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Cost-effectiveness of statins for coronary heart disease patients with hypercholesterolaemia

Key Messages

1. These results suggest that a period of non-pharmacological intervention including dietary classes lowers the blood cholesterol of patients with coronary heart disease. The use of statins can improve the lipid profiles of these patients further.
2. For Hong Kong patients with myocardial infarction and average cholesterol levels on statin therapy, the gross cost per event prevented or per quality-adjusted life year gained is substantial; the potential benefits and savings may outweigh the costs.

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Introduction

There is a strong association between blood cholesterol and the development of ischaemic heart disease (IHD). The Scandinavian Simvastatin Survival Study (4S) was the first of several large-scale clinical trials of an HMG-CoA reductase inhibitor (statin) on cardiovascular events and mortality in patients with known coronary heart disease.[1] Treatment with simvastatin resulted in a 37% reduction in non-fatal myocardial infarction (MI), a 37% decrease in revascularisation procedures, and a 42% reduction in deaths attributable to IHDs. Overall mortality was reduced by 30%. Subsequent large clinical trials such as the Cholesterol And Recurrent Events (CARE) Trial[2] and Long-term Intervention with Pravastatin In Ischaemic Disease (LIPID) study,[3] showed that lower-risk patients also benefited from statins.

Diet modification alone is insufficient to reduce cholesterol level in the majority of patients. For these patients, statins are needed as they are efficacious and reasonably safe. We set out to study coronary heart disease patients requiring lipid-lowering therapy and to analyse the costs, benefits and cost-effectiveness of treating hypercholesterolaemia with statins in these patients.

Methods

Effect of diet and statin therapy

Patients were recruited from the Cardiac Clinic at Sai Ying Pun between November 1996 and January 1997. Patients were included if they had not had their cholesterol checked in the previous 2 years and were diagnosed as having IHD, by virtue of a clinical diagnosis of IHD or angina, a history of MI, positive exercise ECG or thallium scan, coronary angiography showing any significant stenosis, or prescription of nitrates as anti-anginal therapy. Subjects were seen and plasma lipid profile was measured at the time of recruitment, after dietary class, and 3 and 6 months after statin prescription.

Cost-effectiveness of dietary intervention in lowering serum cholesterol

The cost-effectiveness of dietary intervention was assessed in those patients who were started on cholesterol-lowering therapy for the first time. Drug therapy would be started if the plasma total cholesterol (TC) exceeded 5.2 mmol/L and dietary modification for at least 3 months had failed.[4] We used this period to assess the effectiveness of diet. All hypercholesterolaemic patients were asked to attend an afternoon dietary class (3 hours) run by dieticians. The cost in terms of dietician time and the cholesterol-lowering effect of the dietary intervention were used to calculate a cost-effectiveness ratio.

Cost-effectiveness of statins in lowering plasma cholesterol

Assessment of costs

Patients were assumed to receive 40 mg daily of pravastatin, as in the CARE study.[2] The acquisition cost of a 20 mg tablet of pravastatin was HK$7.67 for hospitals in the Hong Kong Hospital Authority. A telephone survey of 10 local private clinics indicated that the market price of a full lipid profile was $440.

Table 1. Lipid profile

Profile*	Blood test 1 (n=143) Mean ± SD (mmol/L)	Blood test 2 (n=40) Mean ± SD (mmol/L)	Blood test 3 (n=30) Mean ± SD (mmol/L)	Blood test 4 (n=16) Mean ± SD (mmol/L)
TC	5.30 ± 0.99	5.80 ± 0.87	5.53 ± 0.95	5.52 ± 0.94
TG	1.39 ± 0.92	1.60 ± 1.10	1.57 ± 1.21	1.48 ± 0.65
HDL	1.17 ± 0.38	1.25 ± 0.42	1.20 ± 0.34	1.20 ± 0.32
LDL	3.51 ± 0.89	3.93 ± 0.82	3.60 ± 1.05	3.63 ± 0.84

* TC denotes total cholesterol, TG triglycerides, HDL high-density lipoprotein cholesterol, and LDL low-density lipoprotein cholesterol

Assessment of benefits

We assessed the benefits of treating a hypothetical cohort of Hong Kong patients with the same demographics and prognosis as in the CARE study. As there were no local data on the long-term benefit of statins, we used the outcome data of the CARE study. Patients in CARE were American and Canadian men (n=3583) and post-menopausal women (n=576), aged 21 to 75 years, who had an acute MI 3 to 20 months previously. The entry criteria included plasma TC levels <240 mg/dL (6.2 mmol/L), low-density lipoprotein (LDL) cholesterol levels of 115 to 174 mg/dL (3.0 to 4.5 mmol/L), fasting triglyceride levels of <350 mg/dL (4.0 mmol/L), fasting glucose levels of no more than 220 mg/dL (12.2 mmol/L), left ventricular ejection fractions of no less than 25%, and no symptomatic congestive heart failure. The patients were randomised to double-blind treatment with either placebo (n=2078) or pravastatin (n=2081) for a median period of 5 years.

