Dietary and antismoking advice and ischemic heart disease mortality in men with normal or high fasting triacylglycerol concentrations: a 23-y follow-up study[1,2]

Ingrid Ellingsen, Ingvar Hjermann, Michael Abdelnoor, Elsa M Hjerkinn, and Serena Tonstad

ABSTRACT

Background: In the Oslo Diet and Antismoking Trial, 1232 high-risk men aged 40–49 y were randomly assigned to either a lifestyle intervention group or a control group for 5 y. The study showed a significant reduction in ischemic heart disease (IHD) events in the intervention group.

Objective: Our objective was to examine this cohort 23 y after the start of the trial.

Design: We examined the effect of group assignment on IHD mortality in subjects with a normal (below the median; range: 0.69–2.00 mmol/L; $n = 615$) or a high (at or above the median; range: 2.01–13.80 mmol/L; $n = 617$) fasting triacylglycerol concentration in 1972–1973 (at inclusion into the study). We recorded vital status on 31 December 1996 and ascertained causes of death by linkage to Statistics Norway.

Results: In the men with a high triacylglycerol concentration, IHD death occurred in 25 (8.13%) subjects in the intervention group and in 44 (14.2%) subjects in the control group (relative risk: 0.57; 95% CI: 0.36, 0.91; $P = 0.02$). An adjusted Cox proportional hazards model yielded a hazard ratio of 0.56 (95% CI: 0.34, 0.93; $P = 0.027$). In the men with a normal triacylglycerol concentration, the intervention had no detectable effect on IHD mortality (adjusted hazard ratio: 1.10; 95% CI: 0.66, 1.83; $P = 0.7$).

Conclusions: These data suggest that advice to change diet and smoking habits reduced the relative risk of IHD mortality after 23 y in men with high triacylglycerol concentrations. Men with normal triacylglycerol concentrations did not appear to achieve this long-term benefit of lifestyle intervention. *Am J Clin Nutr* 2003;78:935–40.

KEY WORDS Oslo Diet and Antismoking Trial, ischemic heart disease mortality, triacylglycerol, middle-aged men

INTRODUCTION

Several studies suggest that men with a high triacylglycerol concentration and a high total or LDL-cholesterol concentration may have a particularly high risk of subsequent ischemic heart disease (IHD) (1–3). High triacylglycerol concentrations tend to cluster with other features of the insulin resistance or metabolic syndrome, including abdominal obesity; low HDL-cholesterol concentrations; the presence of small, dense LDL particles; high blood pressure; and type 2 diabetes (4). Although dietary change, weight loss, and increased physical activity have been shown to improve several aspects of the metabolic syndrome (5), the effect of changes in lifestyle on mortality has not been thoroughly documented.

The Oslo Diet and Antismoking Trial was a 5-y primary prevention trial that showed the protective effect of dietary and antismoking advice against IHD events in high-risk, middle-aged men. The effects of the intervention were described previously at the end of the study (6) and in a further analysis 102 mo after the start of the study (7).

In the present study, we present the results of a 23-y follow-up of the men in the Oslo Diet and Antismoking Trial. We compared the IHD mortality of the men who had a normal triacylglycerol concentration at screening with that of the men who had a high triacylglycerol concentration at screening. Our rationale for doing so included the following considerations. First, the potential of risk reduction in terms of absolute risk may be greater in subjects with a high baseline risk of IHD than in subjects with a low baseline risk (8). Second, subjects with hypertriglyceridemia are often overweight, and dietary changes may reduce body weight in this subgroup. Finally, cigarette smoking worsens insulin sensitivity and may increase the risk of type 2 diabetes (9, 10). Thus, smoking cessation may be especially effective in reducing IHD risk in subjects with the metabolic syndrome.

SUBJECTS AND METHODS

Study population

The Oslo Diet and Antismoking Trial was initiated in 1972 as a primary prevention trial that sought to establish whether reduction in serum lipid concentrations and cessation of smoking reduced the incidence of IHD (6). The study was extensively described in previous publications (6). Briefly, 1232 healthy men aged 40–49 y who had an elevated serum total cholesterol concentration or coronary risk score were included in the study from a pool of 16 202 men who were screened (65% of all men aged 40–49 y in Oslo). All subjects had a normal electrocardiogram at rest and were free of chest pain during exercise testing; they were

[1] From the Department of Preventive Cardiology (IE, IH, EMH, and ST) and the Center of Clinical Research (MA), Ullevål University Hospital, Oslo.

