to some extent reflects the inclusion of angina pectoris,
but the two methods apparently yield different results also for MI.
The questionnaire picks out 79 per cent of the verified MI positive
family histories. It also gives a considerable number of false
positives, but it is a far more practical method, and we have to
search for more precise questions to improve the reliability of
the questionnaires in the future. Our basis for suggesting the

Table 2

QUESTIONNAIRE ANSWERS TO THE QUESTION : "HAS ONE OR MORE OF YOUR PARENTS OR SIBLINGS HAD MYOCARDIAL INFARCTION OR ANGINA PECTORIS ?" DISTRIBUTED ACCORDING TO RESULTS OF VERIFIED INTERVIEW. THE CARDIO-VASCULAR DISEASE STUDY IN FINNMARK, FOUR MUNICIPALITIES, 4,450 HEALTHY MEN AND WOMEN AGED 20-49 YEARS

RESULT OF VERIFIED INTERVIEW

QUESTIONNAIRE ANSWERS	Total	No MI among first degree relatives	Myocardial infarction	Sudden death	Uncertain MI	Angina pectoris	Not traced for verification	Lack of information about relatives
Yes	1034	385	417	30	8	71	96	27
No	2918	2741	53	17	1	7	31	68
Don't know	498	407	40	9	2	8	16	16
Total	4450	3533	510	56	11	86	143	111

family history included in the risk function was that the family-
associated risk could have an independent contribution to the pre-
diction.   Even if it were not so, i.e. the family risk was con-
ferred through the major risk factors already included in the
risk function, the family history would be another way of measuring
the risk, which together with the other measurements could bring
us closer to the true risk level.

The prevention controversy

Even if some controversy still exists concerning the causal role
of the major risk factors, the main controversy is related to the
benefit of intervention measures in individuals or society at
large.   This controversy is partly caused by conceptional diffe-
rences within the medical profession, but the principal cause is
inadequate data.   Unequivocal evidence of a worth-while benefit
of intervention still does not exist.

If we look at the diet-heart controversy, most diet trials to date
have been encumbered by methodological problems or inconsistency
in results (22, 23).   Some studies, however, have been encouraging,
especially with regard to the feasibility of cholesterol reduction
in men by dietary means (24).   With regard to antihypertensive
treatment most studies have shown indisputable effects on the inci-
dence of cerebrovascular strokes, whereas the effect on the incidence
of CHD has been less equivocal striking (25, 26).   In order to
further investigate the effectiveness of antihypertensive treatment
on moderately elevated blood pressure the British Medical Research

Council has recommended a controlled trial including 18,000 subjects,
a number which requires screening of 380,000 - 450,000 subjects (27).
The effect of quitting smoking has been examined in several studies.
A gradual decrease in relative risk for CHD has been observed during
the first two years after having stopped smoking (28). Such results
however, may be biased by other changes in behaviour taken by those
who stop smoking cigarettes. These changes cannot be adjusted for
without controlled trials. Only one controlled trial of smoking
intervention is known, with participants drawn from the Whitehall
study of male civil servants in London (29). In that study approxi-
mately one half of the cigarette smokers did stop smoking, but as
also a rather large group of the controls stopped smoking in the
same period, and the CHD incidence did not differ between the groups,
the results remain inconclusive. The present status of intervention
is, in summary, that the evidence of a beneficial effect of quitting
smoking and the benefit from dietary changes are encouraging,
whereas the effect of medical treatment for hypertension, although
overall clearly beneficial, is debatable with regard to CHD.

Both the risk factor concept with additive effect from each single
factor, and the almost insuperable difficulties in changing one
single factor at a time, have initiated multiple risk factor inter-
vention trials. The future results from the large American Multiple
Risk Factor Intervention Trial (MRFIT), started in 1973 and including
approximately 12,000 men aged 35-57 years, will probably have consi-
derable effect on the policy of intervention (30). Inconclusive
results also from this study must, however, be anticipated in the
light of the recent reports on decreasing CHD mortality rates in USA,

corresponding to changes in life style habits (31). Both this fact, the use of drug intervention (32) and the relatively late onset of intervention may reduce the chances for conclusive results.

It has been argued that the total body of "indirect" evidence - epidemiologic, clinical, animal experiments - only permits formulation of hypotheses, and that only experiments, i.e. randomized controlled trials, permit decisive testing of a hypothesis. If this approach to the methodology of science should prevail, most of the knowledge acquired by modern medicine would have to be classified as hypotheses. It is of course justified to ask for a final proof for the beneficial effect of intervention, but the methodological difficulties of experiments within this field, and the ideal experiment i.e. to randomize and intervene upon newborn babies, are so unrealistic that we probably have to live with circumstantial evidence. Nevertheless, we feel that the time is ripe for more attempts at controlled mass scale preventive action.

The fact that the detrimental way of living is so ordinary, everyday and widespread in modern industrial societies, suggests measures towards society at large rather than the single individual. Measures towards the society must arise from political decisions, but examples of such decisions are rare. In Norway a three-year old parliamentary report suggesting well-founded changes in nutritional habits has still not resulted in any political action. Similar to the ban on tobacco advertisements, which was put into effect anyhow, the suggested changes are so entangled in circumstantial interests that political decisions are very complex. This political dilemma and our inability to provide effective health education, necessitate also individual intervention measures.

Ideally, individual intervention should be a task for the primary
health service. In Norway, however, the resources allocated to
the primary health service do not at present allow any substantial
increase in work-load. A reinforcement both educationally and
financially is needed before the primary health service can handle
these tasks properly.

In the mean-time, the work-sharing exemplified by the County
Studies, where the State Mass Radiography Service performed the
screening and the general practitioners the intervention has proved
to be a feasible model. Besides giving research opportunities such
screening programmes have a health educational value both for the
public and the health personnel.

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