ORIGINAL ARTICLE

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Cost-effectiveness analysis of applying the Cholesterol and Recurrent Events (CARE) study protocol in Hong Kong

在香港應用膽固醇及復發案例(CARE)研究的成本效益分析

Objective. To determine the cost-effectiveness of secondary prevention with pravastatin in Hong Kong patients with coronary heart disease and average cholesterol levels.
Design. Cost-effectiveness analysis based on published results of the CARE study.
Patients. Men and women post–myocardial infarction with average cholesterol levels.
Main outcome measures. Cost-effectiveness analysis: cost per life saved, cost per fatal or non-fatal coronary event prevented, cost per procedure prevented, and cost per fatal or non-fatal stroke prevented. Cost-utility analysis: gross cost and net cost per quality-adjusted life year gained calculated using two alternative models.
Results. Cost per life saved or death prevented was HK$4 442 350 (non-discounted); cost per fatal or non-fatal cardiac event prevented HK$1 146 413; cost per procedure prevented HK$732 759; and cost per fatal or non-fatal stroke prevented HK$2 961 566. Net cost per quality-adjusted life year gained was HK$73 218 and HK$65 280 non-discounted, respectively using the two alternative models.
Conclusions. The results of this study can assist in prioritising the use of health care resources in Hong Kong but should be considered alongside the benefits and costs of alternative interventions for coronary heart disease.

目的：確定在有冠心病和平均膽固醇水平的香港患者中，用 pravastatin 作二級預防方法的成本效益。
設計：基於已發表的 CARE 研究結果之成本效益分析。
患者：曾患有心肌梗塞和有平均膽固醇水平的患者。
主要結果測量：成本效益分析：每挽救一個生命的成本，每防止一個致命或非致命有關冠心病的成本，每預防一項程序的成本，每防止一次致命或非致命中風的成本。成本效用分析：利用兩種不同模式計算出每質素調整的生存年份的總成本和淨成本。
結果：每挽救一個生命或防止死亡的成本為港幣$4 442 350(無折扣)，每防止一個致命或非致命心臟病例的成本為港幣 $1 146 413 ，每預防一項程序的成本為港幣 $732 759 ，每防止一次致命或非致命的中風的成本為港幣 $2 961 566。使用兩種不同模式計算得到的每質素調整的生存年份所獲得的淨成本分別為港幣 $73 218 和 $65 280(無折扣)。
結論：本研究的結果可以幫助香港考慮使用醫護資源時的優先次序，但應同時考慮醫治冠心病的其他療法的效益和成本。

Key words:
Cost-benefit analysis;
Cost of illness;
Myocardial infarction;
Pravastatin;
Quality-adjusted life years

關鍵詞：
成本效益分析；
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Introduction

From the economist's point of view, resources in a society are finite and limited. Every time resources are deployed, the possibility of expending them for alternative purposes (opportunity cost) is foregone. In applying this concept to the health care system, priority must be given to providing maximum benefit from the available resources.[1] However, should more weight be given to maximising possible benefits for a selected set of individuals, or to spreading benefit among a maximum number of suitable persons (societal perspective)? With respect to secondary prevention of coronary disease events, the Scandinavian Simvastatin Survival Study (4S) clearly demonstrated the benefits of lipid-lowering therapy in a group of patients who had high cholesterol levels.[2] Further, the Cholesterol and Recurrent Events (CARE) study raised the possibility that benefits also extend to more typical at-risk patients with average cholesterol levels.[3] The CARE study demonstrated that patients with a history of myocardial infarction (MI) treated with pravastatin experienced a significant reduction in the incidence of coronary events, despite most patients having average cholesterol levels.

The 4S showed the beneficial effect on mortality and morbidity of lowering excessive cholesterol levels with simvastatin in patients with coronary heart disease (CHD). Its cost-effectiveness and favourable pharmacoeconomic implications have also been shown.[4,5] Cost-effectiveness of expensive drug treatments such as the statins, however, depends on the risk of CHD.[6] The cholesterol level of the patient is one determinant of this risk. It has yet to be shown whether treating patients who have normal cholesterol levels with statins is a relatively cost-effective option.

The concern of this study was to evaluate the CARE approach from a Hong Kong perspective, with respect to cost-effectiveness and cost-utility analyses. The major endpoint in the cost-utility analysis was net cost per quality-adjusted life year (QALY) gained, adjusting for other less tangible monetary savings and benefits relevant to the calculations of net costs.

