# Lipid Treatment Assessment Project II in Thailand (LTAP-II Thailand)

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**Objective:** Evaluate treatment practices and their outcomes in Thai patients with hyperlipidemia. The factors contributing to success of treatment were also determined.

*Material and Method:* A multi-center cross-sectional survey with the support of 98 physicians from 48 hospitals was done. Each physician enrolled up to 20 dyslipidemic patients by simple randomization.

**Results:** One thousand nine hundred twenty one cases, 45.1% males with a mean age of 58.6 years (SD = 9.6) were recruited. The patients were divided into three groups: 1,178 patients with coronary heart disease (CHD) and CHD equivalents, 424 patients with high risk, and 319 patients with low risk. The main targets for treatment were LDL-C levels of < 100, < 130 and < 160 mg/dL for each respective group. As a whole, the risk factors listed in order of frequency were age at risk (78%), hypertension (69.8%), diabetes mellitus (43.6%), smoking (24.6%), and family history of CHD (6.9%). Obesity (body mass index  $\ge 25$  kg/m<sup>2</sup>) was found in 53.8% of the patients. Twenty eight percent of the patients experienced CHD or other atherosclerotic diseases. Statin was the commonest prescribed drug (64%) followed by fibrate (25%). The overall success rate was 46.5%. Percentage of cases achieving LDL-C targets in the CHD and CHD equivalents, high and low risk group was 34.6%, 56.4%, and 76.8%, respectively. The patients in the low risk group, being under specialist care and receiving statin therapy reached target of treatment at a significantly higher rate.

**Conclusion:** The present study showed that statin was the most common drug used in the management of hyperlipidemia. Patients with CHD and CHD equivalents were the group with least achievement of LDL-C target. The factors contributing to achievement of LDL-C target were lower risk patient, specialist care, and statin therapy.

#### Keywords: Hypercholesterolemia, Treatment

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Multiple studies have exemplified the efficacy of lipid lowering drugs and showed that the reduction of low density lipoprotein cholesterol (LDL-C) also lowers coronary heart disease (CHD) risk through both primary<sup>(1)</sup> and secondary prevention studies<sup>(2,3)</sup>. These results and other landmark studies spawned an updated version of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults: Adult Treatment Panel (ATP) III<sup>(4)</sup>. This version and its subsequent recommendation<sup>(5)</sup> for clinical management of high blood cholesterol calls for a more intensive LDL-C lowering therapy as the primary focus in patients with CHD and CHD equivalents.

Prior to the dissemination of the NCEP ATP III Guidelines, numerous surveys throughout Australia (VIC I and II)<sup>(6)</sup>, Europe (EUROASPIRE I and II)<sup>(7)</sup> and the United States (Lipid Treatment Assessment Project, LTAP)<sup>(8)</sup> have all reported a wide variety of primary or secondary findings regarding the use of lipid-lowering drugs. Despite variations in the conditions of the target

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population, statins were the most prescribed lipidlowering medication. From these studies, the use of statins in those receiving lipid-lowering therapy ranged from 57.8% in the EUROASPIRE I to 97.4% in the VIC II survey.

CHD is one of the leading causes of death in Thailand since 1989 and mortality rates from CHD were rising<sup>(9)</sup>. It is vital that the treatment of high cholesterol and LDL-C be reached and be maintained at an optimal level. In contrast to the above surveys, the previous LTAP study in Thailand (1997-1998)<sup>(10)</sup> had revealed that the prescription rates of fibrates were higher in all risk groups compared to statins. Moreover, the study reported a lower overall success rate of 40.5%, with the rate of success of 11.9%, 39.2% and 72.7% in the CHD, high, and low risk groups, respectively. According to these data, a Lipid Education Program (LEP) Council was formed in 1999 by Thai cardiologists and endocrinologists. The training programs for the management of dyslipidemia were introduced to help increase awareness and to educate the physicians and the patients as well. Coupled with the updated NCEP ATP III Guidelines, it was anticipated that the training programs would increase effective therapy and better patients' compliance.

The second lipid treatment assessment project (LTAP-II) was therefore, conducted to reassess the percentage of Thai patients on therapy for hyperlipidemia who achieved NCEP ATP III target of treatment. The factors that contributed to achieving their target would also be examined.

