# Cost effectiveness of incremental programmes for lowering serum cholesterol concentration: is individual intervention worth while?

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## Abstract

*Objective*—To evaluate the relative cost effectiveness of various cholesterol lowering programmes.

*Design*—Retrospective analysis.

*Setting*—Norwegian cholesterol lowering programme in Norwegian male population aged 40-49 (n=200 000), whose interventions comprise a population based promotion of healthier eating habits, dietary treatment (subjects with serum cholesterol concentration 6·0-7·9 mmol/l), and dietary and drug treatment combined (serum cholesterol concentration ≥8·0 mmol/l).

*Main outcome measure*—Marginal cost effectiveness ratios—that is, the ratio of net treatment costs (cost of treatment minus savings in treatment costs for coronary heart disease) to life years gained and to quality of life years (QALYs) saved.

*Results*—The cost per life year gained over 20 years of a population based strategy was projected to be £12. For an individual strategy based on dietary treatment the cost was about £12 400 per life year gained and £111 600 if drugs were added for 50% of the subjects with serum cholesterol concentrations ≥8·0 mmol/l.

*Conclusions*—The results underline the importance of marginal cost effectiveness analyses for incremental programmes of health care. The calculations of QALYs, though speculative, indicate that individual intervention should be implemented cautiously and within more selected groups than currently recommended. Drugs should be reserved for subjects with genetic hypercholesterolaemia or who are otherwise at very high risk of arteriosclerotic disease.

## Introduction

Coronary heart disease represents an important health problem in most industrialised countries. There is strong evidence that lowering serum cholesterol concentration will reduce the incidence of the disease.[1-4] Three strategies are available to do so: population based promotion of better eating habits, individual dietary treatment, and diet combined with various drugs. The individual approaches are based on the Norwegian cholesterol lowering programme,[5] which recommends cholesterol testing and subsequent follow up by family doctors or medical specialists and accords with the American national cholesterol education programme,[6] although it places less emphasis on analyses of high density liproprotein cholesterol and lipoprotein concentrations.

Though available analyses of cost effectiveness[7-13] indicate that lowering serum cholesterol concentration compares well with other generally accepted medical practices, they have presented average cost effectiveness ratios rather than incremental ones. In this study we calculate the marginal ratios of the three main strategies, discuss the quality of life aspects of these strategies, and demonstrate the relevance to policy of marginal analysis.

## Methods

After the method of Weinstein and Stason[14] we measured the cost effectiveness of a programme as the ratio of net treatment costs (cost of treatment minus savings in the cost of treating coronary heart disease to life years gained. As a model we used the Norwegian cholesterol lowering programme[5 6 15] applied to the Norwegian male population aged 40-49 years (n= 200 000). We assumed full participation in the programme and compliance with the prescribed treatment and a distribution of serum cholesterol concentration (table I) similar to that in the Tromsø heart study population (E Arnesen, personal communication; see table I).

### INTERVENTION

The population approach, entailing different forms of promoting healthy eating habits, is considered to be the first step in lowering serum cholesterol concentration. The Norwegian nutrition policy, which is explicitly directed at health aspects, is based on two

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TABLE I—*Fatal and non-fatal myocardial infarctions during first and subsequent 10 years of intervention in men aged 40-49 at start of intervention by serum cholesterol concentration*

