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Cost of lipid lowering in patients with coronary artery disease by Case Method Learning

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Objectives: This investigation was undertaken to study the costs of a Case Method Learning (CML) -supported lipid-lowering strategy in secondary prevention of coronary artery disease (CAD) in primary care.
Methods: This prospective randomized controlled trial in primary care with an additional external specialist control group in Södertälje, Stockholm County, Sweden, included 255 consecutive patients with CAD. Guidelines were mailed to all general practitioners (GPs; n = 54) and presented at a common lecture. GPs who were randomized to the intervention group participated in recurrent CML dialogues at their primary health-care centers during a 2-year period. A locally well-known cardiologist served as a facilitator. Assessment of low-density lipoprotein (LDL) cholesterol was performed at baseline and after 2 years. Analysis according to intention-to-treat—intervention and control groups (n = 88)—was based on group affiliation at baseline. The marginal cost of lipid lowering comprised increased cost of lipid-lowering drugs in the intervention group compared with the primary care control group, cost of attendance of the GP's in the intervention group, and cost of time for preparation, travel, and seminars of the facilitator. Costs are as of 2002 with an exchange rate 1 US$ = 9.5 SEK (Swedish Crowns).
Results: Patients in the primary care intervention group had their LDL cholesterol reduced by 0.5 (confidence interval [CI], 0.1–0.9) mmol/L compared with the primary care control group ($p < .05$). No change occurred in controls. LDL cholesterol in the external specialist control group decreased by 0.6 (CI, 0.4–0.8) mmol/L. The cost of the educational intervention represented only 2 percent of the drug cost. The cost of lipid lowering in the intervention group, including the cost of the educational intervention, was actually lower than that of patients treated at the specialist clinic—106 US$ per mmol decrease in LDL cholesterol in the intervention group and 153 US$ per mmol decrease in LDL cholesterol in the specialist group. EuroQol 5D Index, which gives an estimate of global health-related quality of life, was 0.80 (CI, 0.75–0.85) in the present cohort.
Conclusions: The additional cost of CML was only 2 percent of the drug cost. Assuming the same gain in life expectancy per millimole decrease in LDL cholesterol as in the 4S-study gives a cost per gained quality-adjusted life year of US$ 24,000.

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This finding indicates that the CML-supported lipid-lowering strategy is cost-effective. The low cost of CML in primary care should probably warrant its use in the improvement of the quality of care in other major chronic diseases.

Keywords: Coronary artery disease, Lipids, Antilipemic agents, Health-care costs, Education, Medical, Continuing, Quality of life

Unambiguous results from randomized controlled trials show that treatment with statins for patients with coronary artery disease (CAD) are both clinically effective (2;18) and leads to potential savings of health services (13). The higher the CAD event risk, the stronger is the evidence that lipid-lowering therapy is cost-effective (16). Despite this finding, there are still a not-negligible gap between what is achieved in clinical practice and what should be achieved according to scientific evidence-based goals for secondary prevention in patients with CAD, even for patients in high-risk groups (1). The reason for this gap is probably that there are several barriers and complexities between evidence-based guidelines and anticipated behavior change in real clinical practice (5;9). Keys to successful cost-effective implementation of new evidence could be educational methods focusing on how and when to use the content of guidelines in the local context and content of the target physicians, and facilitation of the process of local consensus building (8). However, educational intervention studies with patient-related end points are scarce. Studies measuring the cost-effectiveness of educational/implementation methods are even more scant. Salkeld et al. state that the cost-effectiveness of general practice-based lifestyle interventions is yet to be demonstrated (19).

We have shown that Case Method Learning (CML) for general practitioners (GP) resulted in a significant reduction of lipid levels in patients with coronary artery disease (CAD) to a degree that—according to current knowledge—should decrease mortality and morbidity in CAD (2;14). This study is an economic evaluation of the costs and effects of this intervention.