Methods

Patients

In this analysis, the costs and benefits of using CARE criteria and pravastatin 40 mg daily to treat a hypothetical cohort of Hong Kong patients with the same demographics and prognosis as those enrolled in the CARE study were evaluated.

The CARE study recruited patients from 13 centres in Canada and 67 centres in the United States.[3] Patients included men and postmenopausal women, aged between 21 and 75 years, who had an acute MI between 3 and 20 months before recruitment. Entry criteria included plasma total cholesterol levels of less than 240 mg/dL (<6.2 mmol/L), low-density lipoprotein cholesterol levels of 115 to 174 mg/dL (3.0 to 4.5 mmol/L), fasting triglyceride levels of less than 350 mg/dL (<4.0 mmol/L), fasting glucose levels of 220 mg/dL or less (≤12.2 mmol/L), left ventricular ejection fractions of 25% or greater, and absence of symptomatic congestive heart failure.

Perspective

The cost-effectiveness of lipid-lowering therapy using the CARE criteria was analysed from a societal perspective with respect to the benefits. The perspective of the health service was considered with regard to costs and savings.

Costs

Local costs of treatment were used in the analysis and were derived by combining the costs of drug treatment and lipid measurements for a period of 5 years. All monetary values were calculated for 1997/1999 in Hong Kong dollars (US$1 = HK$7.78).

In the CARE study, patients randomised to the active treatment group received pravastatin 40 mg/d. The acquisition cost of a 20 mg tablet of pravastatin was HK$7.67 for hospitals in the Hong Kong Hospital Authority.[7] The total drug cost was thus calculated as the annual cost of two 20 mg tablets daily per patient, multiplied by the number of patient years of treatment (ie the total number of patients multiplied by the number of years of treatment). The second cost considered was that of serum lipid measurements. In the CARE study, measurements were completed at baseline, at 6 and 12 weeks after randomisation, thereafter at the end of each quarter during the first year (ie six measurements in the first year), and semi-annually for the remaining 4 years. Thus for patients surviving 5 years, the number of measurements equalled 14 in total (6 + 2 x 4). The authors undertook a telephone survey of 10 local private clinics to estimate the market price of a full lipid profile in Hong Kong. The median cost of a single lipid profile measurement was calculated at HK$440.

Cost-effectiveness analysis

Cost-effectiveness analysis is concerned with the measurement of outcomes in natural units (eg cost per event prevented).[8] In this study, the primary endpoint was the cost per life saved. Secondary endpoints included:

(1) cost per fatal or non-fatal coronary event (ie death from CHD or non-fatal MI) prevented;
(2) cost per procedure prevented; and
(3) cost per fatal and non-fatal stroke prevented.

The endpoint figures—cost per prevention of event—were also calculated based on the 95% confidence intervals (CI) for the risk reduction of cardiovascular events by pravastatin (in percentages) as determined from the CARE trial.[3] The upper limits of the CI for risk reduction of events were used to determine the corresponding upper limits of the number of events prevented (original number of events prevented multiplied by the upper limit of CI for risk reduction/ original risk reduction). Thus, the lower limits of cost per event prevented were derived. Similarly, the upper limits of cost per event prevented were derived from the lower limits of the CI for risk reduction of events.

Cost-utility analysis

In the cost-utility analysis, the endpoints were gross cost and net cost per QALY gained. This calculation involved the summation of QALYs gained from two sources: fatal and non-fatal MIs prevented, and fatal and non-fatal strokes prevented. In the 4S, the average quality of life (QOL) for the patients post-MI was assumed as 0.88.[4] Various other published studies have proposed a QOL value for those surviving MI of approximately 0.8 to 0.9.[9,10] Thus, in this study the average QOL for the hypothetical patients was taken as approximately 0.85.