[2] Address reprint requests to I Ellingsen, Department of Preventive Cardiology, Ullevål University Hospital, N-0047 Oslo, Norway. E mail: ingrid.ellingsen@ulleval.no.

Received November 22, 2002.

Accepted for publication May 16, 2003.

also free of cardiovascular disease, hypertension, diabetes mellitus, cancer, disabling diseases, psychopathologic diseases, and alcoholism. Men on lipid-lowering diets were excluded. The subjects in the intervention group ($n = 604$) visited the clinic every 6 mo and were seen by the doctor and dietitian at each session, whereas the subjects in the control group ($n = 628$) were seen at 12-mo intervals. Body weight was measured at screening and at subsequent clinic visits. The study was performed in accord with the Helsinki Declaration of 1975 as revised in 1983.

Diet and lifestyle history and interventions

A short diet history of 8 food items was evaluated at screening. The subjects were asked to quantify their consumption of hard margarine or butter, soybean oil, whole milk, cream, cheese, eggs, cakes and pastries, and lean or fatty meats. The scores for all 8 dietary items were summed to obtain a total score, with a low total score indicating a high-risk diet. The maximum possible score was 50 points. Thus, for example, consumption of $>$ 250 g margarine or butter/wk, consumption of $>$ 1 L whole milk/wk, daily consumption of cream or cakes and pastries, consumption of $>$ 60 g cheese/d, consumption of $>$ 3 eggs/wk, consumption of 0–50 g soybean oil/wk, and avoidance of lean meat gave a total score of 0 points (0 points for each item), whereas consumption of 0–50 g margarine or butter/wk, 0–0.25 L whole milk/wk, or $>$ 250 g soybean oil/wk gave a score of 8 points for each item. Consumption of wine, beer, and liquor was recorded as none, occasional, 1–2 d/wk, or daily.

At the time the dietary questionnaire was administered, the subjects were asked about marital status, current cigarette smoking (exsmokers and never smokers were counted as nonsmokers), and physical activity at work and during leisure time. Smoking status was reevaluated at 2 and 5 y.

A trained dietitian and the lead investigator (IH) gave dietary advice individually and during group sessions (6). Subjects with elevated total cholesterol concentrations were advised to reduce their saturated fat intake and to slightly increase their polyunsaturated fat intake. Subjects with elevated triacylglycerol concentrations were asked to reduce their total energy intake (mainly by reducing their intakes of sugar, sweet drinks, chocolate, alcohol, and fat). For breakfast and evening meals, all subjects were asked to consume fiber-rich bread with no or only a thin layer of highly polyunsaturated, low-fat margarine. Preferred bread fillings included fish, vegetables, fruit, low sugar jam, and low-fat meats and cheeses. Skim milk and $\leq$ 1 egg/wk were recommended. For main meals, the use of lean meat, fish, and low-fat fish products, together with potatoes and vegetables, was advised. Cigarette smokers were urged to stop smoking. Each subject was monitored individually and given nutritional advice in groups. The results of the blood tests were also used during the nutrition sessions as a monitoring tool.

Laboratory methods

Blood samples were collected by venipuncture at an initial screening (nonfasting), at a second screening (fasting), at half-yearly intervals, and after 3 and 5 y of follow-up. Concentrations obtained at the second screening were used in determining baseline lipid concentrations for study eligibility and were collected at the same time as questionnaire and other clinical data. Thus, the fasting values obtained in the second screening were used in the present study. These samples were taken after a 12-h fast. Samples were assayed for serum total cholesterol, triacylglycerol, and glucose concentrations but not for HDL-cholesterol concentrations (OP Foss, unpublished observations, 1975). The same methods of analysis were used for samples taken at all visits. For missing values at 5 y, the last available value was used in the present analysis.

Endpoints

The inclusion date was the date of screening in 1972–1973. We set a census date of 31 December 1996. Outcomes were identified by linkage to Statistics Norway. Linkage was based on the unique 11-digit identification number given to all Norwegian citizens and was approved by the Norwegian data inspectorate. Outcome status was available for every participant included in the original study. The main outcome measure was IHD mortality. Codes were defined according to the *International Classification of Diseases* (ICD). For IHD mortality, the ICD 8th revision (codes 410–414 and 795), the ICD 9th revision (codes 410–414 and 798.1), and the ICD 10th revision (codes I21.0–I21.9, I25.0–I25.9, and R96.0) were used. Death from causes other than IHD was censored (11). Other causes of death included cerebrovascular disease, other vascular disease, infections, accidents, alcoholism, asthma, and cancer.