Benefits evaluated included (i) benefits to the hospital: the prevention of IHD (costs of hospitalisation, clinic attendance, cardiac investigations, cardiac intervention procedures, rehabilitation), and other cardiovascular diseases (eg stroke, peripheral vascular disease), and (ii) patient benefits: reduction in loss of earnings. We used data from the CARE study to estimate the number of cardiac events prevented by treatment with statins.

Cost-effectiveness analysis

The cost-effectiveness in terms of reduction in cardiac events and mortality was analysed from the perspective of a hospital-based cardiological service providing in-patient and out-patient care, specifically the diagnosis, treatment, rehabilitation, follow-up and secondary prevention of IHD.

Cost-utility analysis

In our cost-utility analysis, the endpoint was gross cost per quality-adjusted life year (QALY) gained. In the 4S study, the quality of life (QOL) in their population of post-MI patients was 0.88. Other studies reported the QOL as between 0.8 and 0.9. We therefore used 0.85. Based on official statistics, the remaining average life expectancy was estimated to be 16.7 and 22.3 years respectively in males and females. We assumed that at age 59 a prior MI decreased life expectancy by half, as observed in the 4S study.

Cost-benefit analysis

Benefits and savings arose from life years gained, prevention of MIs, strokes and procedures. The life years gained was translated to earnings according to the employment pattern for the working population aged 55 to 59 years. Prevention of non-fatal MIs would lead to fewer hospitals admissions. The average cost of an admission to Queen Mary Hospital for an acute MI patient was $46 720. The median cost of a percutaneous transluminal coronary angioplasty (PTCA) procedure was $35 000 and the median price for a stent was $12 000. Calculation of benefits due to stroke prevention was based on the assumption of equal numbers of severe and mild disabilities prevented. Severe disabilities was assumed to require attendance at a day hospital with supervised daily training ($1430 per attendance). Mild disabilities were assumed to require community nursing services (twice per week at $360 per visit).

Results

Effect of diet and statin therapy

There were 106 males and 95 females (mean age, 71±10 years) recruited. Results of lipid profiles are shown in Tables 1 to 3. For those patients who had raised cholesterol levels in their first blood test, they were asked to attend diet class and have their second blood test measured 3 months later.

Cost-effectiveness of dietary intervention and statin therapy in lowering serum cholesterol

The cost of the dietary intervention was $55.44 per patient. The mean reductions in TC and LDL cholesterol after the dietary intervention were 0.24 mmol/L and 0.22 mmol/L, respectively. Therefore, the cost per mmol/L reduction was estimated as $231 for TC and $252 for LDL cholesterol. The mean cost of statin therapy was $8.41 per patient per day. The average LDL cholesterol level of patients who had received statin treatment until the end of the study decreased from 4.58±0.77 to 3.59±0.86 (P=0.003). The mean reduction due to statin treatment was 0.99 mmol/L per patient. The cost-effectiveness of statin therapy was $8.49 per patient per day per mmol/L reduction in LDL cholesterol.

Cost-effectiveness of statins in lowering plasma cholesterol

Costs and benefits of lipid-lowering therapy with a statin

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Table 2. Effect of diet class on lipid profiles (n=40)

Profile*	Before class Mean ± SD (mmol/L)	After class Mean ± SD (mmol/L)	Change in mean (mmol/L)
TC	6.04 ± 0.72	5.80 ± 0.87	-0.24†
TG	1.63 ± 1.16	1.60 ± 1.10	-0.03
HDL	1.21 ± 0.42	1.24 ± 0.42	0.03
LDL	4.15 ± 0.56	3.93 ± 0.82	-0.22†

* TC denotes total cholesterol, TG triglycerides, HDL high-density lipoprotein cholesterol, and LDL low-density lipoprotein cholesterol
† P<0.05

Table 3. Effect of statin on lipid profiles (n=16)

Profile*	Before statin Mean ± SD (mmol/L)	Blood test 3 Mean ± SD (mmol/L)	Blood test 4 Mean ± SD (mmol/L)	Change in mean (mmol/L)
TC	6.33 ± 0.73	5.62 ± 1.20	5.52 ± 0.94	-0.81†
TG	1.57 ± 0.84	1.59 ± 1.31	1.48 ± 0.65	-0.09
HDL	1.14 ± 0.34	1.25 ± 0.31	1.23 ± 0.30	0.09
LDL	4.58 ± 0.77	3.64 ± 1.25	3.59 ± 0.86	-0.99†

* TC denotes total cholesterol, TG triglycerides, HDL high-density lipoprotein cholesterol, and LDL low-density lipoprotein cholesterol
† P<0.05