Unified approach

In the 4S, it was estimated that the individual's remaining life expectancy was approximately halved by a CHD event at around the age of 60 years.[5] According to government statistics, the remaining average life expectancy in Hong Kong at the age of 59 years is 21.28 years for males and 25.34 years for females.[11] Thus, using the 4S approach, a prior MI at 59 years in men in Hong Kong could be expected to reduce average life expectancy by 10.64 years. For males meeting the entry criteria for the CARE study (ie past MI), a further MI (fatal or non-fatal) was assumed on average to decrease remaining life expectancy at the age of 59 years by a further half (ie 10.64/2 years). Thus, the QALYs gained from the prevention of MI could be calculated as: (number of second MIs prevented) x (average number of life years gained) x 85%. Consequently, in males the average QALYs gained per MI prevented was estimated as 10.64/2 years x 85%. Correspondingly in females, this equated to 12.67/2 x 85%. In Hong Kong, the ratio of males to females with MI at the age of 50 to 59 years is 6.45:1,[12] giving an average life expectancy in these combined groups of 10.91 years. Thus, assuming that the total number of MIs (fatal and non-fatal) prevented by pravastatin treatment would be the same as in the CARE study (ie 50), the QALYs gained in Hong Kong could be estimated as 50 x 10.91/2 x 85%.

By analogy with ischaemic heart disease, it was assumed that in patients meeting CARE entry criteria, the average remaining life expectancy following a fatal or non-fatal stroke would similarly decrease by half (ie 10.91/2). Thus, the QALYs gained from strokes prevented were calculated as: (number of strokes prevented) x (number of corresponding life years gained) x 85%. Extrapolating from the total number of strokes prevented in the CARE study (ie 24),[13] the QALYs gained in Hong Kong could be estimated as 24 x 10.91/2 x 85%.

Alternative approach

For this approach to the calculations, the assumption made was of a 50% average reduction in remaining life expectancy for patients sustaining a non-fatal MI. For patients sustaining a fatal MI at some time during the ensuing 5 years of the trial, a 75% average reduction in remaining life expectancy (at age of 59 years) was assumed. The resulting gain in QALYs from the prevention of fatal MIs (ie 14 x 10.91 x 0.75 x 0.85), non-fatal MIs (ie 38 x 10.91 x 0.5 x 0.85), and strokes attributed to statin therapy was recalculated on this basis.

Discounting of costs

The budget for the pravastatin tablets and the lipid level testing was estimated as if such costs were incurred at the beginning of a typical 5-year treatment course. In actuality, such expenditure was incurred throughout the course of treatment. For this reason, a further calculation was made, discounting gross cost at the respective rates of 6% and 4% per annum. These discounted rates were applied to the cost-effectiveness and cost-utility (unified and alternative approach) analyses.

Discounting of quality-adjusted life years gained

In addition to discounting gross cost to calculate gross cost per QALY gained, the number of QALYs gained was also discounted at 6% per annum in the cost-utility analysis under both unified and alternative approaches.

Sensitivity analysis

The endpoint results could be varied if different assumptions were made in the calculations of the two approaches. Two types of sensitivity analyses were performed on the gross cost per QALY gained before discounting: (1) by changing the expected QOL after MI; and (2) by modifying the extent to which fatal and non-fatal MIs decreased the average remaining life expectancy of patients. Thus, QOLs of 0.8 and 0.9 instead of 0.85 were considered. Similarly, average remaining life expectancy after fatal or non-fatal MI (unified approach) were considered to decrease by 40% and 60% instead of 50%. For the alternative approach, 40% and 65% as well as 60% and 85% reductions (instead of 50% and 75%) in life expectancy for non-fatal and fatal MIs respectively, were taken into account.

Further analysis of net cost: potential savings

In order to estimate net cost per QALY gained in the cost-utility analysis, all potential savings were deducted from the gross cost to obtain the net cost. In addition to estimations without discounting, the potential savings were discounted at 6% per annum. The net cost per QALY gained was thus calculated with both non-discounted and discounted net costs and benefits. Savings that were considered arose from three sources:

(1) prevention of non-fatal MIs;
(2) prevention of procedures; and
(3) prevention of non-fatal strokes.

Prevention of non-fatal MIs implied the saving of an acute admission (38 x cost of admission). The average cost of each admission for a patient with acute MI was determined as HK$46 720, based on a cost estimation provided by accountants in the finance division of Queen Mary Hospital.

The rate of procedures was reduced by treatment and a corresponding reduction in the use of stents was expected. A survey of the prices charged for percutaneous transluminal coronary angioplasty (PTCA) and the use of stents in patients with heart disease was undertaken at Queen Mary Hospital. The most recent patients (n=120) who underwent PTCA were evaluated. The median cost of a PTCA procedure was $35 000 (mean, $29 195.83; standard deviation [SD], $11 504.92; range, $14 000-$48 000) and the median price for stenting was $12 000 (mean, $12 767.50; SD, $13 963.24; range, $0-$65 600). By using these median costs, the savings resulting from the prevention of the 47 PTCA and stenting procedures were estimated.