Statistical methods

The subjects were classified according to the median triacylglycerol concentration, and risk factors were compared between the normal and high triacylglycerol groups according to intervention or control status. For continuous variables, a two-factor analysis of variance with terms for interaction between triacylglycerol concentration and treatment group was applied. For categorical variables, the Cochran and Mantel-Haenszel statistics test was applied by using the Wolf test for interactions.

The subjects' age on 1 January 1972 was used in all analyses. The inclusion period lasted 2 y; thus, the age range of subjects was 40-51 y. Person-time for each subject was calculated from the date of screening to the date of confirmation of death due to IHD or until 31 December 1996, whichever came first. The relative risk (RR) of IHD mortality for assignment to the intervention or the control group was estimated for men whose triacylglycerol concentration was below the median (0.69–2.00 mmol/L) or equal to or greater than the median (2.01–13.80 mmol/L). To test our main hypothesis that the RRs of men with high triacylglycerol would differ from those of men with normal triacylglycerol, we used Cox regression analysis with treatment group (intervention or control), triacylglycerol concentration (below the median or equal to or greater than the median), and their product as confounders (12). A Wald test was applied to test whether the product (interaction term) was statistically significant (13). The test was done by linear regression analysis using triaclyglycerol concentration, treatment group, and triacylglycerol concentration $\times$ treatment group. Further analyses were based on 615 men with triacylglycerol concentrations below the median and 617 men with triacylglycerol concentrations equal to or greater than the median. Comparison of univariate survival curves between the treatment groups within each of the triacylglycerol subgroups was performed by using log rank statistics (14).

The following variables were specified for inclusion in the multivariate model because of their potential relation with IHD

TABLE 1
Baseline characteristics and dietary intakes according to median fasting triacylglycerol concentrations and assignment to the intervention or the control group[1]

	Normal triacylglycerol concentration (< 2.01 mmol/L)		High triacylglycerol concentration (≥ 2.01 mmol/L)	
	Intervention group (n = 297)	Control group (n = 318)	Intervention group (n = 307)	Control group (n = 310)
Characteristic				
Age (y)	46 ± 3[2]	46 ± 3	46 ± 3	46 ± 3
Married (%)	89	87	87	87
Current cigarette smoker (%)	79	79	79	79
Active at work (%)	57	56	51	52
Active during leisure time (%)	82	78	72	76
BMI (kg/m^2)[3]	24.2 ± 2.5	24.5 ± 2.4	25.6 ± 2.6	25.9 ± 2.7
Systolic BP (mm Hg)	125 ± 15	127 ± 63	126 ± 11	126 ± 11
Diastolic BP (mm Hg)	81 ± 9	80 ± 9	82 ± 9	82 ± 9
Total cholesterol (mmol/L)	7.6 ± 0.8	7.6 ± 0.7	7.8 ± 0.7	7.9 ± 0.7
Plasma glucose (mmol/L)	5.8 ± 2.0	5.8 ± 0.5	5.8 ± 0.8	5.8 ± 0.9
Triacylglycerols (mmol/L)	1.6 ± 0.3	1.6 ± 0.3	2.8 ± 0.9	3.0 ± 1.3
Dietary intake				
Margarine or butter, ≥ 50 g/wk (%)	97	94	95	96
Soybean oil, ≥ 50 g/wk (%)	33	33	31	30
Whole milk, ≥ 0.25 L/wk (%)	81	82	79	80
Cream, daily (%)	26	21	22	23
Cheese, ≥ 60 g/d (%)	67	68	61	64
Eggs, ≥ 3/wk (%)[4]	21	21	15[5]	25
Cakes or pastries daily (%)	42	38	39	39
Lean meat, regularly (%)	2	1	2	1
Dietary score[6]	14 ± 6	14 ± 6	15 ± 6	14 ± 6
Alcohol (%)				
Wine, ≥ 1–2 times/wk	8	6	7	7
Beer, ≥ 1–2 times/wk	27	23	30	30
Liquor, ≥ 1–2 times/wk	50	48	52	51