| | | Unchanged incidence of infarctions | | Reduced incidence of infarctions | | | | | |
|---|---|---|---|---|---|---|---|---|---|
| | | | | Population strategy | | Dietary treatment | | Dietary and drug treatments | |
| Serum cholesterol | No of men | Non-fatal | Fatal | Non-fatal | Fatal | Non-fatal | Fatal | Non-fatal | Fatal |
| *First 10 years' intervention* | | | | | | | | | |
| ≤4·9 | 40 000 | | | | | | | | |
| 5·0-5·9 | 40 000 | 640 | 320 | 64 | 32 | 128 | 64 | 128 | 64 |
| 6·0-6·9 | 70 000 | 1 960 | 980 | 245 | 123 | 490 | 245 | 490 | 245 |
| 7·0-7·9 | 30 000 | 1 240 | 620 | 155 | 78 | 310 | 155 | 310 | 155 |
| ≥8·0 | 20 000 | 1 226 | 614 | 184 | 92 | 368 | 184 | 552 | 276 |
| Total | 200 000 | 5 066 | 2534 | 648 | 325 | 1296 | 648 | 1480 | 740 |
| *Subsequent 10 years' intervention* | | | | | | | | | |
| ≤4·9 | 40 000 | | | | | | | | |
| 5·0-5·9 | 40 000 | 1 920 | 960 | 192 | 96 | 384 | 192 | 384 | 192 |
| 6·0-6·9 | 70 000 | 5 880 | 2940 | 735 | 369 | 1470 | 735 | 1470 | 735 |
| 7·0-7·9 | 30 000 | 3 720 | 1860 | 465 | 234 | 930 | 465 | 930 | 465 |
| ≥8·0 | 20 000 | 3 678 | 1842 | 552 | 276 | 1104 | 552 | 1656 | 828 |
| Total | 200 000 | 15 198 | 7602 | 1944 | 975 | 3888 | 1944 | 4440 | 2220 |

government white papers. The Norwegian Nutrition Council has an important role as a broker of information among the scientific community, the agricultural sector, the food industry, and health authorities, as well as schools and the general public. The impact on eating habits may be enforced by a more targeted use of the mass media as well as through levying taxes on fatty foods or subsidising low fat foods.

The next step in lowering serum cholesterol concentration is screening for hypercholesterolaemia and following up subjects whose serum values exceed certain defined limits. The Norwegian programme defines any person with a serum cholesterol concentration >5·0 mmol/l as being at risk of premature death and recommends a confirmatory cholesterol test. If the average value of the two tests is 5·0-5·9 mmol/l a new test should be performed in five years. Above this concentration dietary treatment is recommended, with visits to the doctor and additional blood sampling at intervals depending on the actual value. We assumed 1·5 visits a year for subjects with a serum cholesterol concentration of 6·0-7·9 mmol/l and 2·0 visits a year above this value. Visits involving cholesterol testing would be somewhat more frequent in the first two years of the programme. This represents fewer visits and tests than the recommendations in the American programme,[6] and it does not include the more expensive lipoprotein analyses.

The possible third step is the use of drugs in combination with dietary treatment for subjects with the highest risk. We did not consider any specific drug but assumed that half of all subjects with an initial concentration ≥8·0 mmol/l would be prescribed a lipid lowering drug—that is, about 5% of the population, which is in line with experience in the United States.[16] The prescription of drugs would necessitate an extra visit by the doctor each year. To cover side effects we included additionally 0·3 extra visits and four blood tests a year.

CONSEQUENCES FOR HEALTH

We assumed that a systematic population programme leads to 5% lower cholesterol concentrations, but the evidence is sparse. The North Karelia project showed a 4% reduction[17] and Norwegian studies a 5% reduction.[18] We further assumed that individual counselling on diet in combination with the population strategy would accomplish a total reduction of cholesterol concentration by 10%.[12 19] Traditional cholesterol lowering agents reduce cholesterol concentration by 15-20% and the new statins somewhat more.[20] In this study we assumed an average reduction of 20% by diet and drugs combined.

A 2% reduction in the incidence of coronary heart disease is normally assumed when serum cholesterol concentration is reduced by 1%.[25] This may be too conservative. Consequently, we assumed that a 1% reduction in serum cholesterol reduces the risk of the disease by 2% at concentrations of 5·0-5·9 mmol/l, by 2·5% at 6·0-7·9 mmol/l, and by 3% above 7·9 mmol/l. The number of myocardial infarctions at different lipid concentrations was based on a 10 year follow up of 3725 men aged 40-49.[21] We further assumed that a third of myocardial infarctions were fatal (table I).[21] The gradually increasing effect of cholesterol lowering might be expected to start three years after the onset of the programme.[23] We used the causes of death statistics[22] to assume a threefold increase in myocardial infarctions when the programme was followed over the subsequent 10 years. To calculate the number of life years saved we assumed that all myocardial infarctions in the first 10 years occurred in year 7 and those in the subsequent 10 years in year 15.

