Journal of Epidemiology and Community Health 1994;48:22-25

# Randomised controlled trial in northern England of the effect of a person knowing their own serum cholesterol concentration

P J Elton, A Ryman, M Hammer, F Page


## Abstract

***Subject objective*** **– To test the hypotheses that the knowledge that the serum cholesterol concentration *is* raised (⩾6·5 mmol/l) will lead to a *reduction* in the concentration after education intervention and that the knowledge that the concentration *is not* raised does not lead to an *increase* in the serum cholesterol concentration after education intervention.**

***Design*** **– Prospective randomised trial, with investigators blind to the randomisation.**

***Setting*** **– An industrial site in Manchester, England.**

***Participants*** **– A total of 495 employees of Imperial Chemical Industries, 469 of whom completed the trial.**

***Main result*** **– There was a significant reduction in the serum cholesterol concentration of those whose initial concentration was ⩾6·5 mmol/l and who were given the result. This reduction was 0·28 mmol/l greater than in the control group. The reduction was similar, however, to the increase in the serum cholesterol concentration in those whose initial concentration was <5·2 mmol/l, regardless of whether or not they had been given the result.**

***Conclusion*** **– These results support the hypotheses, although the lack of regression to the mean in the control group with high serum cholesterol suggests that this conclusion should be treated with caution.**


(*J Epidemiol Community Health* 1994;48:22-25)

**Tameside and Glossop Health Authority, Hyde, Cheshire**
P J Elton

**Lothian Health Board, Royal Edinburgh Hospital, Edinburgh**
A Ryman

**North Manchester General Hospital, Manchester**
M Hammer

**Zeneca Specialties, Blackley**
F Page

Correspondence to:
Dr P Elton, Tameside and Glossop Health Authority, Greenfield Street, Hyde, Cheshire.

Accepted for publication July 1993

There is a consistent association between the serum cholesterol concentration and coronary heart disease, and there is consensus that this relationship is causal.[1-4] Strong evidence exists that both morbidity and mortality from coronary heart disease are reduced by lowering the serum cholesterol, although the effect on total mortality is less clear.[3-10] There is also doubt about the advantages of using cholesterol reducing drugs rather than diet.[11,12] The possibility that drugs increase mortality from non-cardiac causes is particularly worrying.[13] The disadvantage of diet is that it may be relatively ineffective.[14]

Two strategies that are not necessarily incompatible have been advocated. A reduction across the spectrum of serum cholesterol concentrations in the population has consensus support.[15-16] A small shift across the entire population can have a greater effect on morbidity and mortality than a large shift in selected individuals. Not everyone, however, will respond to a population approach. It has been suggested that if people knew that their serum cholesterol concentration was high they would be more likely to change their behaviour.[17] This not only remains unproved,[18,19] it is supported by a quasi-experimental study only,[20] and may also lead those with lower cholesterol concentrations to leave their diet unchanged, thereby adversely affecting a population approach.[21]

This trial was designed to address these issues, to indicate whether serum cholesterol screening affected peoples' responses to education designed to encourage a change in diet. In particular, the following hypotheses were tested:

(1) The knowledge that the serum cholesterol concentration is raised (⩾6·5 mmol/l) will lead to a reduction in the concentration after educational intervention.

(2) The knowledge that the serum cholesterol concentration is not raised will not lead to an increase in concentrations after educational intervention.

## Methods

The trial took place between August 1991 and June 1992. Subjects were drawn from the Imperial Chemicals Industry site at Blackley, Manchester, with the following exclusions:

(1) Aged under 20 or over 65 years;

(2) Previous knowledge of their own serum cholesterol concentration.

Subjects were given sealed envelopes which randomly allocated them to an intervention group, who were told their serum cholesterol level, or a control group who were not.