#### **Material and Method**

#### Study design

The LTAP-II was a cross-sectional, randomized, nation-wide survey in Thailand between December 2002 and June 2003. The LTAP-II targeted secondary and tertiary care settings and physicians who regularly treated patients with dyslipidemia. The number of sampled hospitals for each region was in proportion with the number and type of hospitals in that region. The physicians in those sampled hospitals were invited to participate in the present study.

The subjects were considered successful if their LDL-C level determined at the entry of the study visit were at or below the target level determined by their risk group. The patients were classified into three groups by their cardiovascular risk factors according to NCEP ATP III recommendation<sup>(4)</sup>. The risk factors included age at risk (age  $\geq$  45 years for men,  $\geq$  55 years for women or premature menopause without estrogen

replacement therapy), family history of premature CHD (definite myocardial infarction or sudden death before 55 years of age in male first-degree relative or before 65 years of age in female first-degree relatives), current cigarette smoking, hypertension (blood pressure  $\geq 140/$ 90 mmHg or taking antihypertensive medication), low HDL-C level (< 0.91 mmol/L [35mg/dL]), and diabetes mellitus. High-density lipoprotein cholesterol (HDL-C) level of 1.55 mmol/L (60 mg/dL) or more was a "negative" risk factor, which allows subtracting 1 from the number of risk factors. The low-risk group included patients without CHD who had fewer than two risk factors (LDL-C target level was < 4.14 mmol/L [< 160 mg/dL]). The high-risk group included patients without CHD who had two or more risk factors (LDL-C target level was < 3.36 mmol/L [< 130 mg/dL]). The CHD group included all patients with a previous heart attack, bypass surgery, or angioplasty and CHD equivalents (LDL-C target level was  $\leq 2.59 \text{ mmol/L} [\leq 100 \text{mg/dL}]$ ).

#### Patient enrollment

Each physician enrolled up to 20 dyslipidemic patients who met the inclusion and exclusion criteria. Inclusion criteria consisted of dyslipidemic patients aged 20 to 75 years who were being maintained on the same therapy for at least 3 months, with dietary therapy with or without lipid-lowering drug regimens. The patients who had recent major trauma, recent surgery that required anesthesia, including coronary artery bypass graft or post-myocardial infarction (within 12 weeks before enrollment), acute infections that required antibiotic therapy (within 2 weeks), recent or abrupt changes in usual diet (within 4 weeks) were ineligible. Women who were pregnant, breast feeding, or 6 months or less post partum, and those who had an unstable medical condition or life expectancy of less than 6 months were also ineligible.

A written informed consent was obtained from each individual patient. The study protocol was approved by an institutional review board at each study site and was conducted in compliance with the ethical principles of the most recent version of the Declaration of Helsinki, the International Conference of Harmonization (ICH) of Good Clinical Practice (GCP) Guidelines and all local regulatory requirements.

#### Laboratory determination

Blood specimens were collected for assessment of lipid levels after the patient had been fasting for 9-12 hours. Lipid profiles including total cholesterol, HDL-C, and triglyceride were measured using a serological analysis conducted by certified local laboratories. LDL-C was obtained by calculation using Friedewald formula. Known lipid data measured before treatment were used to compare with those taken at the time of enrollment to the present study.

#### Statistical analysis

Descriptive statistics on the demographic and clinical data and the overall success rate are presented as mean  $\pm$  SD for continuous variables, as a number (percentage) for dichotomous variables. The Chi-squares test was utilized to see if the success incidences among the three risk groups were different. The statistical test was performed at the alpha level of 0.05, 2-tailed. The data was analyzed using logistic regression implemented under GEE's framework. Effect of risk level was also determined for each patient category. By this, the percent achievement of LDL-C targets by groups of the factor and odds ratios with 95% CI were presented. All analyses were performed using STATA 7 (College Station, TX).

#### **Results**

Forty-eight qualified hospitals across seven regions of Thailand were randomized and 98 physicians were invited to participate in the present study. The physicians consisted of 68 internists (69.4%), 26 cardiologists or endocrinologists (26.5%) and four non-internist (4.1%). Most cardiologists and endocrinologists (57.7%) worked in Bangkok (Table 1). The study enrolled 1,963 patients with 1,921 patients (97.9%) eligible for analysis.

