Randomised trial of lipid lowering dietary advice in general practice: the effects on serum lipids, lipoproteins, and antioxidants

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Abstract

***Objective*—To determine the relative efficacy in general practice of dietary advice given by a dietitian, a practice nurse, or a diet leaflet alone in reducing total and low density lipoprotein cholesterol concentration.**

***Design*—Randomised six month parallel trial.**

***Setting*—A general practice in Oxfordshire.**

***Subjects*—2004 subjects aged 35-64 years were screened for hypercholesterolaemia; 163 men and 146 women with a repeat total cholesterol concentration of 6·0-8·5 mmol/l entered the trial.**

***Interventions*—Individual advice provided by a dietitian using a diet history, a practice nurse using a structured food frequency questionnaire, or a detailed diet leaflet sent by post. All three groups were advised to limit the energy provided by fat to 30% or less and to increase carbohydrate and dietary fibre.**

***Main outcome measures*—Concentrations of total cholesterol and low density and high density lipoprotein cholesterol after six months; antioxidant concentration and body mass index.**

***Results*—No significant differences were found at the end of the trial between groups in mean concentrations of lipids, lipoproteins, and antioxidants or body mass index. After data were pooled from the three groups, the mean total cholesterol concentration fell by 1·9% (0·13 mmol/l, 95% confidence interval 0·06 to 0·22, P<0·001) to 7·00 mmol/l, and low density lipoprotein cholesterol also fell. The total carotenoid concentration increased by 53 nmol/l (95% confidence interval 3·0 to 103, P=0·039).**

***Conclusions*—Dietary advice is equally effective when given by a dietitian, a practice nurse, or a diet leaflet alone but results in only a small reduction in total and low density lipoprotein cholesterol. To obtain a better response more intensive intervention than is normally available in primary care is probably necessary.**

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Introduction

Dietary advice is the recommended initial treatment for moderate hypercholesterolaemia, and lipid lowering drugs should be restricted to patients at highest overall risk of coronary heart disease who do not respond to dietary modification.[1,2] Unfortunately, the level of overall risk above which treatment with lipid lowering drugs is of benefit is poorly defined,[3] and a recent descriptive overview of 16 controlled trials concluded that the effect of the usual diet advised was too small to be of value in clinical management.[4] Relatively small reductions in low density lipoprotein cholesterol concentrations may, however, be clinically useful if accompanied by other nutritional changes, including an increased intake of antioxidants. Biochemical and epidemiological evidence is accumulating that oxidative modification of low density lipoprotein cholesterol has an important causative role in atherosclerosis[5] and that dietary advice that results in a higher intake of natural antioxidants, especially of vitamins E and C and carotenoids, may protect against coronary heart disease.[6-8]

About a quarter of the British population aged 25 to 59 years have a total cholesterol concentration above 6·4 mmol/l,[9] and current guidelines recommend supervised management and follow up for such patients.[2] However, the relative efficacy of dietary advice given in general practice by a dietitian, a practice nurse, or only printed leaflets has not been compared despite the different resource implications. The aim of our study was to determine the effect of these interventions on serum lipid, lipoprotein, and antioxidant concentrations in patients with type IIa or IIb hyperlipoproteinaemia.

Subjects and methods

The trial consisted of a randomised six month parallel comparison of the efficacy of three dietary interventions. Patients were recruited from a group practice in Oxfordshire with nearly 11 600 patients. Men and women of European origin, aged 35-64 years, with a total cholesterol concentration on screening of 6·5-9·0 mmol/l, and a repeat fasting concentration of 6.0–8.5 mmol/l were eligible for inclusion in the trial. The exclusion criteria were total cholesterol:high density lipoprotein cholesterol ratio $<4{\cdot}0$; low density lipoprotein cholesterol concentration $<3{\cdot}5$ mmol/l; fasting triglyceride concentration $\geq 5{\cdot}6$ mmol/l; diagnosed diabetes, hypothyroidism, or renal disease; current treatment with a lipid lowering drug; admission to hospital with a severe illness within the previous three months; pregnancy or breast feeding.

