Lipid-lowering therapy using statins in patients with cardiovascular risk in clinical practice in Thailand

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ABSTRACT

Background Since the release in Thailand in 2001 of the Third Guidelines by the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation and Treatment of High Blood Cholesterol in Adults or the Adult Treatment Panel (ATP III), there have been no nationwide studies on the proportion of dyslipidaemic patients who have achieved the low-density lipoprotein cholesterol (LDL-C) goals. The authors therefore aimed to estimate the percentage achievement of LDL-C goals based on the modified NCEP ATP III guidelines in intermediate- to high-risk patients.

Methods The authors conducted a hospital-based, cross-sectional, epidemiological survey. Patients (1240) were selected consecutively from 50 hospitals across Thailand. Patients were included if they had been treated with statins for at least 3 months.

Results Two-thirds were female, and the mean age was 61.7±9.5 years. The median duration of statin treatment was 21 months. Half (633/ 1240) of the patients achieved the LDL-C goal levels as defined by the NCEP guidelines (51.1%, 95% CI 48.3% to 53.8%). The very-high-risk group had the lowest percentage achievement (11.6%; 95% CI 1.6% to 21.6%), compared with 54.2% (95% CI 50.9% to 57.4%) for the high-risk group and 47.0% (95% CI 41.1% to 52.8%) for the moderate-risk group. More males achieved the LDL-C goals than females (55.6% vs 48.9%; p=0.029).

Conclusions Overall, 51.1% of the patients with cardiovascular risk, on statins treatment, achieved the NCEP ATP III LDL-C goal levels.

INTRODUCTION

Elevated, low-density, lipoprotein cholesterol (LDL-C) is a major risk factor of coronary heart disease (CHD): it is possible, however, to reduce it. Since 1993, the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel or ATP) has periodically updated the treatment guidelines which identify LDL-C as a cause of CHD and the primary aim for diagnosis and treatment of hypercholesterolaemia.[1–2]

In 2001, the latest recommendations were released in the Third ATP Report (NCEP ATP III),[3] which reaffirmed the risk of CHD from increased LDL-C, the benefit of LDL-C-lowering therapy and maintaining intensive treatment of patients with CHD. The report also added a call for more intensive LDL-C-lowering therapy as the primary aim for patients with a CHD risk equivalent. Although the guidelines have been widely available, achieving the lower LDL-C goals in practice has been suboptimal. In a US study, only 38% of 4888 patients under primary care in five regions achieved the LDL-C target levels.[4] The respective success rates were 68% and 37% in the low- and high-risk groups. Only 18% of the patients with established CHD with the highest risk of future CHD events achieved the lower LDL-C targets. Another study, based on the records of 461 patients in rural areas, covering all risk levels from four practices, found that only 54% of dyslipidaemic patients achieved the NCEP ATP III goals.[5] In 1998, a survey in Thailand assessing the achievement of LDL-C goals in high-risk patients indicated an unsatisfactorily low percentage of 39.2%.[6] The most recent nationwide survey was conducted between December 2002 and June 2003.[7] The study involved 1921 patients from 48 hospitals across Thailand. Percentage achievements of LDL-C targets in the CHD and CHD equivalents, high-, and low-risk group were 34.6%, 56.4% and 76.8%, respectively.[7] In 2004, several changes were made to the guideline, released as the Modified NCEP ATP III in that year.[8] There has, however, been no recent nationwide study in Thailand investigating the proportion of dyslipidaemic patients who have achieved the updated LDL-C goals.

Our study aimed to estimate the percentage of LDL-C goals achievement based on the NCEP ATP III guidelines in intermediate- to high-risk patients receiving statins for at least 3 months in clinical practice in Thailand.

METHODS

This was a hospital-based, cross-sectional, epidemiological survey and retrospective chart review, in both secondary and tertiary care across Thailand (http://ClinicalTrials.gov Identifier: NCT00684151). The hospitals studied were randomly selected using a simple random scheme generated by Stata V.10 Statistical Software (StataCorp). Each hospital selected was evaluated as to whether it had diabetes or any other types of outpatient clinics that involved lipid-lowering drug prescriptions. If not, it was replaced by another hospital based on the stated sampling method. This process was repeated until a total of 50 hospitals were selected, which represents approximately half of the total number of secondary- and tertiary-care hospitals in Thailand. The investigators, who were not attending physicians, were confidentially scheduled to do the data collection, and the selected hospitals were informed that the physicians would be attending 1 week prior to the date of data

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collection. Lipid levels were based on an analysis conducted by local laboratories on the day of the data collection, if not available on the most recent visit.