Both groups were scheduled to have two serum cholesterol concentration measurements with a week's interval in between, and an average was taken as it is recognised that there can be substantial fluctuations in intra-subject serum cholesterol measurements.[22] Total cholesterol was measured on a Monarch 2000 centrifugal analyser using Biostat CHOD/PAP cholesterol reagent, catalogue no 510019 (as used on the routine departmental Technicon SMAC multichannel analyser), and calibrated using the same SMAC Set Point 2 calibrator for consistent results. Normal quality control procedures were followed and full participation in external quality assur-

ance schemes was maintained throughout the study. All subjects were asked questions about their social demographic characteristics and their perception of other risk factors.

All subjects were invited to a health education session, introduced by a doctor (AR) and then run by a dietitian, within two weeks of the second serum measurement. The session, which lasted about an hour, advocated a diet equivalent to the step 1 diet.[14] All subjects were handed the sealed envelope a quarter of an hour before the start of the formal session. Subjects were asked not to discuss the contents of the letter. In the intervention group, the envelope contained one of three different letters according to whether their cholesterol concentration was $\geqslant 6{\cdot}5$ mmol/l, 5·2–6·45 mmol/l, or $<5{\cdot}2$ mmol/l. While the three letters stated whether the result was "high", "not particularly high", or "below average", all three indicated that the advice in the health education session should be followed either to reduce or maintain the serum cholesterol concentration. The description of the result meant that motivation was most clearly intended for those with a cholesterol concentration $\geqslant 6{\cdot}5$ mmol/l in line with the hypotheses. For the control group there was only one letter informing the subject that they were in the control group but, that as it is worthwhile for everybody to reduce their blood cholesterol concentration, the health education would be relevant to them too. The doctor (AR) and the dietitian remained blind to the allocation.

Thirteen weeks after the initial serum measurements, two further serum cholesterol concentration determinations with a week's interval were scheduled. Analysis of serum cholesterol concentrations was based on the two means before and after the intervention. If the difference between the two measurements at either stage was more than 1·0 mmol/l, a third sample was taken and the two measurements closest to each other were used to calculate an average.

The calculation of sample size required[23] depends on using values from studies with a different design. In these studies, serum cholesterol was reduced as a result of dietary intervention in which all subjects with a high serum cholesterol knew this to be the case. These indicated a reduction in serum cholesterol of about 10%.[24] This would produce a reduction in the serum cholesterol concentration of about 0·7 mmol/l. For an SD of this reduction of 0·9 mmol/l[25] to achieve a power of 90% at a significance level (one tailed) of 5%, 26 subjects with an initial serum cholesterol $\geqslant 6{\cdot}5$ mmol/l would be required in each group. The proportion of people in this country with a serum cholesterol $\geqslant 6{\cdot}5$ mmol/l has been reported to be 26%.[26] Since this was based on one measurement, however, it is likely to be a higher proportion than results based on two measurements. If 20% of subjects were to have a serum cholesterol of $\geqslant 6{\cdot}5$ mmol/l, then a total of 260 subjects would be required to complete the trial.

The absolute values of the serum cholesterol concentration within each result band would not be expected to follow a normal distribution, whereas the differences in the measurements between the two stages would be expected to approximate more closely to such a distribution. Because of this, the Student's *t* test was performed on the differences between the serum cholesterol concentrations at the two stages rather than on the absolute values.

## Results

A total of 239 people in the intervention group had their initial serum cholesterol concentration measured but 10 (4%) failed to complete the trial, including one with an initial serum cholesterol concentration $>6{\cdot}5$ mmol/l. The control group comprised 256 subjects who had their initial serum cholesterol measured, but 16 (6%) failed to complete the trial, including three with an initial serum cholesterol concentration $>6{\cdot}5$ mmol/l.

Except for gender, the social and other characteristics of the two groups at entry were similar (table 1). The higher proportion of men with low serum cholesterol concentrations in the intervention group compared with the control group does just reach the conventional level of significance ($p<0{\cdot}05$), but this is one of 18 comparisons of characteristics that were made. The lower proportion of subjects with a cholesterol concentration of 5·2–6·45 mmol/l in the intervention group was not statistically significant.