In the CARE study, 28 non-fatal strokes were prevented. Calculation of benefits due to stroke prevention was based on the assumption of an equal distribution of severe and mild disabilities prevented. The health care for stroke patients depends on the degree of severity of their disabilities. For the prevention of 14 severe disabilities, it was assumed that savings from attending a geriatric day hospital with supervised daily therapy were made. According to a local publication on hospital charges for persons not entitled to government subsidised services,[14] the cost of geriatric day hospital care was HK$1430 per attendance. This saving was interpreted as the daily cost multiplied by the life span of those with severe disabilities (10.91 x 0.5) expressed in days (HK$1430 x 14 x 10.91 x 0.5 x 365). For the prevention of 14 mild disabilities, it was assumed that community nursing services (two visits per week per patient) might be saved. The cost of the community nursing service was HK$360 per patient per visit in Hong Kong.[14] Thus, the savings from care of mild disabilities prevented were calculated as the weekly cost multiplied by the life span of patients with mild disabilities (10.91 x 0.5) expressed in weeks ($360 x 2 x 14 x 10.91 x 0.5 x 52).

Results

Cost figures

The cost of prescribing pravastatin 40 mg/d (365 days x 5) for 2081 patients was estimated to be HK$58 258 636. Using the median market price for a full lipid profile of HK$440 (mean, $441; range, $350-$650) derived from the telephone survey, the cost of lipid measurements was estimated at HK$12 818 960. Hence, the combined costs comprised a total of HK$71 077 596.

Cost-effectiveness results

To evaluate the benefits of active treatment, the results of the pravastatin and placebo groups in the trial were compared. The number of events prevented by pravastatin treatment, including deaths (all-cause including CHD), non-fatal MI, procedures, and strokes are shown in Table 1, together with the respective cost per event prevented. The calculated endpoints of cost per life saved or death prevented was HK$4 442 350; the cost per fatal or non-fatal cardiac event (CHD death or non-fatal MI) prevented was HK$1 146 413; the cost per procedure prevented was HK$732 759; and the cost per fatal or non-fatal stroke prevented was HK$2 961 566. The corresponding upper and lower estimates for cost per event prevented is also shown in Table 1. In the case of all deaths and CHD deaths, the upper limits for cost per event prevented were undefined, because the lower limits of the 95% CI for risk reduction of these events with active treatment

Table 1. Cost-effectiveness over 5 years without and with discounting

Event	No. of event prevented	Cost per event prevented (HK$) (lower limits to upper limits)		
		No discounting	4% discounting	6% discounting
Deaths	16	4 442 350 (1 537 736 to undefined*)	3 982 955 (1 378 715 to undefined*)	3 782 055 (1 309 173 to undefined*)
Coronary heart disease deaths	23	3 090 330 (1 584 785 to undefined*)	2 770 751 (1 420 898 to undefined*)	2 630 995 (1 349 228 to undefined*)
Non-fatal MIs†	38	1 870 463 (1 103 094 to 10 755 162)	1 677 034 (989 020 to 9 642 944)	1 592 444 (939 134 to 9 156 554)
Fatal or confirmed non-fatal MIs	50	1 421 552 (911 251 to 4 442 350)	1 274 546 (817 016 to 3 982 955)	1 210 258 (775 806 to 3 782 055)
Coronary heart disease deaths or non-fatal MIs	62	1 146 413 (764 275 to 3 057 101)	1 027 859 (685 240 to 2 740 958)	976 014 (650 676 to 2 602 704)
Procedures	97	732 759 (534 716 to 1 318 966)	626 982 (479 420 to 1 182 568)	623 844 (455 238 to 1 122 919)
Fatal and non-fatal strokes	24	2 961 566 (1 822 502 to 23 692 532)	2 655 304 (1 634 033 to 21 242 428)	2 521 370 (1 551 612 to 20 170 959)
All events (deaths + non-fatal MIs + non-fatal strokes + procedures)	179	397 082	356 018	338 061

* The upper limits of costs are undefined since no events were prevented as implied by the lower limits of the 95% CI of risk reduction with pravastatin given in the CARE study
† MI myocardial infarction

were negative numbers, implying that no deaths were prevented.