Primary outcome

The primary outcome of this study was the percentage of dyslipidaemic patients on lipid-lowering therapy who had achieved their respective LDL-C target levels as defined by the NCEP ATP III guidelines (table 1).

Criteria for study subject selection

The data collection was conducted at the selected hospitals between March and July 2008, where patients were selected consecutively as they attended hypertension or diabetes clinics. The maximum number of patients per site was 40.

Patients enrolled in the study were outpatients seen in the hypertension or diabetes clinics, between 20 and 80 years of age, having at least one established risk factor, viz., coronary artery disease, postmyocardial infarction, acute coronary syndrome, peripheral artery disease, poststroke, CHD risk equivalent (ie, abdominal aortic aneurysm, diabetes mellitus, and peripheral vascular disease) or type 2 diabetes mellitus, and had been on the same type of statin as treatment of dyslipidaemia for at least 3 months.

Study procedures

The study was conducted in full conformity with Good Clinical Practice, and the investigators obtained Institutional Review Board approval prior to conducting the study. All subjects were informed about the study's purpose and thereafter signed an informed consent form.

Each subject was screened for eligibility for the study. The data-collection process involved a face-to-face interview with each subject and a review of medical records. Laboratory results were transcribed from the medical records.

Statistical analysis

The results of two previous studies in Thailand, conducted in 1998 and 2003,[6 9] suggest that the respective rates of achieving the lower LDL-C targets among the high-risk group were 39% and 35%. Our sample size calculation was based on the latter using methods suggested by Kish.[10] A sample size of 1260 was therefore planned. The study was conducted in 50 hospitals, each of which enrolled between 10 and 40 patients depending on case availability on the date the survey was conducted.

The percentage achievement of LDL-C goals and 95% CIs (95% CI) were estimated based on normal approximation to binomial distribution. We estimated the effect of selected factors on the LDL-C goals achievement using multiple logistic regressions performed by Stata version 10. The level for statistical significance was set at 0.05.

RESULTS

Number of patients and participating hospitals

There are 95 secondary- and tertiary-care hospitals across Thailand, 50 (52.6%) of which were selected for the study. The number of selected hospitals in each region was proportional to the total number of eligible hospitals in each region (ie, the North, the Northeast, the South and Central). A total of 1730 patients attending OPD clinics were screened by interviews, and 167 (9.6%) were excluded: 161 not currently treated with statin, five not consented and one not within 20–80 years of age (figure 1). After the chart review was conducted, a further 323 (20.7%) cases were excluded: 216 treated <3 months before lipid profile became available, 32 lipid profile not available and 75 having not received the same statin before lipid profile became available. The final number of subjects included in the analysis was 1240.

Time from the most recent lipid profile to data collection

The duration between the date of data collection and the most recent lipid profile ranged between 0 and 41 months (median 5.5 months). The treatment outcome was measured at a mean of 5.5 months prior to the study date.

Duration of statin treatment prior to the most recent lipid profile

The duration of statin treatment prior to the date of the most recent lipid profile ranged between 3 and 191 months (median 21 months), which represented the period of statin treatment at the time of assessing the treatment outcome.

Patients characteristics

The high-risk group accounted for the largest number of patients, followed by moderate- and high-risk patient types. The mean age was 61.7±9.5 years, and approximately two-thirds were female (table 2). The mean age of each risk group was similar. For each sex, the percentage distribution was similar across all risk groups. Overall, the majority of males at risk (94%) were 45 years of age or higher. A similar percentage was seen in each risk group. For females at risk, about three-quarters were aged 55 years or older. Most common cardiovascular risks were diabetes mellitus (66.1%) and hypertension (57.6%).

Treatments at the most current visit

More than 90% of the patients received statins without any other lipid-lowering drugs (table 3). Simvastatin was used by 85.4% of the patients, and about 89.0% of the patients had been treated for more than 6 months. Almost all of the attending physicians (99.0%) were mainly internal medicine non-subspecialists (84.1%).