[1] BP, blood pressure.
[2] $\bar{x}$ ± SD.
[3] Significant difference between the subjects with a normal triacylglycerol concentration and those with a high triacylglycerol concentration, $P = 0.01$ (two-factor ANOVA).
[4] Significant interaction between treatment group and baseline triacylglycerol concentration, $P = 0.02$.
[5] Significantly different from the control group, $P = 0.03$ (Mantel-Haenszel test).
[6] A high score (up to 50 points possible) indicates a diet that confers a low risk of ischemic heart disease.

mortality: age, body mass index (BMI; in kg/m^2), cigarette smoking, total cholesterol and triacylglycerol concentrations, glucose concentration, systolic and diastolic blood pressure, total dietary score (or score for each dietary item), alcohol intake, and activity at work or during leisure time. The relations between assignment to the intervention or the control group and IHD mortality were then analyzed with the multivariate Cox proportional hazards model, with initial adjustment for age followed by adjustment for potential confounders. Because of intercollinearity between systolic and diastolic blood pressure, only diastolic blood pressure was entered into the multivariate model. We did not account for the effect of the intervention on IHD risk factors at the end of the intervention because the intention of this analysis was to examine the effect of the intervention on total IHD deaths including deaths during the intervention period. All calculations were done with SPSS (version 10; SPSS Inc, Chicago).

RESULTS

Between 1972 and 1996, we accumulated 26 734 person-years of follow up, and 322 deaths, including 136 IHD deaths (5.1/1000 person-years), occurred. The mean length of follow up was 22.8 y (maximum: 24.7 y). In the entire cohort, IHD death occurred in 77 of the 628 men in the control group and in 59 of the 604 men in the intervention group ($P = 0.14$). The Wald interaction term between group assignment and triacylglycerol concentration (ie, below the median or equal to or above the median) was marginally significant ($P = 0.06$).

As shown in **Table 1**, the subgroups with normal or high triacylglycerol concentrations were well balanced with regard to baseline characteristics: there were only minor differences between the 2 subgroups with regard to BMI and egg consumption. In the subgroup with high triacylglycerol concentrations, IHD death occurred in 44 of 310 (14.2%) subjects in the control group and in 25 of 307 (8.1%) subjects in the intervention group, which gave a risk ratio of 0.58 (95% CI: 0.35, 0.94; $P = 0.02$) (**Table 2**). Survival curves show that, relative to the control group, the intervention group had an early and persistent decrease in cumulative IHD mortality (log rank $\chi^2 = 5.9$, $P = 0.015$) (**Figure 1**A).

In the subgroup with normal triacylglycerol concentrations, IHD death occurred in 33 of 318 (10.4%) subjects in the

TABLE 2
Relative risks of mortality from ischemic heart disease (IHD) in 1232 men in the Oslo Diet and Antismoking Trial according to median fasting triacylglycerol concentrations and assignment to the intervention or the control group

	Normal triacylglycerol concentration (< 2.01 mmol/L)		High triacylglycerol concentration (≥ 2.01 mmol/L)	
	Intervention group (n = 297)	Control group (n = 318)	Intervention group (n = 307)	Control group (n = 310)
Follow-up time (person-years)	6772	7250	7000	7068
Number of IHD deaths	34	33	25	44
Rate ratio	1.10 (0.68, 1.78)[1]		0.58 (0.35, 0.94)	
Relative risk, adjusted for age[2]	1.09 (0.68, 1.72)		0.55 (0.33, 0.89)	
Relative risk, multivariate model[2,3]	1.10 (0.66, 1.83)		0.56 (0.34, 0.93)	

[1] 95% CI in parentheses.
[2] Values obtained with a Cox proportional hazards analysis.
[3] Adjusted for age, BMI, cigarette smoking, total cholesterol and triacylglycerol concentrations, glucose concentration, diastolic blood pressure, dietary score, alcohol intake, and activity at work and during leisure time.

control group and in 34 of 297 (11.4%) subjects in the intervention group, which resulted in a risk ratio of 1.10 (95% CI: 0.68, 1.78; $P = 0.7$) (Table 2). Survival curves show that the cumulative incidence of IHD deaths was not significantly different between the intervention group and the control group (log rank $\chi^2 = 0.13$, $P = 0.7$) (**Figure 1**B).