The mean initial and final concentrations and the change in cholesterol values in the two groups are shown in table 2.

## Discussion

The a priori hypotheses that knowledge that the serum cholesterol concentration is *raised* will lead to a *reduction* after educational intervention and that knowledge that the concentration is *not raised* will not lead to an *increase* after educational intervention seem to be

*Table 1 Social characteristics of the two groups*

| | *Serum cholesterol (mmol/l)* | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | *Intervention* | | | | *Control* | | | |
| | *<5·2* | *5·2–6·45* | *≥6·5* | *Total* | *<5·2* | *5·2–6·45* | *≥6·5* | *Total* |
| No | 77 | 94 | 58 | 229 | 75 | 112 | 53 | 240 |
| Mean age (y) | 34·4 | 38·0 | 43·6 | 38·2 | 31·6 | 39·3 | 44·0 | 37·9 |
| Male (%) | 52 | 63 | 66 | 60 | 36 | 60 | 75 | 56 |
| Social class I or II (%) | 77 | 80 | 84 | 80 | 85 | 76 | 72 | 78 |
| Present smokers (%) | 8 | 16 | 35 | 18 | 12 | 14 | 34 | 18 |
| Subjects classifying themselves as overweight (%) | 32 | 27 | 45 | 33 | 25 | 34 | 49 | 35 |
| 1st degree relative died of heart attack before age of 60 y (%) | 5 | 4 | 5 | 5 | 3 | 6 | 8 | 5 |

*Table 2 Serum cholesterol measurements (mmol/l)*

| | < 5·2 mmol/l | 5·2–6·45 mmol/l | ⩾6·5 mmol/l |
|---|---|---|---|
| Intervention initial serum cholesterol | 4·62 | 5·74 | 7·13 |
| Control initial serum cholesterol | 4·59 | 5·83 | 7·12 |
| Intervention final serum cholesterol | 4·84 | 5·81 | 6·84 |
| Control final serum cholesterol | 4·85 | 5·81 | 7·12 |
| Intervention mean change | +0·22 | +0·07 | −0·29* |
| (95% CI) | (0·13, +0·31) | (−0·02, +0·17) | (−0·48, −0·11) |
| Control mean change | +0·26 | −0·02 | −0·01* |
| (95% CI) | (0·13, +0·38) | (−0·15, +0·11) | (−0·16, +0·15) |
| p (for mean change) | 0·67 | 0·26 | 0·024 |

* The difference between these two values reaches the conventional level of significance given in the last line of the table.

statistically confirmed. However, the results do throw some doubts on this conclusion. Regression towards the mean in the subjects with high and low serum cholesterol concentrations is to be expected. In those with a high concentration who were told their results, the regression towards the mean is similar to that in those with a low concentration. The aberrant result seems to be in those in the control group with high cholesterol values. It should also be noted that there were overall mean increases of 0·03 mmol/l and 0·07 mmol/l in the intervention group and the control group respectively.

These results may be due to chance, although an alternative explanation is available. In a quasi-experimental study from Australia,[20] public screening participants who were self selected were told their serum cholesterol concentration and asked to speak to a cholesterol advisor. They were compared with blood donors, who unknowingly had their serum cholesterol measured. In those with a value > 5·5 mmol/l who returned after three months, there was a significant mean fall of 0·19 mmol/l in the public screening participants compared with a significant mean increase of 0·26 mmol/l in the blood donors. It was suggested that the increase in the blood donors was due to Christmas intervening between the measurements of serum cholesterol. In the present study, Christmas intervened between the initial and final serum cholesterol measurements for 87% of the subjects. There has also been a reported trend towards higher blood cholesterol in the cooler months in the USA.[27] The reported increase was about 0·03 mmol/l per month between the end of June and the end of December, with a similar increase each month for the following six months.