METHODS

Patients

The patient registry of Stockholm County Council allows identification of all inpatients and outpatients visiting the hospital clinics. The Department of Medicine at Södertälje Hospital, located in the southern most part of Stockholm County, Sweden, provides planned and emergency health care for acute and elective cardiac patients in a catchment area of approximately 95,000 habitants. Thus, we could identify all these patients, during the preceding year, with a diagnosis of CAD (ICD-9 code 410-414). We identified 429 patients $\leqslant$ 70 years of age with such a diagnosis and scrutinized their medical records.

Criteria for a confirmed diagnosis of CAD in the patient record were as follows: (i) A diagnosis of angina pectoris, either by objective criteria based on coronary angiography, or pathologic findings on exercise test or stress test, or a clinical assessment based on typical angina symptoms at exercise with or without electrocardiographic (ECG) evidence of possible or definite ischemia. (ii) A diagnosis of myocardial infarction based on either World Health Organization criteria (21) or on unequivocal ECG findings.

A total of 323 patients fulfilled the inclusion criteria. We had identified, thus, all the patients in the population with a recent need for specialist care. We invited all of these patients to participate in the main study (January 1995); 68 patients refused to participate, leaving 255 patients to be included in the main study (79 percent of the identified unselected population). Hypertension was considered to be present if systolic blood pressure was $>$ 140 mm Hg, if diastolic blood pressure was $>$ 90 mm Hg, or if antihypertensive medication were used. Diabetes mellitus was defined as fasting plasma glucose of $\geqslant$ 7.0 mmol/L, a self-reported history of diabetes mellitus, or treatment for diabetes.

The patients were randomly assigned into two groups according to which group the physician responsible for their care belonged to. The intervention group (I) for a GP participating in the CML seminars and the control group (C) for a GP working at a primary health-care center only receiving the local practice guidelines. A specialist group (S) representing patients treated by a specialist in cardiology or internal medicine served as an external control group. A total of 220 patients completed the 2-year study.

Intervention

New evidence-based guidelines were presented to all participating physicians. The physicians in the intervention group also participated, together with a locally well-known facilitator (cardiologist), in recurrent interactive CML seminars at their own primary health-care center. Details of the intervention in the randomized controlled educational study have been published previously (14).

Costs

Data were gathered prospectively during the 2-year study period. *Direct costs* of health-care resources (utilization of lipid-lowering drugs) were measured. Resources attributable to cholesterol-lowering drugs were recorded, and changes from baseline were calculated. Lipid-lowering drugs were recorded both as defined daily doses (DDD) and as actual cost. *Cost of the educational intervention* was based on time consumption in hours and corresponding salary cost for

attendance of the GPs, and preparation, travel, and seminar time and corresponding salary cost of the facilitator. Mean salaries for GPs and the mean salary of hospital-based consultants—for the facilitator—in Stockholm County Council were used in the cost analysis. Payroll taxes were included. All costs are calculated on the basis of Swedish prices in 2002 and converted to US$ at the 2002 exchange rate (1 US$ = 9.5 SEK [Swedish Crowns]).

Quality of life

EuroQol 5D Index (EQ-5D) is a quality of life instrument well-established for use as weight in calculation of quality-adjusted life years (QALYs). The respondents may classify their present health status in five dimensions—mobility, self-care, usual activities, pain/discomfort, and anxiety/depression. Each question can be answered in three levels—no problems, moderate problems, and severe problems. The UK EQ-5D index tariff was used to obtain single index values between 0 (dead) and 1 (full health) for the QALY calculations (6). EQ-5D is an easy and rapid generic instrument, well-validated and found to be reliable in different cultures and in different diseases (3;4;17).

Ethical Considerations

All participating patients gave written informed consent. The study complies with the Declaration of Helsinki and was approved by the ethics committee of Karolinska Institute at Huddinge University Hospital.