Based on the risk categories of NCEP ATP III, there were 1,178 patients (61.3%) who established CHD and CHD equivalents, 424 high-risk patients (22.1%) and 319 low-risk patients (16.6%). In CHD and equivalents group, the frequency of patients who had disease (one risk factor), two, three, four, and five risk factors were 30.1%, 41.0%, 23.4%, 5.2% and 0.3%, respectively. The majority of patients (66.3%) in the high-risk group

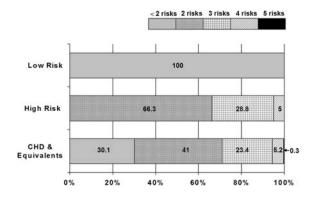


Fig. 1 Number of risk factors observed in each risk category

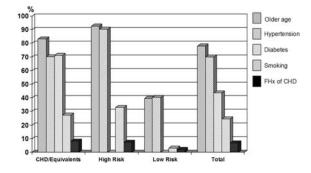


Fig. 2 Frequency of risk factors found in each risk category and all patients

had two risk factors while 28.8% had three risk factors and 5.0% had four risk factors (Fig. 1).

The most common risk found within the study population was age factor with 1,498 patients (78.0%) having age at risk as a risk factor (Fig. 2). The lowest risk factor found was having a family history of CHD, reported in 133 patients (6.9%).

The demographics of the patients are displayed in Table 2 with the low risk group having patients with the least mean age of 51.4 years. The CHD and equivalents and high-risk groups had a higher body mass index (BMI) and more obese patients.

Table 1. Profile of participating hospitals, physicians, and patients

Profile	North	North-east	Bangkok	Central	West	East	South	Total, n (%)
Number of hospitals	8	7	10	7	4	4	8	48
Number of physicians	17	14	20	15	8	8	16	98 (100)
Cardiologist or Endocrinologist	2	3	15	1	1	2	2	26 (26.5)
Internist	14	10	5	13	6	6	14	68 (69.4)
Non-Internist	1	1	0	1	1	0	0	4 (4.1)
Number of patients	336	278	373	297	160	159	318	1921

Characteristics	CHD or CHD risk equivalence (n = 1178)	High-risk (n = 424)	Low-risk (n = 319)	Total (n = 1921)
Age (mean $\pm$ SD)	$60.0 \pm 8.9$	$60.0 \pm 8.6$	$51.4 \pm 10.3$	58.6 <u>+</u> 9.6
Sex				
Male total number (%)	555 (47.1)	234 (55.2)	78 (24.5)	867 (45.1)
45 year or higher	509 (91.7)	219 (93.6)	40 (51.3)	768 (88.6)
Female total number	623 (52.9)	190 (44.8)	241 (75.5)	1054 (54.9)
55 year or higher	470 (75.4)	174 (91.6)	86 (35.7)	730 (69.3)
Height (mean $\pm$ SD)	159.7 <u>+</u> 8.2	$160.2 \pm 8.1$	158.0 <u>+</u> 7.3	159.5 <u>+</u> 8.1
Weight (mean $\pm$ SD)	$66.2 \pm 11.9$	66.7 <u>+</u> 11.8	62.3 <u>+</u> 10.9	65.6 <u>+</u> 11.8
Body mass index (mean $\pm$ SD)	25.9 <u>+</u> 3.9	25.9 <u>+</u> 3.9	24.9 <u>+</u> 3.8	25.7 <u>+</u> 3.9
Lower than 18.5 (underweight)	16 (1.4)	4 (0.9)	6 (1.9)	26 (1.4)
18.5-24.9 (acceptable weight)	510 (43.3)	181 (42.7)	170 (53.3)	861 (44.8)
25.0-29.9 (obese)	495 (42.0)	186 (43.9)	111 (34.8)	792 (41.2)
30 or higher (severe obese)	157 (13.3)	53 (12.5)	32 (10.0)	242 (12.6)
Consumes alcohol	228 (19.4)	115 (27.1)	53 (16.6)	396 (20.6)
History of CHD and/or a therosclerotic $\mbox{disease}^1$	544 (46.2)	0 (0)	0 (0)	544 (28.3)