Cost-utility results

Unified approach

The total gain in QALYs under the unified method of calculation was 231.84 years from the prevention of fatal and non-fatal MIs, and 111.28 years from the prevention of fatal and non-fatal strokes. Total QALYs gained thus amounted to 343.12 years and the resulting gross cost per QALY gained was HK$207 151, assuming no overlap and without discounting.

Alternative approach

When fatal MIs during the 5 years of the trial were assumed to decrease remaining life expectancy by 75% on average, the QALYs gained from their prevention totalled 97.37 years. For non-fatal MIs, prevention led to a gain in QALYs of 176.20 years. Thus, the total QALYs gained were 384.85 years, together with 111.28 QALYs gained from the prevention of fatal and non-fatal strokes, calculated previously. The gross cost per QALY gained, assuming no overlap and without discounting, was thus HK$184 689 using this second method of calculation.

Discounting of costs

The cost of drugs prescribed and lipid level measurements decreased to HK$49 081 313 and HK$11 431 563, respectively when they were discounted at 6% per annum. Thus, discounted total costs at 6% amounted to HK$60 512 876. With discounting at 4% per annum, the cost of drug and lipid measurements amounted to HK$51 871 419 and HK$11 855 865, respectively; hence HK$63 727 284 in total. Non-discounted and discounted costs per event prevented are summarised in Table 1. Gross costs per QALY gained with, and without discounting costs, using the unified and alternative approaches are summarised in Table 2.

Discounting of quality-adjusted life years gained

Using the unified approach to estimating QALYs gained, the discounted QALYs at 6% per annum were 195.32 years from fatal and non-fatal MIs prevented, and 93.75 years from fatal and non-fatal strokes prevented. Thus, the total discounted QALYs gained were 289.07 years using the unified approach. Using the alternative approach, the discounted QALYs gained were 82.03 years from fatal MIs prevented, 148.44 years from non-fatal MIs prevented; and 93.75 years from fatal and non-fatal strokes prevented. Thus, the total discounted QALYs gained were 324.22 years using the alternative approach. In combination with the discounted gross costs at 6% ($60 512 876) as calculated previously, discounted gross costs per QALY gained using the unified and alternative approaches in the cost-utility analysis were HK$209 336 and HK$186 641, respectively.

Table 2. Cost-utility analysis: gross cost per quality-adjusted life year gained over 5 years without and with discounting costs

	Gross cost per quality-adjusted life year gained (HK$)		
	No discounting	4% discounting*	6% discounting*
Unified approach	207 151	185 729	176 361
Alternative approach	184 689	165 590	157 237

* Costs of drug treatments and lipid measurements were discounted at 4% and 6% per annum for 5 years. The present value of drug cost=$\sum c / (1 + r)^n$, for n=1 to 5; where c=cost of drug treatments for 2081 patients per year and r=discount rate. The present value of lipid measurements = $m + m / [(1 + r)^{1/8} - 1] + \sum m / [(1 + r)^{1/4} - 1]^n$, for n=1 to 4 and n=6, 8, 10, 12, 14, 16, 18, 20; where m=cost of each lipid measurement for 2081 patients and r=discount rate

Sensitivity analysis

Gross cost per QALY gained was tested for sensitivity to the values for expected QOL after MI. The degree to which non-fatal and fatal MIs reduced the average remaining life expectancy of patients, and thus the gain attributable to their prevention, was subject to uncertainty. In the unified approach, gross cost per QALY gained increased from HK$207151 to HK$220098 when QOL was taken as 0.8, whereas when QOL increased to 0.9, it decreased to HK$195643. Similar results were obtained with respect to 40% and 60% reductions in average life expectancy. For the alternative method, gross cost per QALY gained rose less, from HK$184689 to HK$196232, and fell to HK$174428 when QOL was assumed to be 0.8 and 0.9, respectively, with all other variables unchanged. The results of the sensitivity analysis are summarised in Table 3.

Further analysis: net cost per quality-adjusted life year gained

Savings from avoiding acute admissions resulting from the prevention of non-fatal MIs amounted to HK$1775360. The prevention of PTCA procedures saved HK$1 645 000 and the prevention of stent deployment, HK$564 000. Thus, the procedures prevented saved HK$2209000 in total. The savings from avoiding geriatric day hospital care for stroke patients with severe disabilities was HK$39861322. The savings due to avoiding community nursing services for stroke patients with mild disabilities was estimated at HK$2859293. Thus, the monetary savings resulting from the prevention of non-fatal strokes was estimated at HK$42720615 and the total of all potential savings HK$46704975 (Table 4).