RESULTS

Baseline characteristics of the primary health-care centers and general practitioners are shown in Table 1. Baseline characteristics of the patients are shown in Table 2. Patients in the intervention group had their LDL cholesterol reduced by 0.5 (confidence interval [CI], 0.1–0.9) mmol/L compared with controls ($p < .05$; Figure 1). No change did actually occur in the control group. LDL cholesterol in the specialist group—the external control group—decreased by 0.6 (CI, 0.4–0.8) mmol/L. Consumption of DDD of lipid-lowering drugs increased by 0.2 (CI, 0.04–0.3) in the primary care intervention group and 0.3 (CI, 0.2–0.5) in the specialist group ($p < .03$; Figure 2) but did not change in the primary care control group 0.0 [CI, −0.1–0.1].

Costs

The costs of CML—seminar time of GPs and travel, planning, and seminar time of the facilitator—in the intervention group were US$ 3.3 per treated patient during the 2 years of the study (Table 3). Costs of lipid-lowering drugs were US$ 106 during the second study year in the intervention group (Table 4) as opposed to US$ 52 in the control group. This finding means that the increase in costs of lipid-lowering drugs was US$ 47 higher per patient and year in the primary care intervention group than in the primary care control group. Total costs for lipid-lowering drugs and CML in the intervention group were US$ 154 during the 2 years and US$ 87 in the control group. As a comparison, the costs of lipid lowering were US$ 307 in the external specialist control group. The additional costs of the educational intervention did only represent 2 percent of the drug cost (Tables 3 and 4).

Table 1. Baseline Characteristics of Primary Health Care Centers and General Practitioners in Intervention and Control Groups

Characteristic	Intervention	Control
No. of general practitioners	26	28
Mean (SD) age (yr)	47.0 (6.3)	46.4 (4.8)
No. (%) women	9 (35)	9 (32)
No. (%) specialized in general medicine	26 (100)	28 (100)
No. of physicians with known relation to a physician in other group	0	0
No. of included patients	43	45
No. of included patients per physician [median (range)]	1 (0–4)	1 (0–5)
No. of primary health-care centers	7	7
No. of primary health-care centers with:		
1–3 physicians	3	3
4–5 physicians	3	2
>5 physicians	1	2
<5,000 inhabitants	2	2
5,000–9,999 inhabitants	2	3
>10,000 inhabitants	3	2
Mean population income[a]		
<150 kSEK	1	1
150–199 kSEK	5	4
>199 kSEK	1	2
Urban population	5	5
Mixed urban and rural population	2	2

[a] Part of the population > 16 years of age (kSEK = 1,000 Swedish Crowns).

Quality of Life

Quality of Life according to EQ-5D was 0.80 (CI, 0.75–0.85) in the intervention group at baseline and did not change during the study (Table 4). In the control group, EQ-5D was 0.79 (CI, 0.71–0.86) at baseline and 0.76 (CI, 0.71–0.86) at 2 years (not significant). The EQ-5D in the specialist group at baseline was slightly lower than for patients treated in primary care ($p = .048$). In the specialist group, EQ-5D increased ($p = .03$) from 0.72 (CI, 0.69–0.76) to 0.76 (CI, 0.73–0.80). There were no significant differences between the groups at the end of the study.

DISCUSSION

We have shown that the use of CML improves the quality of care of the patients at only a marginal additional cost of 2 percent of the drug cost. It can be argued that the effect of the CML strategy is that more patients suitable for lipid

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Table 2. Baseline Characteristics of Patients