The primary end point for the trial was the total cholesterol concentration measured at six months, and the secondary end points were concentrations of low density and high density lipoprotein cholesterol and antioxidants and body mass index (kg/m^2). The trial was designed to have a 90% statistical power to detect a difference of $\geq 0{\cdot}3$ mmol/l between the groups in mean total cholesterol concentration at the end of the trial with a 5% level of significance.

Patients of eligible age were identified either opportunistically or from the practice's age-sex register and were invited to attend a cardiovascular screening clinic. Screening was undertaken by five practice nurses using the existing practice protocol, which included standardised measurement of height and weight and a record of cigarette smoking. A non-fasting venous blood specimen was taken, and patients with a total cholesterol concentration of 6·5-9·0 mmol/l

were informed of the result and asked to reattend after an overnight fast. A fasting venous blood sample was then obtained for measurement of total cholesterol, high density lipoprotein cholesterol, triglyceride, and antioxidant concentrations. Patients with a fasting total cholesterol concentration of 6·0-8·5 mmol/l who met the entry criteria were informed of the result and were invited to participate. The purpose of the trial was explained, and informed consent was obtained. The study protocol had been approved by the central Oxford research ethics committee.

The study coordinator randomised the eligible patients to one of the three interventions before they next attended. Randomisation was done by using a list of consecutive random treatment assignments. Patients living at the same address were randomised to the same intervention group to avoid contamination. The results of lipid and lipoprotein measurements were not entered in the clinical case notes until the end of the trial to avoid the possible confounding effect of dietary advice offered opportunistically, and similarly no advice on smoking, exercise, or alcohol consumption was given until the end of the trial to ensure that the outcome was unconfounded by lifestyle changes.

DIETARY INTERVENTION

Patients randomised to receive advice from the study dietitian attended a 30 minute appointment at the practice; a standard diet history was taken and patients were given individual advice based on their dietary habits and weight. They were advised to reduce the percentage of total dietary energy contributed from fat to 30% or less and to consume up to 10% of energy each from saturated, monounsaturated, and polyunsaturated fatty acids. The recommended percentage of energy derived from carbohydrates was 50-60% and that from protein 10-20%. A daily intake of less than 300 mg of cholesterol and about 35 g of fibre was recommended.[2]

Patients randomised to receive advice from the practice nurses attended a 30 minute individual appointment and were advised to make changes in food intake to reduce the amount of total and saturated fat and to increase the amount of dietary fibre and complex carbohydrate in their usual diet. Habitual diet was estimated by using a prescored food frequency questionnaire of 19 groups of foods which account for about 70% of the fat and fibre in the typical British diet.[10] The questionnaire combined groups of foods with similar nutrient content and dietary use and assigned each group a score proportional to the fat or fibre content of a standard portion size. The scores were weighted by the frequency of consumption. The total score and the pattern of individual food scores were used by the nurse to suggest specific changes in food choices. The nurses had a day's training in using these methods before the trial started. Standard current clinical practice was used by the dietitian and nurses in trying to facilitate behavioural changes.

The group receiving written advice only were posted a leaflet containing dietary guidance that was consistent with the advice provided by the study dietitian. The content and format of the dietary leaflet have been published.[11]

Subjects in the dietitian and nurse intervention groups were reviewed eight weeks after their initial visit. During a 10 minute appointment further advice was given, and a non-fasting venous blood sample was taken to measure total cholesterol concentration. The leaflet intervention group received additional written advice by post after two months. At the end of the six month trial, subjects were weighed and a fasting venous blood sample was taken for measurement of total cholesterol, high density lipoprotein cholesterol, triglyceride, and antioxidant concentrations. They were given a brief questionnaire for self completion which asked what dietary changes they had made.