A reduced serum cholesterol concentration presumably reduces the number of coronary artery bypass graft operations for angina pectoris. The extent of this reduction was estimated from records of the total number of such operations in Norway.

ESTIMATING COSTS

We followed Weinstein's approach for costing,[14] and, as with Williams's analysis of coronary artery bypass grafting,[23] we considered only health care costs. The different cost components were based on current fee schedules or recent cost calculations (table II). As we lacked other data these charges were used even if they only approximate to actual consumption of resources.[24] To calculate resource savings owing to avoided myocardial infarctions we used data specific to myocardial infarctions for average hospital costs in Norway[25] and assumed that a quarter of patients with fatal myocardial infarctions would be admitted to hospital. Avoided costs of treatment after infarction with β blockers were estimated, as were increased costs associated with use of health care as a result of increased life expectancy (table II).

TABLE II—Cost components of lowering serum cholesterol concentration

| Component | Unit of cost | Cost (£) |
| --- | --- | --- |
| Screening | Per individual | 6·40 |
| Confirmatory screening test | Per individual | 3·20 |
| Doctor's visit | Per visit | 16·20 |
| Cholesterol testing | Per test | 2·30 |
| Treatment of coronary heart disease | Per hospital stay | 2 318·00 |
| Coronary artery bypass grafting | Per operation | 9 922·00 |
| Treatment after infarction | Per person per year | 227·00 |
| Average health care cost | Per person per year | 455·00 |
| Drugs | Per person per year | 909·00 |
| Population strategy | Per year | 454 545·00 |

With respect to the population strategy the annual budget of the Norwegian Nutrition Council is about £450 000. We assumed that a stronger commitment to health education programmes in schools and the increased use of the mass media would cost ten times as much—that is, about £4·5m per year. We allocated 10% of this amount to our target group (men aged 40-49).

QUALITY OF LIFE

As, to our knowledge, no analyses of quality of life have been performed in this field (individual intervention in asymptomatic subjects) we arbitrarily assumed that quality of life is reduced by 0·2% when a subject is identified as being at risk of premature death and included in the individual intervention programme (serum cholesterol concentration >5·0 mmol/l). The reduction is conceivably greater (say 0·5%) when the risk is such that drugs are prescribed. The gain in quality of life was assumed to be 10% for a non-fatal myocardial infarction avoided[26] and 100% for a death avoided. Future costs and benefits were discounted according to normal practice[14 27] at a rate of 7%, that recommended by the Norwegian Treasury.

Results

The discounted total net cost of the population strategy was estimated at £36 700 (Kr 136 836 in 1990) with a gain of 3100 discounted life years, giving a cost effectiveness ratio of £12 for men aged 40-49 at entry to the programme (table III). The incremental cost of cholesterol screening and individual dietary treatment was £38·8m, increasing to £99·2m when drug treatment was added. The incremental life years gained were 3100 years and 900 years for dietary treatment and drug treatment respectively. Hence the marginal cost effectiveness ratios were about £12 400

for dietary treatment and about £111 500 for the combined dietary and drug treatment modality. As women have about the same serum cholesterol concentrations as men but less than a fifth the risk for coronary heart disease the cost effectiveness ratios for women are at least five times higher.

| Strategy | Life year | QALY |
| --- | --- | --- |
| No action | 0 | 0 |
| Population approach | 12 | 10 |
| Dietary treatment | 12 440* | 100 546 |
| Dietary and drug treatments | 111 549 | 125 860 |

The population approach represented a gain of 3800 quality of life years (QALYs) (£10 per QALY, table III). The net incremental effects of dietary treatment were 400 QALYs (£100 500 per QALY) and 800 QALYs (£125 900 per QALY) for drug treatment. If the reduction in quality of life were only 0·1% by individual interventions the net incremental gains in QALYs would be about 2100 and 700 QALYs for diet and drugs respectively. If the reduction were 1% the individual interventions would represent substantial net losses of QALYs.