 Table 2.
 Demographic characteristics of all patients

<sup>1</sup>Defined as any one or more of the following: angina pectoris, myocardial infarction, coronary revascularization, peripheral vascular disease, or abdominal aortic aneurysm or asymptomatic carotid artery disease

Lipid-lowering therapy	CHD or CHD risk equivalence (n = 1178)	High-risk (n = 424)	Low-risk (n = 319)	Total (n = 1921)
Overall therapy practice				
Drug not being used (%)	113 (9.6)	60 (14.2)	101 (31.7)	274 (14.3)
Statin (%)	772 (65.5)	223 (52.6)	159 (49.8)	1154 (60.1)
Fibrate (%)	224 (19.0)	124 (29.2)	54 (16.9)	402 (20.9)
Statin combined fibrate (%)	53 (4.5)	13 (3.1)	3 (0.9)	69 (3.6)
Others <sup>a</sup> (%)	16 (1.4)	4 (0.9)	2 (0.6)	22 (1.1)
Non-Pharmacologic therapy				
Dietary therapy				
Step I diet (%)	931 (79.0)	356 (84.0)	272 (85.3)	1559 (81.2)
Step II diet (%)	21 (1.8)	12 (2.8)	4 (1.3)	37 (1.9)
Exercise program (%)	572 (48.6)	272 (64.2)	193 (60.5)	1037 (54.0)

Table 3. The distribution pattern of lipid-lowering therapy in practice

<sup>a</sup> Includes any other drug or combination of another drug with statins or fibrates

The majority of the patients surveyed (n = 1,001 or 52.1%) had an education level of primary school or lower, resided in the provincial capitals and Bangkok (n = 1,079 or 56.2%), and had medical insurance stemming from the government or state enterprises (n = 1,078 or 56.1%).

As a whole, 1,647 patients (85.7%) were on drug therapy. Statins or combination of statins was the most common prescribed drug (64.0%) within all risk

groups. Fibrates were the second used drug. The majority of subjects (81.2%) were on the step I diet program while 54.0% of the patients regularly exercised (Table 3).

Among all patients who were taking statins (n = 1,229 or 64.0%), simvastatin was the medication that was taken at the highest frequency followed by atorvastatin, fluvastatin and pravastatin. With those taking fibrates (n = 475 or 24.7%), gemfibrozil was taken

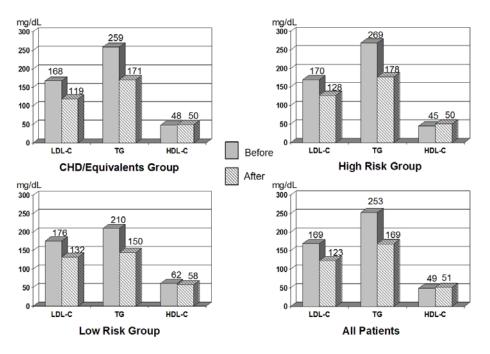


Fig. 3 Changes in the serum level of low density lipoprotein cholesterol (LDL-C), triglyceride (TG), and high density lipoprotein cholesterol (HDL-C) after therapy

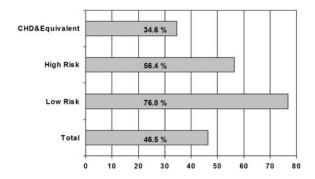


Fig. 4 Frequency of achieving low density lipoprotein cholesterol (LDL-C) target in each risk category and all patients

at the highest rate with the majority taken 600 mg/day. Fig. 3 illustrates the changes of LDL-C, triglyceride and HDL-C after therapy.

The rate of achieving LDL-C target according to the risk categories was highest (76.8%) in the lowrisk group and lowest (34.6%) in the CHD and CHD equivalent group (Fig. 4). The differences in the rate of achieving LDL-C goals in each group were statistically significant (p < 0.001). As a whole, achievement of LDL-C goal levels was significantly higher in the group of patients treated by cardiologists or endocrinologists than those treated by internists (56.6% vs. 41.8%, p < 0.001). Comparing the types of medication for the overall study population, the patients treated with statins alone or statin plus fibrate had a higher rate of achieving LDL-C goal level than other treatments (Table 4).