BIOCHEMICAL ANALYSES

Venous blood specimens (10 ml) were collected in plain tubes and were transported daily to the laboratory in ice and centrifuged immediately on arrival. Serum was removed and stored at −50° C in airtight tubes until analysis of lipids. In fasting subjects additional 0·5 ml aliquots of serum for analysis of retinol and antioxidants were stored at −50° C for two to three weeks and then transferred to −75° C storage until analysis. The laboratory was unaware of which intervention group the subjects were allocated to.

All serum lipids were measured on a Cobas Fara centrifugal analyser (Roche Diagnostic Systems, Welwyn Garden City). Samples were analysed once a week, usually during the week of collection. Cholesterol concentration was measured with the Monotest cholesterol reagent (Boehringer Mannheim, Lewes) and triglyceride with Peridochrom reagent (Boehringer Mannheim). High density lipoprotein cholesterol concentration was measured by precipitation of the non-high density lipoprotein fraction with phosphotungstic acid. The between batch coefficient of variation of internal and external quality control material over the range of results found in the study was $<2\%$ for cholesterol, $<3\%$ for triglycerides, and $<6\%$ for high density lipoprotein cholesterol. Serum low density lipoprotein cholesterol concentrations were calculated by using the Friedewald equation.[12]

Retinol and antioxidants samples taken before and after dietary intervention were analysed in the same batch at the end of the study concurrently with six month lipid and lipoprotein samples. Serum concentrations of retinol, α tocopherol, lutein, cryptoxanthin, lycopene, α and β carotene were measured in duplicate by high performance liquid chromatography.[13] The concentration of total carotenoid was calculated by integrating all the peaks absorbing at 450 nm and using the response factor for β carotene. The overall within batch coefficient of variation for antioxidant measurements was 6·7% and ranged from 1·7% to 9·7%, except for α carotene (15·6%).

STATISTICAL ANALYSES

The results were analysed by using the statistical package SPSS/PC+.[14] Data were analysed on the basis of intention to treat, and a secondary exposure analysis was also done. For patients who were randomised but did not proceed to the allocated intervention or were lost to follow up, the baseline prerandomisation results were used in the outcome analyses. The triglyceride measurements were log transformed before analysis because the data were positively skewed. Results for α tocopherol were also expressed as tocopherol:total cholesterol ratio (μmol/mmol) because there was a significant positive correlation ($r=0{\cdot}21$, $P<0{\cdot}001$). For continuously distributed variables statistical comparisons between the three groups at the end of the trial were made by analysis of variance, and the same procedure was used to adjust for the effects of any initial imbalance between the groups. Analysis of variance was also used to examine differences between groups in the mean individual changes in outcome measures from randomisation to the end of the trial. Comparisons within groups were made by paired t tests. A χ^2 statistic was used to test for differences between categorical variables. We calculated 95% confidence intervals when appropriate.

To reduce the effect of regression to the mean, eligibility for inclusion in the trial was determined on the basis of a second cholesterol measurement with the upper and lower inclusion criteria set 0·5 mmol/l lower than the initial screening selection criteria. To

TABLE I—*Baseline characteristics of 309 subjects randomly allocated to dietary intervention*

	Dietitian advice (n=103)	Nurse advice (n=104)	Leaflet advice (n=102)	Total (n=309)	P value
Male: female	56:47	54:50	53:49	163:146	NS
Median (interquartile range) age (years)	55·0 (49·1-60·5)	55·6 (46·6-60·0)	55·3 (48·5-59·4)	55·4 (48·7-59·9)	NS
Mean (SD) body weight (kg)	76·4 (12·7)	74·8 (11·7)	75·9 (13·6)	75·7 (12·7)	NS
No (%) of cigarette smokers	14 (14)	20 (19)	33 (32)	67 (22)	P=0·0037
Mean (SD) screening total cholesterol (mmol/l)	7·19 (0·58)	7·29 (0·62)	7·35 (0·55)	7·28 (0·59)	NS
No (%) receiving no advice or lost to follow up	8 (8)	16 (15)	6 (6)	30 (10)	NS