The independent multivariate relation obtained with the Cox proportional hazards model between assignment to the intervention or the control group and IHD mortality in the men with high or normal triacylglycerol concentrations is shown in Table 2. Relative to the incidence of IHD deaths in the control group, the incidence of IHD deaths in the intervention group decreased after adjustment for age in the subgroup with high triacylglycerol concentrations but not in the subgroup with normal triacylglycerol concentrations. Adjustment for age, BMI, cigarette smoking, total cholesterol and triacylglycerol concentrations, glucose concentration, diastolic blood pressure, dietary score, alcohol intake, and activity at work and during leisure time reduced the RR minimally, from 0.58 to an adjusted hazard ratio of 0.56 (95% CI: 0.34, 0.93; $P = 0.03$). In the subgroup with normal triacylglycerol concentrations, there was no effect of assignment to the intervention or the control group on IHD mortality after adjustment for the same variables (RR: 1.10; 95% CI: 0.66, 1.83; $P = 0.7$). Results of the Cox proportional hazards model were not different when separate dietary items (eggs, cream, and cakes or pastries) were entered in the model instead of the total dietary score. The RRs were then 0.50 (95% CI: 0.30, 0.83; $P = 0.007$) and 1.14 (95% CI: 0.69, 1.90; $P = 0.6$) in the groups with high and normal triacylglycerol concentrations, respectively.

Total cholesterol and triacylglycerol concentrations were lower in the intervention group than in the control group after 5 y, regardless of baseline triacylglycerol concentrations (**Table 3**). Smoking prevalence was lower in the intervention group than in the control group.

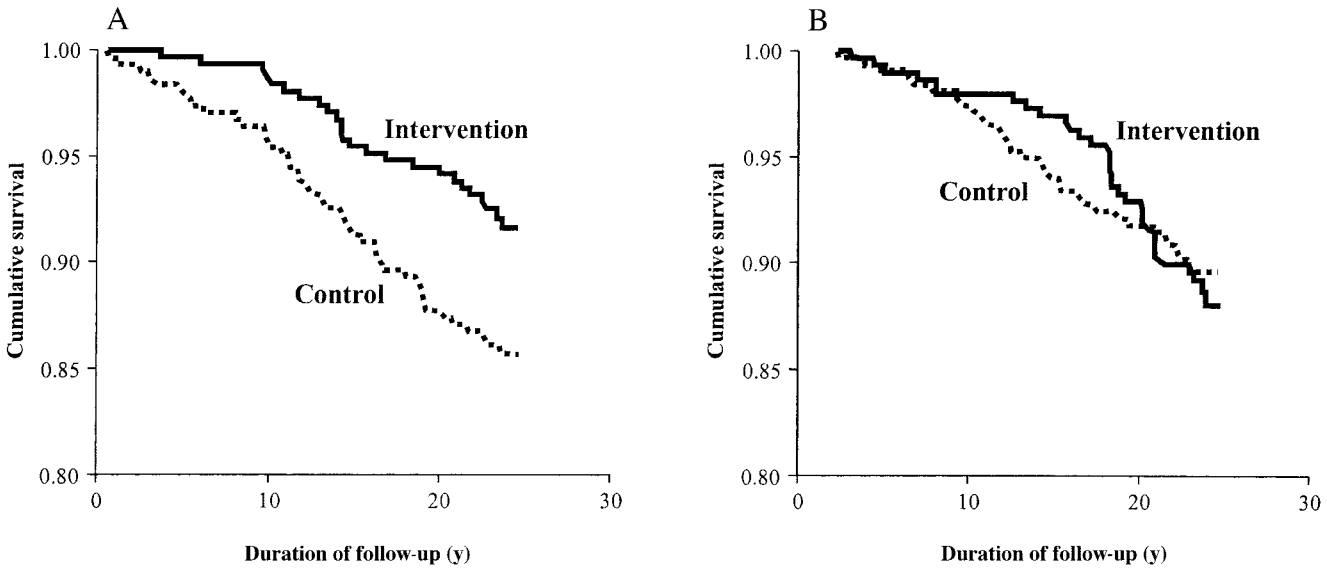

FIGURE 1. Kaplan-Meier survival curves showing the relation between survival from ischemic heart disease and assignment to the intervention or the control group in men with high (n = 617; log rank $\chi^2 = 5.9$, $P = 0.015$) or normal (n = 615; log rank $\chi^2 = 0.13$, $P = 0.7$) triacylglycerol concentrations.