Table 4. Cost-effectiveness of statin treatment

Event*	No. prevented	HK$ cost/event prevented Mean (95% CI)	
		No discounting	6% discounting
Deaths	16	4 442 350 (1 537 736 to undefined†)	3 782 055 (1 309 173 to undefined†)
CHD deaths	23	3 090 330 (1 584 785 to undefined†)	2 630 995 (1 349 228 to undefined†)
Non-fatal MI	38	1 870 463 (1 103 094 to 10 755 162)	1 592 444 (939 134 to 9 156 554)
Fatal or confirmed non-fatal MI	50	1 421 552 (911 251 to 4 442 350)	1 210 258 (775 806 to 3 782 055)
CHD deaths or non-fatal MI	62	1 146 413 (764 275 to 3 057 101)	976 014 (650 676 to 2 602 704)
Procedures	97	732 759 (534 716 to 1 318 966)	623 844 (455 238 to 1 122 919)
Fatal and non-fatal strokes	24	2 961 566 (1 822 502 to 23 692 532)	2 521 370 (1 551 612 to 20 170 959)
All events (deaths + non-fatal MIs + non-fatal strokes + procedures)	179	397 082	338 061

* CHD denotes coronary heart disease, and MI myocardial infarction
† The upper limit is undefined as the 95% confidence interval crosses zero

Table 5. Cost-benefit analysis

Source of benefits and savings*	Amount (HK$)
Benefits	
Potential increase in earnings due to life years gained	36 596 390
Savings	
Acute admission from non-fatal MI prevention	1 495 692
PTCA procedures prevented	1 385 868
Deployment of stents prevented	475 155
Community nursing services for mild disabilities prevented from stroke	2 408 876
Geriatric day hospital for severe disabilities prevented from stroke	33 582 077
Total discounted benefits and savings	75 944 058

* MI denotes myocardial infarction, and PTCA percutaneous transluminal coronary angioplasty

40 mg pravastatin daily for 2081 patients was estimated to be $12 818 960 and $58 258 635.5, respectively. Total undiscounted cost was $71 077 596. The cost-effectiveness ratios are set out in Table 4. Total undiscounted benefits and savings would be $90 144 231 (Table 5). As the potential benefits and savings exceed the costs, there is a net benefit of $19 066 635 before discounting. After discounting at 6%, benefits and savings ($75 944 058) are still larger than the discounted costs ($60 512 876), resulting in a net benefit of $15 431 182. Pravastatin treatment for 5 years resulted in 343.12 QALYs gained. Net cost per QALY gained was $71 032 ([$71 077 596 - $46 704 975]/343.12) and after discounting at 6%, $73 218 ([$60 512 876 - $39 347 668]/289.07) [Table 6].

Table 6. Gross and net cost per QALY gained

	Amount (HK$)	
	No discounting	6% discounting
Gross cost/QALY gained	207 151	209 336
Net cost/QALY gained	71 032	73 218

Cost-effectiveness of statins under different circumstances

The cost-effectiveness of statins was also estimated for other types of patient population. In a patient population similar to 4S, drugs and biochemical monitoring would cost $8331.23 per patient per year. It would cost $524 867.49 to prevent one coronary event and $1 357 990.49 to prevent one death. In a patient population similar to WOSCOP study,[5] drugs and biochemical monitoring would cost $7359.10 per patient per year. It would cost $1 596 924.70 to prevent one coronary event and $4 054 864.10 to prevent one death. In a patient population similar to AFCAPS/TexCAPS study,[6] drugs and biochemical monitoring would cost $5707.48 per patient per year. It would cost $1 461 114.88 to prevent one coronary event. In this study, there was no significant reduction in mortality.

Discussion

Dietary class

These results suggest that dietary classes help to lower the cholesterol level of patients with coronary heart disease.

The use of statins can improve the lipid profiles of these patients but at a considerable cost. Dietary intervention is less effective than drug treatment in lowering cholesterol but it is inexpensive. Since a proportion of patients respond to dietary modification, long-term prescription of expensive lipid-lowering drugs might be avoided in these patients.

Cost-effectiveness of lipid-lowering therapy

Previous clinical trials suggest that all at-risk patients will benefit from treatment with statins, regardless of the level of their risk. The cost-effectiveness of statins depends on the risk of coronary heart disease. For patients at high risk treatment with a statin has been shown to be cost-effective. In our analysis of a patient population similar to that in the CARE study, the gross cost per QALY gained is substantial. Care should be taken in the prescription of statins and in deciding whom to treat. Cholesterol per se is a weak indicator of future coronary risk. The majority of coronary event patients have average cholesterol levels. To be more cost-effective, statins should be prescribed according to the baseline risk of individual patients.

Treatment with statins can also reduce the risk of stroke, the second leading cause of death. We therefore included stroke in our analysis and found that its inclusion increases the cost-effectiveness of statin therapy. Prevention of heart attacks and strokes result in other benefits and savings that ultimately outweigh the costs of statins. These include increased life expectancy and earnings, as well as avoidance of costs due to acute hospitalisation, more frequent out-patient follow-up, procedures, and rehabilitation.

Conclusions

If coronary heart disease patients in Hong Kong derive as much benefit from statin therapy as patients in clinical trials, statin therapy may be economically sound. Although the short-term costs appear high, there are long-term benefits in terms of lower mortality, fewer hospitalisations and cardiac catheterizations, angioplasties and coronary artery bypass operations, especially if stroke reduction is also considered. Therefore, our analysis supports the use of statins in addition to dietary intervention for patients with coronary heart disease. Cholesterol-lowering therapy in patients with coronary heart disease should be enthusiastically implemented and allocated appropriate resources.

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