TABLE II—*Mean (SD) fasting plasma lipid and lipoprotein concentrations and body mass index at start and end of six month trial*

	Dietitian advice (n=103)		Nurse advice (n=104)		Leaflet (n=102)	
	Start	6 months	Start	6 months	Start	6 months
Concentration (mmol/l)						
Total cholesterol	7·01 (0·61)	6·91 (0·73)	7·15 (0·65)	6·97 (0·74)**	7·23 (0·63)	7·10 (0·63)
Low density lipoprotein cholesterol	5·11 (0·60)	5·00 (0·70)	5·17 (0·67)	4·99 (0·69)**	5·25 (0·65)	5·06 (0·62)**
High density lipoprotein cholesterol	1·18 (0·26)	1·17 (0·26)	1·23 (0·27)	1·28 (0·30)**	1·23 (0·28)	1·25 (0·30)
Triglycerides†	1·48 (0·94-2·31)	1·53 (0·99-2·37)	1·56 (1·01-2·41)	1·46 (0·98-2·19)*	1·54 (0·99-2·41)	1·57 (1·01-2·46)
Body mass index	26·64 (4·06)	26·40 (4·00)**	26·31 (3·93)	26·24 (4·22)	26·32 (4·32)	26·08 (4·29)

*P<0·05, **P<0·01, ***P<0·001 compared with initial value. †Geometric mean (range).

TABLE III—*Pooled mean (SD) plasma concentrations of lipids and lipoproteins (mmol/l) at start and end of six month trial and change from baseline concentration*

	Start	6 Months	Change (95% confidence interval)
Total cholesterol	7·13 (0·64)	7·00 (0·71)***	−0·13 (−0·22 to −0·06)
Low density lipoprotein cholesterol	5·17 (0·64)	5·02 (0·67)***	−0·16 (−0·22 to −0·08)
High density lipoprotein cholesterol	1·21 (0·27)	1·24 (0·29)*	0·03 (0·01 to 0·05)
Triglycerides†	1·53 (0·98-2·37)	1·52 (0·99-2·34)	−0·01 (−0·03 to 0·02)

*P<0·05, **P<0·01, ***P<0·001 compared with initial value. †Geometric mean (range).

distinguish between a treatment effect and any remaining effect of regression to the mean a Monte Carlo simulation [15] was undertaken to estimate the expected mean total cholesterol at the end of the trial for the whole study population and also for each tertile of the prerandomisation cholesterol concentrations. The simulation assumed a screened population with a mean total cholesterol concentration of 5·9 (SD 1·1) mmol/l. The variance was split into two components: that due to the "true" underlying distribution (SD 1·0) and that due to within person variation (SD 0·45). The simulation model then generated observations from the underlying distribution with a random element added for each observation until 309 individual sets of observations that fulfilled the screening criteria had been generated.

Results

Screening began in February 1992 and continued until April 1993. A total of 4374 patients aged 35 to 64 years were registered with the practice, and 2004 of these patients were screened (988 men). The mean serum cholesterol concentration in these patients was 5·92 (SD 1·14) mmol/l. Five hundred and fifty two patients were screened opportunistically, and systematic invitations were sent to a further 3658 patients. A single reminder was sent to patients who did not reply, and 1452 patients responded. Non-fasting cholesterol concentrations of 6·5-9·0 mmol/l were found in 520 patients, and a fasting lipid profile was obtained from 472 patients, of whom 329 were eligible for inclusion in the trial; 309 subsequently consented to be randomly allocated to intervention.