From all risk groups, cardiologists and endocrinologists had the highest achievement rates followed by internists. Similarly, all three risks groups also had the highest achievement ratings when prescribed statins alone. In the CHD and CHD equivalents and the high risk group, the combination of statins and fibrates were the next treatment providing achievement to target (p = 0.004 and p = 0.035, respectively). The patients in the low risk group who used fibrates, unlike the other two groups, also had significant achievement levels (Table 5).

According to the NCEP ATP III definition of non-HDL cholesterol, it was found that 570 (52.6%) of the 1,083 patients who had triglyceride levels of 200 mg/dL or more, had achieved their non-HDL cholesterol targets. By risk categories, percentages of low-risk, high-risk and CHD or CHD equivalent patients whose non-HDL cholesterol level achieved the targets were 76.0%, 60.5% and 42.4%, respectively. In the aspect of physician categories, patients who were treated by

Factors	Total (n)	n	% reach target	Adjusted odds ratio	95% CI	p-value
Risk categories						
CHD or CHD risk equivalence	1148	397	34.6	1		
High-risk	415	234	56.4	2.8	2.2, 3.6	< 0.001
Low-risk	314	241	76.8	7.5	5.5, 10.2	< 0.001
Total	1877	872	46.5		,	
Physicians categories						
Cardiologist or Endocrinologist	509	288	56.6	1		
Internist	1292	540	41.8	0.41	0.3, 0.6	< 0.001
Non-Internist	76	44	57.9	0.52	0.2, 1.1	0.089
Treatments						
Without any drugs	267	86	32.2	1		
Statin alone	1131	625	55.3	5.4	3.7, 7.7	< 0.001
Fibrate alone	391	127	32.5	1.8	1.2, 2.7	0.003
Statin + fibrate	69	29	42.0	3.6	1.9, 6.7	< 0.001
Others <sup>a</sup>	19	5	26.3	1.9	0.6, 5.9	0.287

 Table 4. The factors contributing to achievement of LDL-C target

<sup>a</sup> Other drugs or in combination with statins or fibrates

Table 5.	Achieving LDL-	C target in each i	risk category i	in relation to	physicians and	l treatment

Factors	n	% reach target	Adjusted odds ratio	95%CI	p-value
CHD or CHD risk equivalence					
Physicians categories					
Cardiologist or Endocrinologist	181	48.5	1		
Internist	209	27.7	0.4	0.3, 0.6	< 0.001
Non-Internist	7	33.3	0.6	0.2, 1.8	0.345
Treatments					
Without any drugs	13	11.9	1		
Statin alone	328	43.6	5.0	2.7, 9.3	< 0.001
Fibrate alone	36	16.4	1.5	0.7, 3.0	0.238
Statin and fibrate	19	35.8	3.4	1.5, 7.8	0.004
Others <sup>a</sup>	1	7.1	1.1	0.2, 5.6	0.911
High-risk				,	
Physicians categories					
Cardiologist or Endocrinologist	60	72.3	1		
Internist	157	51.6	0.4	0.2, 0.7	0.002
Non-Iinternist	17	60.7	0.6	0.2, 1.8	0.359
Treatments				,	
Without any drugs	15	25.9	1		
Statin alone	159	71.6	6.7	3.4, 12.9	< 0.001
Fibrate alone	49	41.5	2.0	0.9, 3.9	0.056
Statin and fibrate	8	61.5	3.9	1.1, 14.1	0.035
Others <sup>a</sup>	3	75.0	8.1	0.8, 82.4	0.077
Low-risk				,	
Physicians categories					
Cardiologist or Endocrinologist	47	88.7	1		
Internists	174	74.4	0.3	0.1, 1.0	0.050
Non-Internists	20	74.1	0.4	0.1, 1.9	0.247
Treatments				,	
Without any drugs	58	58.0	1		
Statin alone	138	87.9	3.9	2.0, 7.6	< 0.001
Fibrate alone	42	79.2	2.5	1.1, 5.7	0.026
Statin and fibrate	2	66.7	1.5	0.1, 18.5	0.733
Others <sup>a</sup>	1	100.0		, -	