Characteristics	Total (n = 255)	Intervention group (n = 45)	Control group (n = 43)	Specialist group (n = 167)
Mean (SD) age (yr)	60.1 (7.5)	62.6 (6.1)	62.3 (7.4)	59.0 (7.6)
Female sex	57 (22)	8 (18)	5 (12)	44 (26)
Family history of coronary artery disease	97 (38)	13 (29)	15 (35)	69 (41)
Diabetes	37 (15)	5 (11)	6 (14)	26 (16)
Hypertension	67 (26)	16 (36)	10 (23)	41 (25)
History of stroke	3 (1)	0	0	3 (2)
History of peripheral artery disease	5 (2)	0	2 (5)	3 (2)
History of comorbidity	71 (28)	11 (24)	12 (28)	48 (29)
Smoking status				
Never smoked	107 (42)	21/44 (48)	17 (40)	69 (41)
Ex-smoker	85 (33)	13/44 (30)	16 (37)	56 (34)
Current smoker	61 (24)	10/44 (23)	9 (21)	42 (25)
Mean (SD) body mass index (kg/m^2)	28 (4.2)	28.1 (5.5)	27.2 (3.4)	28.1 (3.9)
Mean (SD) waist:hip ratio	0.95 (0.1)	0.96 (0.1)	0.96 (0.1)	0.94 (0.1)
Mean (SD) systolic blood pressure (mm Hg)	139 (20)	142 (19)	139 (20)	138 (21)
Mean (SD) diastolic blood pressure (mm Hg)	84 (9)	84 (10)	85 (8)	84 (9)
Mean (SD) duration of coronary artery disease (yr)	6.0 (5.6)	5.6 (5.8)	6.2 (5.9)	6.0 (5.4)
History of myocardial infarction	167 (65)	29 (64)	23 (53)	115 (69)
History of coronary artery bypass graft surgery	95 (37)	12 (27)	13 (30)	70 (42)
History of percutaneous coronary intervention	29 (11)	2 (4)	3 (7)	24 (14)
Current angina (n = 250)				
CCS 0	100 (39)	18/42 (43)	25 (58)	57 (34)
CCS 1	47 (18)	7/42 (17)	4 (9)	36 (22)
CCS 2	75 (29)	15/42 (36)	7 (16)	53 (32)
CCS 3	17 (7)	2/42 (5)	4 (9)	11 (7)
CCS 4	11 (4)	0	2 (5)	9 (5)
Use of cardiovascular drugs				
Acetyl salicylic acid	205 (80)	38/44 (86)	33 (77)	134 (80)
β-blockers	166 (65)	25 (56)	21 (49)	119 (71)
Lipid lowering drugs	49 (19)	6/44 (14)	3 (7)	40 (24)
Mean (SD) lipid concentrations (mmol/L)				
Total cholesterol	6.4 (1.1)	6.3 (1.0)	6.2 (1.0)	6.4 (1.2)
Triglycerides	2.1 (1.1)	2.1 (1.2)	2.1 (1.0)	2.1 (1.1)
High density lipoprotein cholesterol	1.2 (0.3)	1.2 (0.4)	1.1 (0.3)	1.2 (0.3)
Low density lipoprotein cholesterol	4.2 (1.0)	4.2 (0.8)	4.1 (1.0)	4.3 (1.0)

Values are numbers (percentages) unless stated otherwise. No significant difference between intervention and control groups for any parameter. CCS, Canadian Cardiovascular Society classification system of current angina pectoris symptoms.

lowering actually start and continue treatment. The extra cost for achieving this end is the cost of the educational program that amounts to US$ 3.3 per patient. What is shown in earlier studies is that secondary prevention is cost-effective (12;13). Only adding a small investment cost for the educational program should not change this conclusion.

To expand a bit further on this, the cost-effectiveness of the CML strategy compared with the control could be viewed in terms of the 4S-study (2). In the 4S-study, the patients LDL cholesterol was reduced by 1.7 compared with control. The average follow-up time in that study was 5.5 years. The increase in life years was estimated at 0.377, whereas the increase in the number of discounted life years (5 percent discount rate) amounted to 0.240 (13).

LDL cholesterol in the present study was reduced at a fraction of 0.29 (0.5/1.7) compared with the 4S-study. A total of 0.5 mmol/L may sound a rather marginal lipid lowering compared with the 1.7 mmol/L in the 4S-study. There are, however, several aspects strengthening the argument that the lipid lowering in the present study is of clinical relevance. The 4S-study was a randomized controlled trial with the intention to give all patients in the active group statin treatment. In the present study, the intention was to give all physicians in the active group education with the purpose to increase statin treatment in their CAD patients. The mean lipid lowering is calculated in the whole group of patients and not only in the subgroup who actually got treatment (the proportion of patients treated with statin increased by 20 percent in the intervention group). This finding means that the patients—who actually had statin treatment instituted during the study—had at least the same lipid lowering as shown to be of clinical significance in the 4S-study. Furthermore, it is known that the clinical benefit from statin treatment is related to baseline risk rather than to actual lipid levels (20). The patients in the present study all had a high baseline risk.