Table 1 Treatment goal definitions

Risk categories	Definitions	Low-density lipoprotein cholesterol goals (mg/dl)
Very high risk	Postmyocardial infarction with diabetes mellitus, poststroke with diabetes mellitus, peripheral arterial disease with diabetes mellitus, poststroke with myocardial infarction, poststroke with peripheral arterial disease and postmyocardial infarction with peripheral arterial disease	<70
High risk	Coronary artery disease, cardiovascular diseases, poststroke and diabetes mellitus	<100
Moderate risk	≥2 risk+(hypertension or dyslipidaemia)	<130
Low risk	0–1 risk+(hypertension)	<160

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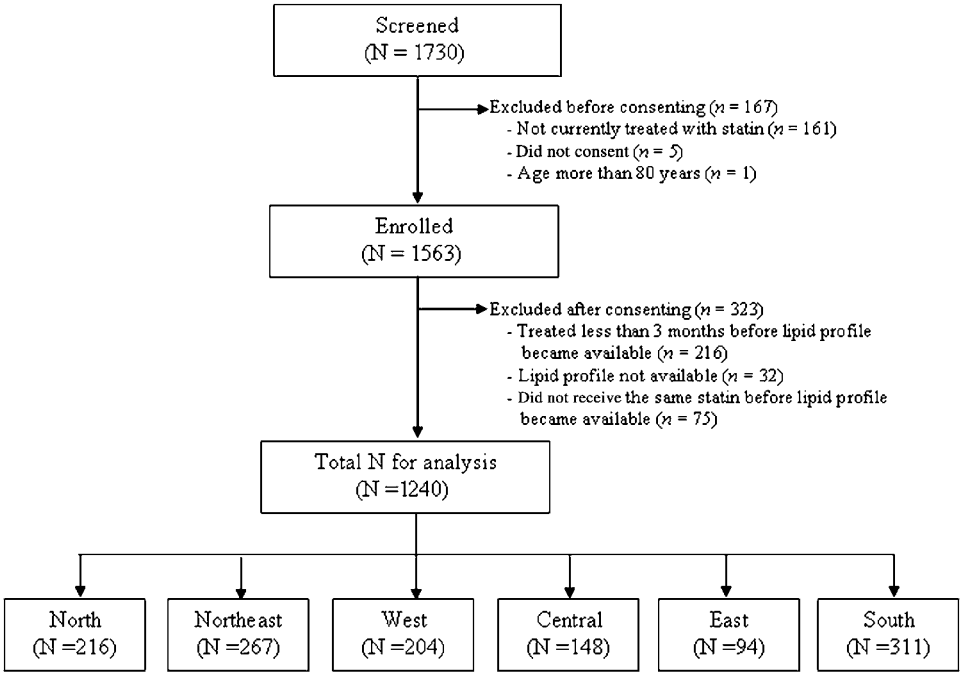

Figure 1 Flow of patients in the study, with number of patients included and reasons for exclusion.

Achievement of LDL-C treatment goals

Percentage achievement of LDL-C goals for all patients

Among the 1240 patients, 633 achieved the lower LDL-C goals as defined by the NCEP ATP III guidelines (51.1%; 95% CI 48.3% to 53.8%) (table 4). The very-high-risk group had the lowest achievement level at about one tenth. The achievement rate varies among regions where the highest achievement rate was 57.4% in the central area, and the lowest achievement rate was 42.6% in the eastern part of the country. On average, the very-high-risk patients were about half, 49.7%, to reach the LDL-C target goal.

Percentage LDL-C goals achievement by selected factors

Males had a statistically higher percentage achievement of the lower LDL-C goals than females (p=0.024) (table 5). The duration of statin treatment and the statin use, either alone or combined with other regimens, had a similar percentage achievement of lower LDL-C goals.

DISCUSSION

The efficacy of statins in atherosclerotic conditions, particularly in the treatment and prevention of CHD, has been well established. Large-scale, randomised, prospective trials involving patients with CHD have shown that statins reduce the clinical consequences of atherosclerosis, including cardiovascular-related deaths, non-fatal MI and stroke, hospitalisation for acute coronary syndrome and heart failure, as well as the need for coronary revascularisation.[11–13]

The Heart Protection Study demonstrated that LDL-C reduction to levels as low as 1.7 mmol/l was associated with significant clinical benefits in a wide range of high-risk individuals, including patients with type 2 diabetes mellitus, or

Table 2 Patient characteristics by patient group, shown as number (%) unless specified otherwise