Table 5 summarises the results of net cost per QALY gained with and without discounting. Using the unified approach with 343.12 QALYs gained and no discounting, net cost per QALY gained from pravastatin treatment for 5 years was calculated as HK$71032 ([$71077 596-$46704975]/343.12). When using the discounted gross cost (at 6%), discounted total potential savings (at 6%), and discounted QALYs gained (at 6%), the net cost per QALY gained became HK$73 218 ([$60 512 876-$39 347 668]/289.07). Applying the same method to the alternative model with 384.85 QALYs gained, net cost per QALY gained was estimated at HK$63330 ([$71077596-$46704975]/384.85); with no discounting and the discounted net cost per QALY gained was calculated as HK$65280 ([$60512876-$39347668]/324.22).

Discussion

In recent years, the efficacy of statins in the prevention of CHD has been well established. Secondary

Table 3. Sensitivity analysis: effect of quality of life adjustments and reduction in life expectancy due to fatal or non-fatal myocardial infarction on costs per quality-adjusted life year gained

	Cost per quality-adjusted life year gained (HK$)		
Unified approach	Reduction in average remaining life expectancy*		
Quality of life	40%	50%	60%
0.8	254488	220098	193896
0.85	239519	207151	182490
0.9	226212	195643	172352
Alternative approach	Reduction in average remaining life expectancy*		
Quality of life	non-fatal MI†: 40% fatal MI: 65%	non-fatal MI: 50% fatal MI: 75%	non-fatal MI: 60% fatal MI: 85%
0.8	224342	196232	174382
0.85	211146	184689	164124
0.9	199415	174428	155006

* at age of 59 years
† MI myocardial infarction

Table 4. Potential savings without discounting

Source of savings	Amount (HK$)
Prevention of:	
Acute admission due to non-fatal MI*	1 775 360
PTCA† procedure	1 645 000
Deployment of stent	564 000
Community nursing services for mild disabilities secondary to stroke	2 859 293
Geriatric day hospital for severe disabilities secondary to stroke	39 861 322
Total savings	46 704 975

* MI myocardial infarction
† PTCA percutaneous transluminal coronary angioplasty

Table 5. Cost-utility analysis: net cost per quality-adjusted life year gained over 5 years without and with discounting

	Net cost per quality-adjusted life year gained (HK$)	
	No discounting	6% discounting*
Unified approach	71 032	73 218
Alternative approach	63 330	65 280

* Calculated with discounted gross cost, discounted total potential savings, and discounted quality-adjusted life years gained

prevention studies have shown that patients benefit whether they have high or normal cholesterol levels.[2,3] In primary prevention, the West of Scotland Coronary Prevention study[15] revealed benefits from treating hypercholesterolaemic men with pravastatin. Moreover, the Air Force/Texas Coronary Atherosclerosis Prevention study[16] suggested that treatment with lovastatin conferred benefits in subjects without CHD and with average serum cholesterol levels. The results of the above trials suggest that, regardless of the level of risk, recipients benefit from treatment with statins in terms of cardiovascular event prevention.[17] Hence, economic evaluation is needed to determine whether such benefits are affordable and whether spending money on statins for those with normal cholesterol levels is a good use of resources.

The definition of economic evaluation is "the comparative analysis of alternative courses of action in terms of both costs and consequences".[18] This study involved both a cost-effectiveness and cost-utility analysis. Cost-effectiveness analysis is one method of economic evaluation which allows comparisons of interventions by their cost per consequence in natural units, such as cost per life saved or life year gained.[19] Cost-utility analysis, a form of cost-effectiveness analysis, is used when single-dimension outcomes are not possible, for example, when the interventions produce differing consequences in terms of quantity and quality of life. The latter takes into account the quality of the individual's resulting health state as well as the number of extra years of life and expresses the combination of these in a unit of utility such as QALYs. Interventions can then be compared by means of a cost per unit of utility gained, for example, cost per QALY gained.[19]

In the economic model of this study, estimations derived from stroke prevention are included. Apart from the risk reduction data for stroke obtained from the CARE study, there is recent evidence confirming that treatment with statins can reduce the incidence of stroke. The Long-Term Intervention with Pravastatin in Ischaemic Disease study,[20] a secondary prevention study in 9014 patients with a broad range of cholesterol levels, shows that treatment with pravastatin reduces the risk of stroke by 19%. This finding is consistent with that of the 4S, which illustrated that a risk reduction of 28% in stroke could be achieved with simvastatin treatment.[21] These results support the inclusion of stroke in the current economic evaluation.