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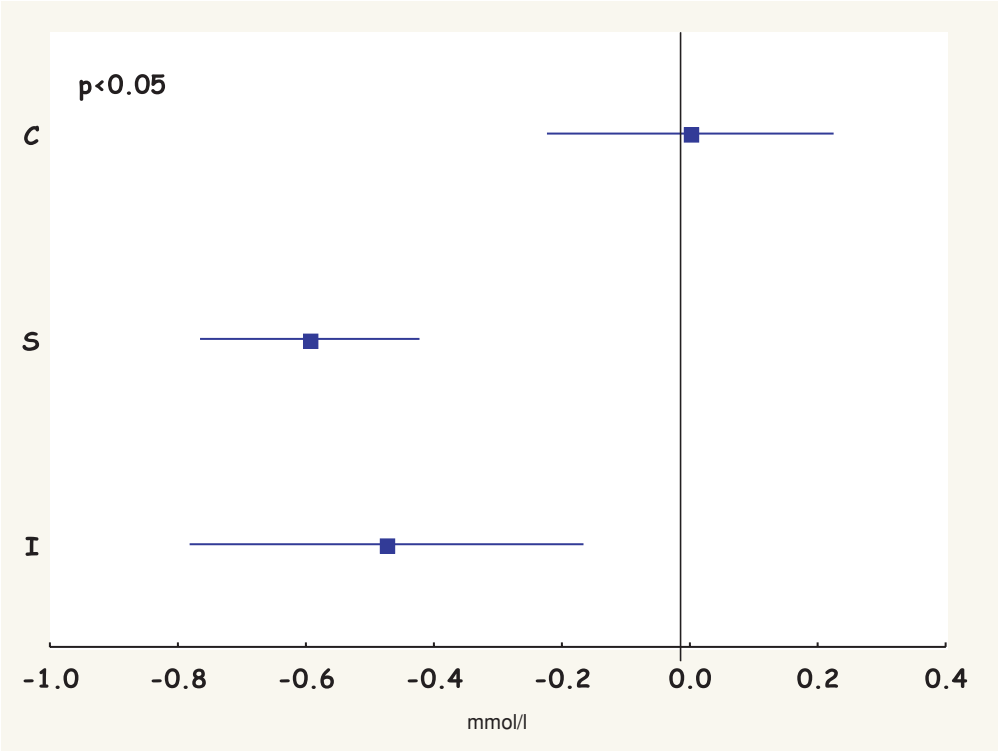

Figure 1. Decrease in low-density lipoprotein cholesterol (mmol/L) at 2 years compared with baseline in the intervention (I), control (C), and specialist (S) groups. Means and 95 percent confidence intervals.