Of the randomised patients, 42 (14%) were aged 35 to 44 years, 106 (34%) were 45 to 54 years, and 161 (52%) were 55 to 64 years. Table I shows the characteristics at randomisation. Forty two per cent (127/303) of patients were overweight with a body mass index of 25 to 29 and 17% (53/303) were obese with a body mass index ⩾30 (results were missing for six patients). Overall 22% of patients (67/309) were cigarette smokers, but the percentage was significantly higher in the leaflet group than in the other two intervention groups. Twenty randomised patients did not proceed to the allocated intervention; none was withdrawn during the course of the study, but 10 were lost to follow up.

Table II shows the mean fasting plasma lipid and lipoprotein concentrations and body mass index in the three groups at the beginning and end of the trial. The mean total cholesterol concentration was significantly higher at randomisation in the leaflet advice group compared with the dietitian advice group (7·23 *v* 7·01 mmol/l, difference 0·22, 95% confidence interval 0·05 to 0·40), but the mean low density lipoprotein cholesterol concentrations were not significantly different and there were no other significant differences between the intervention groups at randomisation. Measurements of total cholesterol concentration were available at two months for 76 patients reviewed in the dietitian advice group and for 70 patients reviewed in the nurse advice group, and there was no significant difference in concentration between them (6·89 (SD 0·78) mmol/l *v* 6·94 (0·76)).

There were no significant differences at the end of the trial between intervention groups in the mean lipid and lipoprotein concentrations or body mass index, nor were there significant differences between groups in the mean individual changes from baseline to the end of the trial. No significant differences were found in responses of men and women. Table II shows that within intervention groups there were small but significant reductions in the body mass index in the dietitian advice group; in total cholesterol, low density lipoprotein cholesterol, and triglyceride concentrations in the nurse advice group; and in low density lipoprotein cholesterol concentration in the leaflet group. High density lipoprotein cholesterol concentration increased significantly only in the nurse advice group. The results were essentially unchanged when analysed on an exposure basis after patients not completing the trial were excluded (data not shown).

Two hundred and forty patients (78%) completed the questionnaire after the study, and 192 (80%) stated that they had made one or more specific food substitution or changes in intake (mean number of changes 3·8 (SD 2·0)).

Table III shows the mean difference in lipid and lipoprotein concentrations between randomisation and the end of the trial after pooling the data from the three

TABLE IV—*Mean (SD) differences and correlation between plasma antioxidant concentrations at start and end of trial*

	No of patients	Start	6 months	Correlation	Difference (95% confidence interval)	P value
α Carotene (nmol/l)	300	88 (53)	88 (47)	0·76	−0 (−4·1 to 3·8)	NS
β Carotene (nmol/l)	305	386 (248)	375 (230)	0·89	−11 (−24 to 1·1)	NS
Cryptoxanthin (nmol/l)	305	209 (185)	218 (194)	0·65	9 (−8·9 to 27)	NS
Lycopene (nmol)	304	559 (286)	581 (289)	0·78	22 (0·7 to 43·7)	0·044
Lutein (nmol/l)	305	363 (147)	376 (150)	0·80	13 (2·8 to 24·1)	0·014
Total carotenoids (nmol/l)	304	2453 (886)	2506 (877)	0·87	53 (3·0 to 103)	0·039
α Tocopherol (μmol/l)	305	38·86 (8·29)	38·72 (9·03)	0·79	−0·14 (−0·77 to 0·50)	NS

groups. There was a small but significant decrease of 0·13 mmol/l (1·9%) in total cholesterol concentration with a corresponding decrease in low density lipoprotein cholesterol; the response did not differ between men and women (−0·13 *v* −0·15 mmol/l) or with age. The results of the simulation model suggest that regression to the mean might account for 0·04 mmol/l of this decrease. A subgroup analysis showed a mean change of 0·18 mmol/l in patients in the lowest tertile of cholesterol concentration before randomisation (6·00-6·78 mmol/l), of −0·06 mmol/l in those in the middle tertile (6·78 to 7·40 mmol/l), and of −0·53 mmol/l in those in the top tertile (7·40-8·50 mmol/l). The simulation model suggests that changes of 0·12, −0·09, and −0·28 mmol/l respectively might be accounted for by regression to the mean.