The current economic model may not contain all potential savings in net monetary terms. The net cost per QALY gained, however, based on available data has been calculated. Since the estimation of costs in these models is from a service provider's perspective, potential savings are similarly calculated from this perspective. Indirect and intangible costs from the patient's perspective, for example, loss of earnings, were not included.

For the calculation of cost per QALY gained, no overlap of patients for the events was assumed. This assumption, however, may not be correct. If there were patients who had more than one event, then the QALYs gained would have been overstated. This assumption was made due to the limited information available. In addition, the endpoint results of the current analyses may be subject to high variability as shown by the upper and lower estimates for cost per event prevented.

A major difficulty in determining whether an intervention is cost-effective or not is the fact that there is no absolute level of cost-effectiveness. No standard is available in Hong Kong to assist in determining the appropriate cost per outcome for an intervention. For example, does this study's finding of a cost of almost HK$4 million per death prevented imply that the use of statins is cost-effective? The purpose of this study has been to provide a basis for future comparison. In theory, different interventions, the same intervention for different risk groups or interventions targeted at preventing different outcomes can be compared. From this study, the cost per coronary event prevented (HK$1.03 million) and the cost per stroke prevented (HK$2.66 million) with pravastatin treatment has been identified. The gross cost per QALY of approximately HK$0.16 to 0.21 million (US$20 000-27 000), and net lost per QALY of approximately HK$0.06 to 0.07 million (US$8000-9000), might be considered an efficient investment in other health care systems where reasonable costs per QALY range from £10 000[22] to US$50 000.[23]

Results of economic evaluations vary because of differences in methodologies and the underlying assumptions used in different studies. The problem is magnified when studies are performed in different countries, as respective social, cultural, and economic factors may influence the corresponding methodology and results. This is why data must be derived for Hong Kong. As well as considering local cost data, QOL data from patients in Hong Kong should be determined. In this study, assumptions concerning QOL were based on patient data from overseas. By applying overseas data, it is possible that the cost per QALY gained in the cost-utility analysis has been underestimated if the QOL in Hong Kong patients is lower than that reference group. Similarly, the cost per event prevented in the cost-effectiveness analysis may have been underestimated if the number of events prevented with treatment is lower in patients in Hong Kong than those overseas.

The cost-effectiveness of treatment with statins is highly dependent on the baseline risk of the individual patient. Cholesterol level in itself can be a poor indicator of future coronary risk, since the majority of coronary events occur in patients with average cholesterol levels. Further data is needed from economic evaluations comparing patients at different levels of risk and treatment with statins, an expensive option, with other possibly more cost-effective interventions.

Data on the cost-effectiveness of the CARE study has not been published. There are, however, cost-effectiveness studies available reporting the use of statins. Ebrahim et al[24] compared the cost-effectiveness of statins with a range of other CHD prevention therapies. They found that the discounted gross cost per life year gained ranged from £3800 to £9300 at levels of risk consistent with secondary prevention, and was high compared to other drug therapies and lifestyle changes. Nevertheless, with a net cost per life year gained of approximately £8000, treatment with statins compared favourably with several other interventions currently provided by the National Health Service.

Coronary heart disease is an increasing problem in Hong Kong. According to local guidelines for treatment with lipid-lowering drugs, treatment is not currently recommended for patients with heart disease but normal cholesterol levels.[25] There is a lack of large local clinical trials in line with the CARE study. By using the results of the CARE study and local cost data, this study has attempted to assess the cost-effectiveness of such an intervention in Hong Kong. This study has assumed that the CARE findings would be applicable to the population in Hong Kong and that similar benefits and gains would be observed in local patients. More local studies are needed investigating these issues, in particular appropriate weightings for QOL following CHD events. This information would allow accurate estimations of costs, and decision-makers to consider whether these costs can be met given the identified benefits. The results of this study and others like it will assist in appropriate prioritisation and allocation of health care resources in Hong Kong.

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