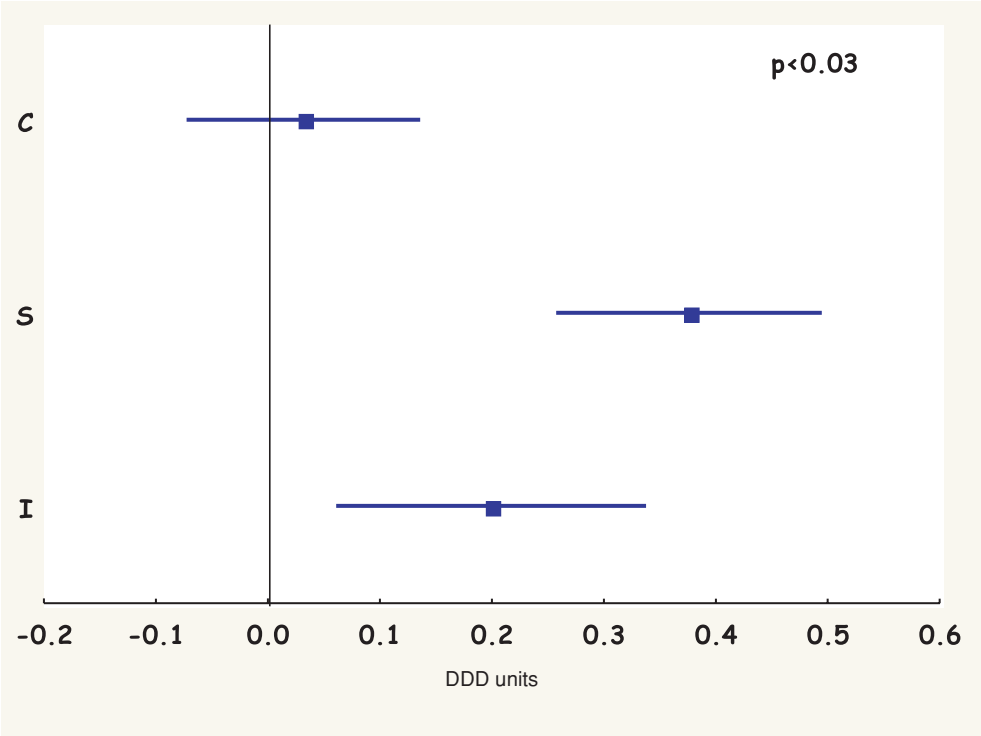

Figure 2. Increase in defined daily doses (DDD) of statins at 2 years as compared with baseline in the intervention (I), control (C), and specialist (S) groups. Means and 95 percent confidence intervals.

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Table 3. Resource Consumption of CML in the Intervention Group

	Total time	Time/ year/GP	Total cost	Cost/ year/GP	Cost per CAD patient
GPs CML (seminar time)	73.7	1.4	3,047.0	58.6	
Facilitator CML (travel, planning, and seminar time)	61	1.2	2,436.1	46.8	
Total CML education	134.7	2.6	5,483.1	105.5	3.3

A Case Method Learning (CML) seminar lasted for 1 hour 3–4 times during the 2-year study period at participating primary health-care centers. Four to seven general practitioners (GPs) participated at each seminar (attendance rate > 82%). Mean salary/hour, including pay roll tax, for GPs, respectively, consultants in Stockholm County Council, Sweden, as of year 2002 is used in the calculations. Time is assessed in hours. Cost is given in US$ with an exchange rate of 9.5 SEK = 1 US$ (2002). Cost per patient with coronary artery disease (CAD) is calculated based on prevalence of CAD patients under treatment at involved primary health-care centers in the catchment area (n = 1,667).