<sup>a</sup> Other drugs or in combination with statins or fibrates

Factors	Total (n)	n	% reach target	Adjusted odds ratio	95% CI	p-value
Risk categories						
CHD or CHD risk equivalence	656	278	42.4	1		
High-risk	210	127	60.5	2.4	1.7, 3.3	< 0.001
Low-risk	217	165	76.0	5.4	3.7, 7.8	< 0.001
Total	1083	570	52.6		,	
Physicians categories						
Cardiologist or Endocrinologist	343	205	59.8	1		
Internist	695	335	48.2	0.5	0.3, 0.7	< 0.001
Non-Internist	45	30	66.7	0.7	0.3, 1.8	0.443
Treatments						
Without any drugs	174	66	37.9	1		
Statin alone	779	457	58.7	4.4	2.9, 6.6	< 0.001
Fibrate alone	98	28	28.6	1.1	0.6, 2.0	0.651
Statin + Fibrate	25	15	60.0	4.5	1.8, 11.2	< 0.001
Others <sup>a</sup>	7	4	57.1	3.7	0.7, 19.6	0.12

Table 6. Achieving non-HDL-C target in relation to treatment factors

<sup>a</sup> Other drugs or in combination with statins or fibrates

cardiologists or endocrinologists achieved non-HDL cholesterol targets with a significantly higher percentage compared to the patients treated by internists but there were no significant differences when compared with non-internist treating groups. Statins or its combination with fibrates had the highest achievement rates at 58.7% and 60.0% respectively (Table 6).

#### Discussion

The present study illustrated that an overall achievement rate of LDL-C reduction to target increased to 46.5% compared to 40.5% in the previous LTAP study in Thailand<sup>(10)</sup>. Although, the difference was only small, the group with the largest change was in the CHD and CHD equivalents with an increase rate of 22.7% (34.6% compared to 11.9%). The difference was 17.2% in the high-risk group and 4.1% in the low-risk group.

The differences in achieving the target between the two LTAP surveys in Thailand could be attributed to two clinical factors. Firstly, the second survey observed that statins were a more widely used therapy compared to the previous finding of fibrates. As a whole, 64% of the patients took either a monotherapy of statins or a combination of statins and others compared to 40.3% in the first Thai LTAP. The authors' analysis illustrates that the use of statins in achieving LDL-C (55.3%; OR = 5.4) was highest compared to all other types of treatment. Secondly, the LTAP II survey consisted of 26.5% cardiologists or endocrinologists compared to 6.8% confirmed cardiologists or endocrinologist. Given that patients treated by cardiologists or endocrinologists in this survey reported a higher and statistically significant achievement rate (56.6%) compared to internist (41.8%). This suggests that specialists probably put more emphasis than the others. Clearly, although the educational programs helped to boost awareness of statins as the primary medication for LDL-C lowering, there is still a considerable difference between physician expertise and their approach in treating dyslipidemic patients.

The present survey also revealed a similar trend in relation to non-HDL cholesterol. Patients from cardiologists or endocrinologists had the highest achievement rates (59.8%) and the monotherapy of statins (58.7%) and combination therapy of statins and fibrates (60.0%) were the two leading treatments attributed to higher achievements of non-HDL cholesterol.

The results showed that statins contributed to an increase in the achievement of LDL-C goal when compared to fibrates. However, as noted in the ATP III guidelines, a more aggressive therapy is needed for high-risk patients. In the present survey, the two most common statins used, simvastatin and atorvastatin were used at doses of 10-20 mg/day and 5-10 mg/day, respectively. For a majority of the patients, these doses were probably suboptimal. Several studies have demonstrated that an increased dosage (10-80 mg/day) of atorvastatin is related to significant incremental clinical benefits<sup>(11-13)</sup>. A study by Jones et al revealed a reduction of LDL-C by 35.7%, 42.2%, 48.6%, and 52.2% on 10, 20, 40, and 80 mg/day of atorvastatin<sup>(12)</sup>.

Therefore, with a more intense treatment regimen, a higher achievement rate would be possible.