We performed a sensitivity analysis of factors most crucial to the conclusions (table IV). Overall the cost effectiveness ratios were fairly robust to realistic changes in the assumptions on which the analysis is based.

TABLE IV — Sensitivity analysis: cost per life year gained under different assumptions for men aged 40-49

| | | | Marginal cost effectiveness ratio (£1000) | | | | | |
| | Estimate (£) | | Population approach | | Dietary treatment | | Dietary and drug treatments | |
| Assumption | Low | High | Low | High | Low | High | Low | High |
| --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Baseline | | | 0 | | 13 | | 112 | |
| Cost per visit | 14 | 27 | 0 | 0 | 11 | 20 | 111 | 113 |
| Cost per screening | 5 | 14 | 0 | 0 | 12 | 13 | 112 | 112 |
| Health care cost per year | 0 | 363 | -0·5 | 0·2 | 12 | 13 | 111 | 112 |
| Cost of drugs | 455 | 1363 | 0 | 0 | 13 | 13 | 57 | 166 |
| Discount rate (%) | 0 | 10 | -0·2 | 0·2 | 8 | 16 | 72 | 136 |
| Life year gain | +20% | -20% | -0·2 | 0·4 | 10 | 16 | 93 | 140 |
| Mass strategy cost | 181 800 | 909 100 | -0·9 | 1·6 | 13 | 13 | 112 | 112 |

## Discussion

### COSTS

As recommended by Weinstein[14] we did not include the production effects of the programmes, nor did we include time costs incurred by patients—for example, in doctor's visits. Thus the analysis is concerned solely with health services cost per QALY (and per life year) as shown earlier by Williams.[23] In general, cost components were estimated conservatively; cost savings are likely if anything to be exaggerated.

### CONSEQUENCES FOR HEALTH

We assumed that dietary treatment would have a smaller effect on cholesterol concentration than was assumed in a recent British report.[13] However, our assumptions accord with large scale intervention trials.[12 19] There is much uncertainty in estimating the long term effects of lowering cholesterol concentration, particularly among women. Lack of available data meant that we could not include the potential effects on cerebral strokes and intermittent claudication. The inclusion of such data, however, would alter the estimates of cost per life year gained little as the mortality from these diseases is low in this age group.[22]

The assumption of full participation and compliance with the programme is not realistic. Though anything less would reduce the costs as well as the benefits, it would probably make the cost effectiveness ratios less favourable as these problems are most likely to occur in the high risk group, in which the potential benefit is greatest. Further, the estimates of cholesterol lowering through dietary treatment may be too optimistic.

For angina pectoris we considered only a reduced amount of coronary surgery. Cholesterol lowering may also mean a lower incidence of less severe angina, but the impact of including this would not have affected the cost effectiveness ratios much.

### COST EFFECTIVENESS

As with other economic studies our analysis is based on numerous assumptions. Hence the calculated costs per life year and per QALY are approximate. They are comparable, however, to other studies on the average cost effectiveness of different approaches for cholesterol lowering.[7-13] When the potential for implementing cholesterol lowering programmes stepwise is examined, however, a somewhat different picture emerges. The cost per life year saved by the mass strategy is negligible. However, the extra (marginal) cost of dietary treatment is substantial compared with the extra life years saved and that for drug treatment is even more so. The analysis clearly shows the importance of a marginal analysis when incremental programmes are available.