Antioxidant and retinol measurements were available for 305 of the 309 patients (table IV). The baseline and six month concentrations for each antioxidant were significantly and highly correlated. The trial was not designed to have the power to detect significant differences between groups in any of the antioxidant concentrations at the end of the trial, and on an intention to treat analysis there were no such differences. The results for the three groups were therefore pooled. Retinol concentrations did not change (2197 (SD 445) nmol/l *v* 2178 (460) at end of trial, NS) but concentrations of most carotenoids increased. Although there was no significant change in the concentration of α tocopherol, the α tocopherol: cholesterol ratio increased significantly 5·46 (1·05) μmol/mmol to 5·54 (difference 0·08, 95% confidence interval 0·003 to 0·16, P=0·042).

Discussion

Current clinical guidelines recommend a lipid lowering diet as the initial treatment for raised total and low density lipoprotein cholesterol concentration, [1 2] although the efficacy of restricting total fat to less than 30% of total energy intake in lowering cholesterol concentrations is disputed[4] and few studies have evaluated the efficacy of lipid lowering dietary advice in general practice. Our trial was restricted to patients with type IIa or IIb hyperlipoproteinaemia with moderately raised cholesterol concentrations of 6·0-8·5 mmol/l. These are the patients who in clinical practice would be most likely to receive dietary advice. Eligibility for inclusion in the trial was determined on the basis of a repeat fasting total cholesterol concentration to reduce the effect of regression to the mean.

The intervention consisted of only dietary advice to ensure that the outcome of the study was unconfounded by other potential effects that may occur with multifactorial interventions in cardiovascular trials. After six months the pooled data from the three intervention groups showed a small but significant reduction in mean total cholesterol concentration from 7·13 to 7·00 mmol/l, a corresponding decrease in low density lipoprotein cholesterol, a small increase in high density lipoprotein cholesterol, and no change in triglyceride concentrations. The outcome is unlikely to have been affected by the known seasonal variation in cholesterol concentration[16] since patients were recruited over 14 months.

Our results are consistent with two recently published trials [17 18] that evaluated the impact of nurse led cardiovascular screening and multifactorial intervention programmes in general practice. We showed no difference in efficacy between dietary advice from a nurse, a dietitian, or a leaflet, but some caution is needed in generalising from the findings for the dietitian group since advice was given by one dietitian. Nevertheless, the results are consistent with those of a recent review of controlled trials of diet lasting at least six months[4]: among five trials of a fat reduced diet, two used dietitians or nutritionists to give advice [19 20], and the net reduction in serum cholesterol ranged from 0% to 4%[4].

EFFECTIVENESS OF DIETARY MODIFICATION

Despite the poor response among our subjects studies in metabolic ward conditions, where dietary compliance can be ensured, have repeatedly shown that dietary change can substantially reduce total and low density lipoprotein cholesterol concentrations.[21 22] In subjects living in the community diets that are more rigorous than that we used have also been shown to reduce cholesterol concentrations by 6·5-15·1%.[4]

A better response to a lipid lowering diet might be achieved with more intensive intervention, better motivation, or improved compliance. The evidence so far, however, is not encouraging; random allocation to a lipid lowering diet in a trial of secondary prevention of myocardial infarction in 2033 men, who might be expected to be highly motivated, resulted in only a 3-4% reduction in total cholesterol concentration.[19] Asymptomatic apparently fit hypercholesterolaemic patients identified by screening, as in our study, would not be expected to be highly motivated. Taking account of habitual diet and current nutrient intake might be predicted to improve the response observed, but our results did not confirm this. Other programmes have been developed that specifically attempt to integrate behavioural and psychological factors into eating patterns by using computers to individually tailor messages.[23] Although this approach has been reported to produce a significantly greater reduction in total and saturated fat scores,[23] the effect on lipids and lipoproteins has not been documented.