TABLE 3
Values for ischemic heart disease risk factors at the end of the intervention (after 5 y or last available values) according to median fasting triacylglycerol concentrations and assignment to the intervention or the control group

	Normal triacylglycerol concentration (< 2.01 mmol/L)		High triacylglycerol concentration (≥ 2.01 mmol/L)	
	Intervention group (n = 297)	Control group (n = 318)	Intervention group (n = 307)	Control group (n = 310)
Cigarette smoking (%)[1]	55	65	64	67
BMI (kg/m^2)[2]	23.4 ± 2.7[3]	24.5 ± 3.0	24.7 ± 2.6	25.9 ± 3.2
Total cholesterol (mmol/L)[2]	6.7 ± 1.0	7.4 ± 1.0	7.0 ± 1.0	7.6 ± 0.9
Triacylglycerols (mmol/L)[2,4]	1.5 ± 0.6	1.6 ± 0.6	2.1 ± 0.9	2.6 ± 1.4

[1] Significant difference between the intervention group and the control group, $P < 0.01$ (Mantel-Haenszel test).
[2] Significant difference between the intervention group and the control group, $P < 0.001$ (two-factor ANOVA).
[3] $\bar{x}$ ± SD.
[4] Significant interaction between treatment group and baseline triacylglycerol concentration, $P = 0.001$ (two-factor ANOVA).

DISCUSSION

These data show that advice given to hypertriglyceridemic men to change dietary habits and stop smoking may be associated with a > 40% reduction in IHD mortality relative to IHD mortality in the control group after 23 y of follow-up. We found no reduction in IHD mortality in the men with normal triacylglycerol concentrations who were given the same advice, despite apparently similar changes in total cholesterol concentrations in both groups. These findings suggest that the subgroup of high-risk, middle-aged men with hypertriglyceridemia may benefit more from changes in lifestyle than do their counterparts without hypertriglyceridemia.

Our dietary history included only 8 food groups, did not estimate energy intake, and was not repeated at the end of the study. Thus, our ability to provide a detailed analysis of the relation between the diet at baseline or changes in the diet and the primary outcome of the study was limited.

There are several likely mechanisms for the effects of the intervention on IHD risk in the hypertriglyceridemic men; these mechanisms include changes in serum lipid concentrations, body weight, and smoking habits. We were unable to attribute the reduction in IHD mortality to any one of these factors, because the changes achieved did not appear to differ between the subjects with high triacylglycerol concentrations and those with normal triacylglycerol concentrations. Thus, the reasons for these results are unclear but may reflect differences in risk, differences in the responses of biological risk factors to lifestyle changes, or chance.

As hypothesized, IHD mortality in the control group was greater in the hypertriglyceridemic men than in the men with normal triacylglycerol concentrations (14.2% compared with 10.4%). These results are in line with previous data showing that the incidence of IHD in men screened for this study who have high total cholesterol and triacylglycerol concentrations is almost triple that of screened subjects who have high cholesterol but low triacylglycerol concentrations (15). This risk in the latter group of subjects (ie, ≈0.6%/y) is somewhat lower than the usual risk in the population (16). This observation may be explained by the effects of participation in a trial and the yearly follow-up offered to the control group. The risk reduction occurred in the group at higher risk, which mirrored the positive agreement between absolute risk (though not RR) and risk reduction that was reported in a meta-analysis of diet and drug treatments (8). Previous analysis of the results obtained during the Oslo Diet and Antismoking Trial suggested that most of the benefit accrued at the end of the trial was due to the net difference of ≈10% in serum cholesterol concentrations between the groups (17). Our study may have lacked power to show the effect of this modest reduction in serum cholesterol concentration on long-term IHD mortality among men who carried a lower risk of IHD than did the group of hypertriglyceridemic men.