Furthermore, individual intervention as recommended by the Norwegian programme seems to be less cost effective than curative measures for coronary heart disease.[23 28 29]

### QALYS

The Norwegian programme implies that some 160 000 men aged 40-49 would be included for individual intervention of various degrees. Yet only a few have coronary symptoms at entry to the intervention, and some 30-40 000 will develop symptoms during the subsequent 20 years. This means that more than half of the middle aged male population will "unnecessarily" be labelled as subjects at risk. To what extent this labelling detracts from their quality of life is not known, although some indications are evident.[30 31] Avoiding death certainly means an increase in QALYs. Overall, our assumption of a 0·2% reduction in life quality through risk identification, though controversial, seems justified.

### CHOLESTEROL LOWERING POLICIES

The mass strategy for cholesterol lowering seems to be highly cost effective and also acceptable ethically. It may also prevent coronary heart disease in low risk groups which are excluded from the individual programmes.[32]

The individual intervention for men through testing and diet counselling may be comparable with established health care programmes in terms of cost per life year gained. However, ethical and clinical problems exist as the potential long term negative effects of identification of risk have not been studied. Intervention may also counteract the mass strategy in population groups with moderately increased serum cholesterol concentration (5·0-6·5 mmol/l). Kinley and Heller reported that subjects with serum cholesterol concentrations <6·5 mmol/l on screening may believe that their diet is optimal when the test result is all right.[33] The use of drugs with liberally defined indications emerges from our figures as being less cost effective than most other programmes in health care. With a lack of knowledge of the long term effects the ethical issues loom large. Consequently, it would be prudent to reserve such treatment for very high risk groups, and it may be relevant to recall experience with hypertension. There is now evidence that drugs that

were widely used for mild hypertension in the 1960s and '70s might have done more harm than good,[34 35] and this mistake may be potentially repeated in subjects with hypercholesterolaemia.

Doubts are even stronger in women: firstly, the effect of cholesterol lowering remains to be shown and, secondly, the incidence of coronary heart disease is already very low in middle aged women.

Further studies of the long term effects of individual intervention on both biological processes and quality of life are needed, especially for women and other low risk groups. In the mean time it is prudent to recall that a high serum cholesterol concentration is caused by unhealthy eating habits. Our analysis above indicates that individual interventions should be implemented with great caution. The widely recommended intervention limits[5 6 36] should be adjusted to include only a small proportion of the population. To what extent women should be included in such programmes is unclear. The use of drugs should be reserved for subjects with genetic hypercholesterolaemia or those who are otherwise at very high risk of arteriosclerotic disease.

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# Microvascular vasodilatation in feet of newly diagnosed non-insulin dependent diabetic patients

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Patients with non-insulin dependent diabetes have an excess morbidity from foot ulceration, a difference largely attributed to a greater degree of large vessel disease,[1] with a contribution from neuropathy. Microvascular vasodilatation in response to injury is potentially an important part of healing yet the integrity of this response has not been examined at diagnosis in this high risk group.

The maximum vasodilatation (maximum hyperaemic response) to minor thermal injury can be reproducibly measured with laser Doppler fluximetry. An impairment of this response has been shown in type I (insulin dependent) diabetes.[2] We examined the integrity of this response in non-insulin dependent diabetic subjects without significant large vessel disease and compared the results with those from healthy controls and insulin dependent diabetic subjects.

## Patients, methods, and results

Nine non-insulin dependent diabetic patients (assessed on clinical grounds) were recruited from successive referrals to our clinic (four women, five men, median age 42 (range 25-60) years. Controls matched for age and sex (hospital staff with no medical history, mean age 40 (25-60)) and insulin dependent diabetic patients matched for age and sex (mean age 42 (25-60), median duration of diabetes 19 (2-48) years) were recruited for comparison. Hypertensive subjects, those taking vasoactive drugs, and those with large vessel disease (indicated by a previous vascular event, ankle systolic index $<0.1$, or absent foot pulses) were excluded.

Brachial systolic blood pressure was higher in the insulin dependent patients than in the non-insulin dependent patients or the controls (median 144 (112-160) mm Hg, 126 (105-170) mm Hg, and 120 (106-140) mm Hg, respectively; $p<0.05$), although no difference in systolic pressure taken at the ankle or brachial diastolic pressure was found. Ambient blood glucose