Although there was an increase in the overall LDL-C success rate, an improvement of 6% was only minimal. The comparison between the first LTAP<sup>(10)</sup> and present LTAP seemed inappropriate due to the criteria used in grouping patients in risk categories and goals were different. Another major difference between the present survey and its predecessor was the locations of practice. The previous LTAP survey had concentrated in Bangkok (34.6%) and central (12.0%) regions, with sparse distribution in the north (4.5%), northeast (4.5), east (2.3%), west (0.8%), south (9.0%), and unspecified (32.3%) areas. The present survey however, had a smaller number of hospitals in Bangkok (20.8%) and increasing sampling from hospitals in less populated areas: 16.7% in the north, 16.7% in the south, 14.6% in the northeast and central parts and 8.3% in the east and west. The higher number of patients sampled in the rural regions could have some effect on the achievements of reaching LDL-C target levels because behaviors associated with urbanization, such as increased saturated fat consumption and decreased physical activity are associated with adverse changes in the lipid profile<sup>(14-16)</sup>. Moreover, it has been reported that the Thai rural population has a lower LDL-C value compared to urban populations (male: 2.86 mmol/L [SD 0.08] versus 3.61 mmol/L [SD 0.11] and female: 3.28 mmol/L [SD 0.08] versus 3.71 mmol/L[SD 0.07]; p-value < 0.001)<sup>(17)</sup>. Additionally, rural-to-urban difference in mean total cholesterol value is about 0.7 mmol/L translating to urban populations having a 25-35% higher risk of coronary heart disease<sup>(18)</sup>. If the same proportion of patients in Bangkok had been captured, it is possible that the overall achievement level in the present survey could be slightly overestimated since those with higher cholesterol and LDL-C levels could be allocated into a higher risk category and, coupled with non-aggressive treatment, fail to substantially achieve LDL-C targets.

Although patient's demographics and increased availability of statins might affect the overall achievement rates, the present survey has distinguished statins to be a more effective treatment than fibrates, and that being treated by a specialist increases the effectiveness of the therapy. The lipid educational programs might have promoted the use of statins to lower LDL cholesterol. Coupled with the results from other studies that a higher dose of statins could greatly benefit LDL-C reduction, a continuing education on cholesterol lowering must be further enhanced to ensure the same practicing profiles between specialists and non-specialists.

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#### References

- Pignone M, Phillips C, Mulrow C. Use of lipid lowering drugs for primary prevention of coronary heart disease: meta-analysis of randomised trials. BMJ 2000; 321:983-6.
- 2. Randomised trial of cholesterol lowering in 4444 patients with coronary heart disease: the Scandinavian Simvastatin Survival Study (4S). Lancet 1994; 344: 1383-9.
- 3. The Long-Term Intervention with Pravastatin in Ischaemic Disease (LIPID) Study Group. Prevention of cardiovascular events and death with pravastatin in patients with coronary heart disease and a broad range of initial cholesterol levels. N Engl J Med 1998; 339: 1349-57.
- Executive Summary of The Third Report of The National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, And Treatment of High Blood Cholesterol In Adults (Adult Treatment Panel III). JAMA 2001; 285: 2486-97.
- Grundy SM, Cleeman JI, Merz CN, Brewer HB Jr, Clark LT, Hunninghake DB, et al. Implications of recent clinical trials for the National Cholesterol Education Program Adult Treatment Panel III guidelines. Circulation 2004; 110: 227-39.
- Vale MJ, Jelinek MV, Best JD. How many patients with coronary heart disease are not achieving their risk-factor targets? Experience in Victoria 1996-1998 versus 1999-2000. Med J Aust 2002; 176: 211-5.
- Pyorala K, Lehto S, De Bacquer D, De Sutter J, Sans S, Keil U, et al. Risk factor management in diabetic and non-diabetic patients with coronary heart disease. Findings from the EUROASPIRE I AND II surveys. Diabetologia 2004; 47: 1257-65.
- Pearson TA, Laurora I, Chu H, Kafonek S. The lipid treatment assessment project (L-TAP): a multicenter survey to evaluate the percentages of dyslipidemic patients receiving lipid-lowering therapy and achieving low-density lipoprotein cholesterol goals. Arch Intern Med 2000; 160:

459-67.