A lipid lowering diet may be more effective in patients with a very high intake of dietary fat because the scope for behavioural modification is greater. Total fat intake was not measured in our study, but the mean serum cholesterol concentration of 5·9 mmol/l in our population was similar to that found by national surveys of British adults.[9 24] The total fat intake was likely therefore to be similar, accounting for about 38% of total energy.[24] This might partly explain why we failed to achieve a clinically significant reduction in cholesterol concentration.

Other data indicate that people with raised cholesterol concentrations are more responsive to dietary changes than those with low concentrations.[25 26] Although our findings suggest that there may be a somewhat better response among patients with a higher initial cholesterol concentration, caution is

Key messages

- Giving dietary advice to reduce lipid concentrations is recommended treatment for moderate hypercholesterolaemia
- In this study dietary advice had only a modest effect on lipid and lipoprotein concentrations
- Personalised advice from a nurse or dietitian was no more effective than a detailed diet leaflet
- Antioxidant concentrations increased slightly, but this requires further study
- A mass approach to dietary change is needed to produce significant change

needed in interpreting the results of this subgroup analysis. After regression to the mean was allowed for, the mean reduction in total cholesterol concentration among patients in the top tertile of the cholesterol distribution before randomisation (>7·4 mmol/l) was only 0·25 mmol/l. Nevertheless, small reductions in total and low density lipoprotein cholesterol concentrations associated with a decrease in saturated fatty acid intake may be clinically useful, particularly if accompanied by other nutritional changes, such as an increased intake of antioxidants, monounsaturated fatty acids, and a modest increase in ω-3 and ω-6 polyunsaturated fatty acids.[27]

Higher dietary intakes of the natural antioxidants, especially vitamins E and C and carotenoids, may reduce the risk of atherosclerosis by decreasing the susceptibility of low density lipoprotein cholesterol to oxidative modification.[5] The clinical importance of the small increase in carotenoids that we observed is uncertain, and evidence from experimental studies that antioxidants can prevent coronary heart disease is lacking. It is not yet clear whether simple dietary advice can increase antioxidant concentrations sufficiently to reduce the susceptibility of low density lipoprotein cholesterol to oxidative modification.

CONCLUSIONS

In summary, we found no difference in the relative efficacy of lipid lowering dietary advice given by a dietitian, a practice nurse, or a diet leaflet alone. The cost effectiveness of these interventions will therefore differ substantially. Overall, after allowing for regression to the mean, there was about a 1·5% reduction in the concentration of total cholesterol in asymptomatic moderately hypercholesterolaemic patients identified by a screening programme in general practice. This would be expected to reduce coronary heart disease mortality by 3-4%.[28] To obtain a better response it is probably necessary to use more intensive intervention than is normally available in primary care. Cholesterol testing should therefore be targeted at patients at highest overall risk of coronary heart disease in whom treatment with lipid lowering drugs may be warranted if there is an inadequate response to dietary advice.[3] To substantially reduce the mean serum cholesterol concentration of the population as a whole a national nutritional programme is needed.[29]

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ONE HUNDRED YEARS AGO

THE BLOOD SERUM OF THE HORSE AS A REMEDY FOR TUBERCULOSIS.

Dr Paul Paquin, Professor of Bacteriology in the State University of Columbia, and member of the State Board of Health of Missouri, has, as we learn from the New York *Medical Record*, been experimenting for some time with the blood serum of the horse in the treatment of tuberculosis. Having convinced himself that the horse is naturally immune against tuberculosis, he has for some months been using the blood serum of selected horses, carefully injecting the serum under the skin of patients suffering from tuberculosis. Dr. Paquin maintains that the horse being naturally immune against the disease, the blood can be used direct without any artificial immunisation. The serum is said to have been used in about fifty cases with almost uniformly satisfactory results. (*BMJ* 1895;i:660.)