As expected, the men with hypertriglyceridemia in the present study had a higher BMI than did men with low triacylglycerol concentrations, which reflects a clustering of abnormalities consistent with the metabolic syndrome. Several studies have suggested that this subgroup may benefit more from drug treatments for hyperlipidemia or from lifestyle changes than would subjects without features of the metabolic syndrome. A post hoc analysis of the Helsinki Heart Study suggested that the effects of gemfibrozil on IHD events were substantially greater in the subgroup with a high ratio of LDL to HDL cholesterol and high triacylglycerol concentrations than in other subgroups (18). Similarly, in the Simvastatin Survival Study, patients with elevated LDL-cholesterol, low HDL-cholesterol, and elevated triacylglycerol concentrations received greater benefit with simvastatin therapy than did patients with isolated elevation in LDL-cholesterol concentration (19). Persons with hypertriglyceridemia tend to have a predominance of small, dense LDL particles (subclass pattern B). Studies have shown that LDL subclass is an independent predictor of IHD risk (20). Compared with subclass pattern A, subclass pattern B is associated with a greater reduction in LDL-cholesterol concentration and particle number in response to low-fat, high-carbohydrate diets similar to the diet recommended in our study (21). Subjects with hypercholesterolemia and high triacylglycerol concentrations may not experience the adverse effects on HDL-cholesterol and triacylglycerol concentrations noted with dietary fat restriction in subjects with hypercholesterolemia alone, who in addition might experience greater benefits from reducing egg consumption (22, 23). These findings suggest differential effects of the diet on serum lipid concentrations between normotriglyceridemic and hypertriglyceridemic subjects. Moreover, smoking cessation may be particularly advantageous for subjects with hypertriglyceridemia. VLDLs activate the plasminogen activator inhibitor-1

promoter, which increases thrombogenic capacity (24), and may potentiate the hypercoagulable state induced by smoking (25). However, we found no difference in smoking habits between the high and normal triacylglycerol groups after 5 y, which suggests that the difference in outcome was probably due mainly to other lifestyle factors.

Finally, chance is a possible explanation of these findings. Our study had major strengths, including its ability to trace outcomes among all the original study participants and the length of follow-up in a population given lifestyle advice. However, because of its post hoc design, it remains a hypothesis-generating study that only further investigations can confirm or dismiss. These studies are unlikely to be done, primarily because of ethical reasons.

Two clinical issues emerge. Recommendations to lower the intake of fat and to reduce body weight are widely recognized modalities to prevent death from IHD. In practice, it may be very difficult for patients to follow such advice (26). Moreover, the effects of usual dietary advice on lipid concentrations in large trials involving free-living populations are small (27). These findings suggest that resources to effectuate dietary change could be focused first on men with hypertriglyceridemia, who appear to experience salutary long-term effects. Because cigarette smoking increases morbidity and mortality from a wide range of diseases, advice to quit smoking is applicable to all persons.

We thank Ingar Holme for helpful comments and Lise Lund Håheim for assistance with the coding of causes of death.

IE provided the idea for the study, performed the analysis, wrote most of the Subjects and Methods and Results sections, and contributed to the writing of the Introduction and Discussion sections. IH was responsible for the original study and commented on the present analyses. MA was the statistical consultant. EMH assisted in providing the mortality data from Statistics Norway. ST assisted IE with all stages of the work and wrote most of the Introduction and Discussion sections. There were no conflicts of interest.