Characteristics	Very high	High	Moderate	Total
Mean (SD) age, years	n=43	n=914	n=283	n=1240
	61.0 (10.3)	61.5 (9.5)	62.7 (9.3)	61.7 (9.5)
Sex, total	n=43	n=914	n=283	n=1240
Male	17 (39.5)	303 (33.2)	97 (34.3)	417 (33.6)
Female	26 (60.5)	611 (66.8)	186 (65.7)	823 (66.4)
Male at risk by age (years), total	n=17	n=303	n=97	n=417
≥45	16 (94.1)	286 (94.4)	92 (94.8)	394 (94.5)
<45	1 (5.9)	17 (5.6)	5 (5.2)	23 (5.5)
Female at risk by age (years), total	n=26	n=611	n=186	n=823
≥55	22 (84.6)	462 (75.6)	139 (74.7)	623 (75.7)
<55	4 (15.4)	149 (24.4)	47 (25.3)	200 (24.3)
Cardiovascular risks	n=43	n=914	n=283	n=1240
Coronary artery disease, myocardial infarction and acute coronary heart syndrome	22 (51.2)	190 (20.8)	0 (0)	212 (17.1)
Stroke	14 (32.6)	13 (1.4)	0 (0)	27 (2.2)
Peripheral artery disease	11 (25.6)	2 (0.2)	0 (0)	13 (1.1)
DM	42 (97.7)	774 (85.2)	0 (0)	816 (66.1)
Hypertension	28 (65.1)	514 (56.2)	172 (60.8)	714 (57.6)

Very-high-risk patients had postmyocardial infarction with diabetes mellitus (DM), poststroke with DM or peripheral artery disease with DM. High-risk patients had coronary artery disease, cardiovascular disease, poststroke or DM. Moderate-risk patients had two or more risks plus either hypertension or dyslipidaemia.

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Table 3 Treatment pattern by patient group shown as number (%)

Treatments	Very high (n=43)	High (n=914)	Moderate (n=283)	Total (n=1240)
Statin prescriptions				
Statins only	39 (90.7)	847 (92.7)	270 (95.4)	1156 (93.2)
Statins with other lipid-lowering drugs	4 (9.3)	67 (7.3)	13 (4.6)	84 (6.8)
Type of statins				
Pravastatin	0 (0.0)	3 (0.3)	0 (0.0)	3 (0.2)
Simvastatin	38 (88.4)	798 (87.3)	223 (78.8)	1059 (85.4)
Atorvastatin	1 (2.3)	66 (7.2)	32 (11.3)	99 (8.0)
Rosuvastatin	4 (9.3)	47 (5.1)	28 (9.9)	79 (6.4)
Duration (months) of statin treatment				
3–6	4 (9.3)	93 (10.2)	39 (13.8)	136 (11.0)
7–12	10 (23.3)	174 (19.0)	61 (21.6)	245 (19.8)
13–24	13 (30.2)	254 (27.8)	82 (29.0)	349 (28.1)
25–36	11 (25.6)	170 (18.6)	54 (19.1)	235 (19.0)
≥37	5 (11.6)	223 (24.4)	47 (16.6)	275 (22.2)
Field of expertise of the attending physicians				
Internal medicine	41 (95.3)	905 (99.0)	281 (99.3)	1227 (99.0)
General	26	755	248	1029
Cardiologist	13	90	25	128
Endocrinologist, nephrologists or neurologist	2	58	7	67
Unspecified	0	2	1	3
Non-internal medicine	2 (4.7)	9 (1.0)	2 (0.7)	13 (1.0)

Very-high-risk patients had postmyocardial infarction with diabetes mellitus (DM), poststroke with DM or peripheral artery disease with DM. High-risk patients had coronary artery disease, cardiovascular disease, poststroke or DM. Moderate-risk patients had two or more risks plus either hypertension or dyslipidaemia.

peripheral artery disease and cerebrovascular diseases, irrespective of baseline cholesterol levels. There was no apparent lower threshold for LDL-C with respect to risk. In our study, we estimated the percentage of achieving LDL-C goals based on the NCEP ATP III guidelines in patients receiving statins for at least 3 months in clinical practice in Thailand.

Initially, the calculated sample size was 1260, of which 20 (1.8%) patients had a statin treatment of <3 months. These were identified after enrolment and excluded from the analysis. This elimination did not, however, affect the study findings, that is, the percentage achievement of LDL-C goals was 52.5% when they were included, compared with 51.1% when they were excluded.

We, thus, included only patients who had been treated for at least 3 months with no maximum limit of treatment duration. The results in table 5 indeed suggest that the duration of statin treatment had no effect on the percentage achievement of LDL-C goals, which was about 51% for every interval of 12 months (p=0.975). However, there are numerous factors which may confound the goal achievement, including statin dose, potency of statin, culture, socio-economic status, healthcare policy, concomitant medications, etc. Also, the selection bias from selected study sites, which were from diabetes and hypertention clinics even we tried to do the study in various parts of the country. This leads to a higher proportion of high-risk group than general populations.