The only other study that has undertaken a randomised trial of the motivational effect of cholesterol measurement was reported recently from Aylesbury.[19] Although the Aylesbury study gave no evidence of a motivational effect of cholesterol measurements, the results of the two studies are consistent as the confidence limits of the mean changes in all six categories of subjects overlap between the two studies. There were differences between the two studies in both context and study design, which may explain the contrasting results, but these may also be due to chance.

The 4% reduction in serum cholesterol in the intervention group compared with the control group in those with an initial value ⩾6·5 mmol/l was less than anticipated in the power calculation. This was in line with the changes in serum cholesterol values in controlled trials of step 1 or an equivalent diet that were summarised after this study had begun.[14] The power of the trial was increased by the use of two measurements of serum cholesterol to give the initial and final values. This would be expected to increase the reliability of the results and thereby reduce the SDs. The SDs for the mean changes in the intervention and control groups in this study were 0·58 and 0·72 mmol/l respectively. It may be that the power of any future trial with the same number of subjects could be increased by using measurements excluding high density lipoprotein cholesterol, which have an inverse relationship with coronary heart disease[27,28] and do not decline with a conventional lipid-lowering diet.[29] The measurement of low density lipoprotein cholesterol does change the identification of some individuals as having a raised value.[25]

An issue that needs to be considered is whether three months is too short a period to consider. It was not thought practical or ethical to use a longer period, even though it might have been desirable. There is evidence that changes found at five months are similar to those found at one year,[31] indicating that it is worthwhile looking at a short period to ascertain change.

These results do indicate that there might be benefit in a further trial on this matter, despite the previous negative result from the Aylesbury study.[19] Any further trial should consider the nature of the educational content, as effectiveness may depend upon whether this concentrates on dietary advice, as in this study, or is part of a package of health education advice, as in the Aylesbury study. It may be that a much larger trial, based on a factorial design, could elucidate any contribution of either, or both, health education and risk labelling.

The dietitian who ran the educational sessions was E Trier and the administrative work for the study was undertaken by E Lloyd. This study was facilitated by staff at ICI, in particular G Turner, M Davis, S Healey, A Holmes, and S Hadfield. The statistical analysis was undertaken by B Harbin.

1 Kannel WB, Castelli WP, Gordon T, McNamara PM. Serum cholesterol, lipoproteins and risk of coronary heart disease, the Framingham study. *Ann Intern Med* 1971;**74**:1–12.
2 Lipid Research Clinics Program. The Lipid Research Clinics Program coronary primary prevention trial results. I – Reduction in incidence of coronary heart disease. *JAMA* 1984;**251**:351–64.
3 Multiple Risk Factor Intervention Trial Research Group. Multiple Risk Factor Intervention Trial: risk factor changes and mortality results. *JAMA* 1982;**248**:1465–77.
4 Martin MJ, Hulley SB, Browner WS, Kuller LH, Wentworth D. Serum cholesterol, blood pressure and mortality – implications from a cohort of 361 662 men. *Lancet* 1986;ii:933–6.
5 Lipid Research Clinics Program. The Lipid Research Clinics Program coronary primary prevention trial results. II – The relationship of reduction in incidence of coronary heart disease to cholesterol lowering. *JAMA* 1984; **251**:365–74.
6 Frick MH, Eloo O, Haapa K, *et al.* Helsinki heart study: primary prevention trial with gemfibrozil in middle aged men with dyslipidaemia. *N Engl J Med* 1987;**317**:1237–45.
7 National Heart Lung and Blood Institute and National Institute of Health Office of Medical Applications of Research. Consensus conference on lowering blood cholesterol to prevent heart disease. *JAMA* 1985;**253**:2080–6.
8 Muldoon MF, Manuck SB, Matthews KA. Lowering cholesterol concentration and mortality: a quantitative review of primary prevention trials. *BMJ* 1990;**301**:309–13.
9 Rose G, Shipley M. Effect of coronary risk reduction on the pattern of mortality. *Lancet* 1990;i:275–7.