REFERENCES

1. Assmann G, Schulte H. Role of triglycerides in coronary artery disease: lessons from the Prospective Cardiovascular Munster Study. Am J Cardiol 1992;70:10H–3H.
2. Hokanson JE, Austin MA. Plasma triglyceride concentration is a risk factor for cardiovascular disease independent of high-density lipoprotein cholesterol concentration: a meta-analysis of population-based prospective studies. J Cardiovasc Risk 1996;3:213–9.
3. Jeppesen J, Hein HO, Suadicani P, Gyntelberg F. Triglyceride concentration and ischemic heart disease. An eight-year follow-up in the Copenhagen Male Study. Circulation 1998;97:1029–36.
4. Hjermann I. The metabolic cardiovascular syndrome: syndrome X, Reaven's syndrome, insulin resistance syndrome, atherothrombogenic syndrome. J Cardiovasc Pharm 1992;20(suppl):S5–10.
5. Anderssen SA, Haaland A, Hjermann I, Urdal P, Gjesdal K, Holme I. Oslo Diet and Exercise Study: a one year randomized intervention trial: effect on hemostatic variables and other coronary risk factors. Nutr Metab Cardiovasc Dis 1995;5:189–200.
6. Hjermann I, Velve Byre K, Holme I, Leren P. Effect of diet and smoking intervention on the incidence of coronary heart disease. Report from the Oslo Study Group of a randomised trial in healthy men. Lancet 1981;2:1303–10.
7. Hjermann I, Holme I, Leren P. Oslo Study Diet and Antismoking Trial. Results after 102 months. Am J Med 1986;80(suppl):7–11.
8. Sirtori CR, Calabresi L, Marchioli R, Rubings HB. Cardiovascular risk changes after lipid lowering medications: are they predictable? Atherosclerosis 2000;152:1–8.
9. Facchini FS, Hollenbeck CB, Jeppesen J, Chen YD, Reaven GM. Insulin resistance and cigarette smoking. Lancet 1992;339:1128–30.
10. Manson JE, Ajani UA, Liu S, Nathan DM, Hennekens CH. A prospective study of cigarette smoking and the incidence of diabetes mellitus among US male physicians. Am J Med 2000;109:538–42.
11. Kleinbaum DG, Kupper LL, Morgenstern H. Epidemiologic research: principles and quantitative methods. New York: Van Nostrand Reinhold Company, 1982.
12. Cox JR. Regression model and life table. J R Stat Soc [Ser B] 1972;34;187.
13. Kalbfleish J, Prentice R. The statistical analysis of failure time data. New York: Wiley & Sons, 1980.
14. Kaplan EL, Meier P. Non parametric estimation for incomplete observations. J Am Stat Assoc 1958;3:457–81.
15. Holme I. Coronary risk factors and their possible causal role in the development of coronary heart disease. The Oslo Study. PhD thesis. University of Oslo, Oslo, 1982.
16. Sans S, Kesteloot H, Kromhout D. The burden of cardiovascular diseases mortality in Europe. Task Force of the European Society of Cardiology on Cardiovascular Mortality and Morbidity Statistics in Europe. Eur Heart J 1997;18:1231–48.
17. Holme I, Hjermann I, Helgeland A, Leren P. The Oslo Study: diet and antismoking advice. Additional results from a 5-year primary preventive trial in middle-aged men. Prev Med 1985;14:279–92.
18. Manninen V, Tenkanen L, Koskinen P, et al. Joint effects of serum triglyceride and LDL cholesterol and HDL cholesterol concentrations on coronary heart disease risk in the Helsinki Heart Study. Circulation 1992;85:37–45.
19. Ballantyne CM, Olsson AG, Cook TJ, Mercuri MF, Pedersen TR, Kjekshus J. Influence of low high-density lipoprotein cholesterol and elevated triglyceride on coronary heart disease events and response to simvastatin therapy in 4S. Circulation 2001;104:3046–51.
20. Lamarche B, Lemieux I, Després J-P. The small, dense LDL phenotype and the risk of coronary heart disease: epidemiology, pathophysiology and therapeutic aspects. Diabetes Metab 1999;25:199–211.
21. Krauss RM. Dietary and genetic effects on low-density lipoprotein heterogeneity. Annu Rev Nutr 2001;21:283–95.
22. Knopp RH, Walden CE, Retzlaff BM, et al. Long-term cholesterol-lowering effects of 4 fat-restricted diets in hypercholesterolemic and combined hyperlipidemic men. The Dietary Alternatives Study. JAMA 1997;278:1509–15.
23. Knopp RH, Retzlaff BM, Walden CE, et al. A double-blind, randomized, controlled trial of the effects of two eggs per day in moderately hypercholesterolemic and combined hyperlipidemic subjects taught the NCEP step 1 diet. J Am Coll Nutr 1997;16:551–61.
24. Eriksson P, Nilsson L, Karpe F, Hamsten A. Very low density lipoprotein response element in the promoter region of the human plasminogen activator inhibitor-1 gene implicated in the impaired fibrinolysis of hypertriglyceridemia. Arterioscler Thromb Vasc Biol 1998;18:20–6.
25. Miller GJ, Bauer KA, Cooper JA, Rosenberg RD. Activation of the coagulant pathway in cigarette smokers. Thromb Haemost 1998;79:549–53.
26. Berry EM. Why is the treatment of cancer more successful than that of obesity? Public Health Rev 1996;24:147–63.
27. Tang JL, Armitage JM, Lancaster T, Silagy CA, Fowler GH, Neil HAW. Systematic review of dietary intervention trials to lower blood total cholesterol in free-living subjects. BMJ 1998;316:1213–20.