Our study was based on the availability of lipid profiles of patients measured on request, as per real-life clinical practice; however, there were no significant differences between the percentage achievement of LDL-C goals among patients whose lipid profile was assessed before or after the median of 5.5 months prior to the survey date. This result might indicate that LDL-C levels were underutilised to adjust the treatment.

In our study, the percentage of lowered LDL-C according to goal levels, as defined by NCEP ATP III guidelines, among the high-cardiovascular-risk group, was 51.1% compared with 39.2% in a 1997–1998 study[6] and 34.6% in the 2002–2003 study.[9] The higher percentage found in our study could be due to various reasons: (1) we included only patients who used statins and not any other lipid-lowering agent alone; (2) there has been an increasing focus on the benefits of intensive cholesterol reduction; (3) new and more efficacious statins have been developed; (4) 95% of the patients in our study were attended by specialists who might be more likely to adhere to the guidelines; and (5) two-thirds of the patients in our study were females, who might have had a greater rate of compliance to the treatment or might have had a greater response to therapy than males, although there are few data to support this. As with other studies, our study found that the lowest percentage of achieving the recommended LDL-C target was in the very-high-risk group.[6 9]

A number of aspects of our study can be considered strengths. First, the case selection was unbiased, as it was carried out

Table 4 Percentage and 95% CIs of low-density lipoprotein cholesterol (LDL-C) achievement goals by patient group

Patient groups*	Total	Achieved goals	Percentage	95% CI	Mean percentage† to target LDL-C
Very high risk	43	5	11.6	1.6 to 21.6	49.7
High risk	914	495	54.2	50.9 to 57.4	31.8
Moderate risk	283	133	47.0	41.1 to 52.8	9.9
Overall	1240	633	51.1	48.3 to 53.8	27.5

*Very high risk (LDL-C<70 mg/dl); high risk (LDL-C<100 mg/dl); moderate risk (LDL-C<130 mg/dl).
†Calculated based on the percentage difference between LDL-C level and the target goal among patients who did not achieve the LDL-C target.

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Table 5 Percentage low-density lipoprotein cholesterol achievement goals by selected factors

Selected factors	No	Percentage achievement	p Value
Sex			0.029
Male	417	55.4	
Female	823	48.9	
Male by age (years) at risk			0.750
≥45	394	55.6	
<45	23	52.2	
Female by age (years) at risk			0.057
≥55 of age	623	50.7	
<55	200	43.0	
Duration (months) of statin treatment			0.997
3–6	136	50.7	
7–12	245	51.0	
13–24	349	50.4	
25–36	235	51.9	
≥37	275	51.3	
Statins received			0.842
Statins only	1156	51.1	
Statins with other lipid-lowering drugs	84	50.0	
Field of expertise of attending physicians			0.360
Internal medicine	1227	51.2	
Non-internal medicine	13	38.5	
Field of expertise of attending physicians who were in internal medicine			0.598
General	1029	51.2	
Cardiologist	128	53.9	
Endocrinologist, nephrologists or neurologist	67	46.3	

consecutively and independent of the attending physicians. Second, we covered a large number (52.6%) of secondary- and tertiary-care hospitals across the country. Third, almost all of the studied patients (99.0%) were attended by an internal medicine specialist, particularly the very-high-risk and high-risk patients. Finally, our study represented real-life, clinical settings in Thailand, so the percentage achievement of LDL-C goals may represent clinical practice.

In summary, our study demonstrated that 51.1% of patients with cardiovascular risk on statin treatment achieved the LDL-C goal levels defined by the NCEP ATP III guidelines. We suggest that patients with a high CHD risk should be targeted for more aggressive lipid-lowering management. National campaigns to increase the awareness among both physicians and patients of the importance of achieving the LDL-C goals are needed to optimise the prevention of cardiovascular events and to further reduce the burden of cardiovascular diseases. Further investigation is needed to understand the reasons for patients not achieving lower LDL-C levels.

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Competing interests None.

Patient consent Obtained.

Ethics approval Ethics approval was provided by the ethical committees of the participating centres at local level. The Khon Kaen University Ethics Committee for Human Research.

Contributors SS: design and writing of the study protocol, interpretation of the results, writing and final approval of the manuscript. CS: writing and final approval of the manuscript. PR: writing and final approval of the manuscript. RK-N-A: writing and final approval of the manuscript. BT: implementation of the study, data collection, data analysis and drafting the manuscript. PS: reviewing and approval of the protocol, interpretation of the results, writing and final approval of the manuscript.

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