10 Ravnskov U. Cholesterol lowering trials in coronary heart disease: frequency of citation and outcome. *BMJ* 1992; **305**:15–19.
11 Shepherd J, Betteridge DJ, Durrington P, *et al.* Strategies for reducing coronary heart disease and desirable limits for blood lipid concentrations: guidelines of the British Hyperlipidaemia Association. *BMJ* 1987;**295**:1245–6.
12 Smith GD, Pekkanen J. Should there be a moratorium on the use of cholesterol lowering drugs. *BMJ* 1992; **304**:431–4.
13 Oliver MF. Might treatment of hypercholesterolaemia increase non-cardiac mortality? *Lancet* 1991;**337**:1529–31.
14 Ramsay LE, Yeo WW, Jackson PR. Dietary reduction of serum cholesterol concentration – time to think again. *BMJ* 1991;**303**:953–7.
15 Leeder S, Gliksman M. Prospects for preventing coronary heart disease – population based approaches (editorial). *BMJ* 1990;**301**:1004–5.
16 King's Fund Forum. *Blood cholesterol measurement in the prevention of coronary heart disease, a consensus statement.* London: King's Fund, 1989. King's Fund consensus conference.
17 Standing Medical Advisory Committee. *Blood cholesterol testing: report to the Secretary of State for Health.* London: Department of Health, 1990.
18 Australasian Epidemiological Association policy statement on cholesterol testing. *J Public Health Med* 1992;**14**:344–5.
19 Robertson I, Phillips A, Mant D, *et al.* Motivational effect of cholesterol measurement in general practice health checks. *Br J Gen Pract* 1992;**42**:469–72.
20 Van Beurden E, James R, Dunn T, Tyler C. Risk assessment and dietary counselling for cholesterol reduction. *Health Education Research* 1990;**5**:445–50.
21 Kinlay S, Heller RF. Effectiveness and hazards of case finding for a high cholesterol concentration. *BMJ* 1990;**300**:1545–7.
22 Natelson BH, Tapp WN, Munsif A, Burns W. Fluctuating serum cholesterol: implications for coronary prevention. *Lancet* 1989;ii:404–5.
23 Armitage P, Berry G. *Statistical methods in medical research.* Oxford: Blackwell, 1987:181–2.
24 Kottke TE, Gatewood LC, Park H-A. Using serum cholesterol to identify high risk and stimulate behaviour change: will it work? *Ann Med* 1989;**21**:181–7.
25 Turpeinen O, Karvonen MJ, Pekkarinen M, Miettinen M, Elosuo R, Paavilainen E. Dietary prevention of coronary heart disease: the Finnish mental health study. *Int J Epidemiol* 1979;**8**:99–118.
26 Neil HAW, Mant D, Jones L, Morgan B, Mann JI. Lipid screening: is it enough to measure total cholesterol concentration. *BMJ* 1990;**301**:584–7.
27 Gordon DJ, Trost DC, Hyde J, *et al.* Seasonal cholesterol cycles: the Lipid Research Clinics coronary primary prevention trial placebo group. *Circulation* 1987;**76**:1224–31.
28 Gordon T, Kannel WB, Castelli WP, Dawber TR. Lipoproteins, cardiovascular disease, and death. The Framingham study. *Arch Intern Med* 1981;**141**:1123–31.
29 Pocock SJ, Shaper AG, Phillips AN. Concentrations of high density lipoprotein cholesterol, triglycerides, and total cholesterol in ischaemic heart disease. *BMJ* 1989;**298**:998–1002.
30 Hjermann I, Enger SC, Helgeland A, Holme I, Leren P, Trygg K. The effect of dietary changes on high density lipoprotein cholesterol: the Oslo study. *Am J Med* 1979;**66**:105–9.
31 Van Beurden E, James R, Tyler C, Henrikson D. Cholesterol reduction is sustainable: 12 month follow-up of a cholesterol campaign in rural Australia. *Health Education Journal* 1990;**49**:181–4.