Table 4. Results at Patient Level

	Intervention group (n = 45)	Control group (n = 43)	Specialist group (n = 167)	*p* value
BL LDL (mmol/L)	4.2 (4.0–4.5)	4.1 (3.8–4.4)	4.3 (4.1–4.4)	ns
2Y LDL (mmol/L)	3.7 (3.4–4.0)	4.1 (3.8–4.4)	3.6 (3.4–3.8)	0.025[a]
CH LDL (mmol/L)	−0.5 [−0.8–(−0.2)]	0.0 [−0.2–(+0.2)]	−0.6 [−0.8–(−0.4)]	0.004[a]
BL $DDD_{Statins}$	0.1 (0.0–0.1)	0.1 (0.0–0.2)	0.1 (0.1–0.20)	ns
2Y $DDD_{Statins}$	0.3 (0.1–0.4)	0.1 (0.0–0.3)	0.5 (0.4–0.6)	0.0026
CH $DDD_{Statins}$	0.2 (0.1–0.3)	0.0 [−0.1–(+0.1)]	0.4 (0.3–0.5)	0.0081[a]
BL $DDD_{Tot\ lipid\text{-}lowering\ drugs}$	0.1 (0.0–0.2)	0.1 (0.0–0.2)	0.2 (0.2–0.3)	ns
2Y $DDD_{Tot\ lipid\text{-}lowering\ drug}$	0.3 (0.1–0.5)	0.1 (0.0–0.3)	0.6 (0.5–0.7)	0.0005
CH $DDD_{Tot\ lipid\text{-}lowering\ drug}$	0.2 (0.0–0.3)	0.0 [(−0.1)–(+0.1)]	0.3 (0.2–0.5)	0.023
BL Cost lipid-lowering drugs	44.7	35.5	104.6	
2Y Cost lipid-lowering drugs	105.8	51.7	202.1	
CH Cost lipid-lowering drugs	59.2	12.7	90.5	
Cost per mmol decrease in LDL[b]	106.1	—	153.3	
BL EQ-5D[c]	0.80 (0.75–0.85)	0.79 (0.71–0.86)	0.72 (0.69–0.76)	
2Y EQ-5D[c]	0.80 (0.75–0.86)	0.76 (0.67–0.85)	0.76 (0.73–0.80)	

[a] Analysis of variance by group.
[b] Cost in the intervention group includes the time cost for the Case Method Learning seminars.
[c] EQ-5D: EuroQol 5D Index scale (0–1) where high values indicate good health-related quality of life.
BL, values at baseline (total study population); 2Y, values at follow up after 2 years (patients completing the study); CH, the difference between baseline and follow up for the patients who complete the study; LDL, low density lipoprotein cholesterol; DDD, defined daily doses; Cost lipid-lowering drugs, calculated per patient year (statins comprise > 90% of the costs); ns, not significant.

We can assume that the increase in life years in this study is equal to the increase in life years found in the 4S-study multiplied by the fraction of 0.29. Thus, the increase in the number of life years comparing CML with the control for a period of 5.5 years is 0.11 (0.29 ∗ 0.377), whereas the increase in the number of discounted life years is 0.07 (0.29 ∗ 0.24). Adjusting the life years with the quality of life during these years (0.8) results in an increase in the number of QALYs of 0.0875 (0.29 ∗ 0.377 ∗ 0.8), whereas the increase in the number of discounted QALYs is 0.0557 (0.29 ∗ 0.24 ∗ 0.8).

The increase in costs during the study period is equal to US$ 3.3 (education) + US$ (59.2–12.7), which is the annual increase in costs for lipid-lowering drugs during the 2 year study period. The total cost increase during the same follow-up period as in the 4S-study would be equal to 3.3 + 5.5 ∗ (59.2–12.7), which amounts to US$ 256. The corresponding discounted cost increase is US$ 233. From a societal perspective, also costs in added years of life should be included (15). The costs in added years of life are defined as the difference between annual production and consumption in different age groups. Assuming an extra annual cost in added years of life for patients in this study of US$ 16,000 will result in an extra costs per patient of US$ 1,120 (0.07 ∗ 16,000), because consumption exceeds production in gained life years (7). Thus, the total extra discounted costs of CML strategy compared with the control is equal to US$ 1,353.

The resulting discounted cost per gained QALY is then equal to US$ 24,300 = 1,353/0.0557, which is below what is generally accepted as the value of a gained QALY. The value of a gained QALY is usually stated to be approximately US$ 60,000 (10;11). Thus, it is indicated that the CML-supported lipid lowering is a cost-effective strategy in secondary prevention of CAD in primary care.

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CONCLUSIONS

We have shown that CML for physicians in primary care is a cost-effective educational method to implement new evidence in the local context and content of the target physicians. CML resulted in a lipid lowering at a degree that, according to the results in the 4S-trial (2), should decrease mortality and morbidity (14).

Policy Implications

The main finding in the present study is an increase in the quality of care—at only a marginal increase in the cost—by use of the well-established educational method CML. Our findings should probably warrant the use of CML to decrease quality gaps in the care of other major chronic diseases.

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