- 9. Division of International Health, Bureau of Health Policy and Planning, Office of the Permanent Secretary and Ministry of Public Health. Thailand health profile, 1997-1998. Bangkok: Express Transportation Organization; 2000.
- Nitiyanant W, Ngarmukos P, Koanantakul B. Lipid treatment assessment project (L-TAP) in Thailand. Intern Med J Thai 2001; 17: 246-52.
- 11. Wagner AM, Jorba O, Bonet R, Ordonez-Llanos J, Perez A. Efficacy of atorvastatin and gemfibrozil, alone and in low dose combination, in the treatment of diabetic dyslipidemia. J Clin Endocrinol Metab 2003; 88: 3212-7.
- 12. LaRosa JC, Grundy SM, Waters DD, Shear C, Barter P, Fruchart JC, et al. Intensive lipid lowering with atorvastatin in patients with stable coronary disease. N Engl J Med 2005; 352: 1425-35.
- 13. Jones PH, McKenney JM, Karalis DG, Downey J. Comparison of the efficacy and safety of atorvas-

tatin initiated at different starting doses in patients with dyslipidemia. Am Heart J 2005; 149: e1.

- McKenney JM, Davidson MH, Saponaro J, Thompson PD, Bays HE. Use of a treatment algorithm to achieve NCEP ATP III goals with atorvastatin. J Cardiovasc Pharmacol 2005; 46: 594-9.
- 15. Durstine JL, Grandjean PW, Cox CA, Thompson PD. Lipids, lipoproteins, and exercise. J Cardiopulm Rehabil 2002; 22: 385-98.
- Grundy SM, Denke MA. Dietary influences on serum lipids and lipoproteins. J Lipid Res 1990; 31: 1149-72.
- 17. Patel A, Woodward M, Stolk R, Suriyawongpaisal P, Neal B. Serum lipid levels and the prevalence of dyslipidaemia among rural and urban Thai adults are the NCEP III guidelines appropriate? J Med Assoc Thai 2005; 88: 1242-50.
- Hata Y, Nakajima K. Life-style and serum lipids and lipoproteins. J Atheroscler Thromb 2000; 7: 177-97.

## การประเมินผลการรักษาไขมันผิดปกติในประเทศไทย ครั้งที่ 2

### วรรณี นิธิยานันท์, ปียะมิตร ศรีธรา, ชัยชาญ ดีโรจนวงศ์, พึงใจ งามอุโฆษ, บรรหาร กออนันตกูล

**วัตถุประสงค**์: การศึกษาสหสถาบันแบบตัดขวาง เพื่อประเมินผลการรักษาไขมันในเลือดสูงทางเวซปฏิบัติ ในผู้ป่วยไทย ที่มีไขมันในเลือดสูง รวมทั้งศึกษาปัจจัยที่มีผลต่อการบรรลุเป้าหมายการรักษา มีแพทย์ 98 คนจากโรงพยาบาล 48 แห่ง เข้าร่วมการศึกษา โดยแพทย์แต่ละคนจะสุ่มผู้ป่วยเข้าร่วมการศึกษาจำนวน 20 ราย

**ผลการศึกษา**: ผู้ป่วยที่เข้าการศึกษามีจำนวนทั้งสิ้น 1,921 คน เป็นเพศชายร้อยละ 45.1 โดยมีค่าเฉลี่ยอายุที่ 58.6 ปี (ค่าความเบี่ยงเบนมาตรฐาน 9.6) แบ่งผู้ป่วยเป็น 3 กลุ่ม คือ กลุ่มผู้ป่วยโรคหลอดเลือดหัวใจและเทียบเท่า โรคหลอดเลือดหัวใจ 1,178 ราย กลุ่มผู้ป่วยที่มีความเสี่ยงสูง 424 ราย และกลุ่มผู้ป่วยที่มีความเสี่ยงต่ำ 319 ราย เป้าหมายของการรักษาในผู้ป่วยแต่ละกลุ่มความเสี่ยงคือ การลดระดับ LDL-C ในเลือดให้น้อยกว่า100, 130 และ 160 มิลลิกรัมต่อเดซิลิตร, ตามลำดับ ปัจจัยเสี่ยงของโรคหลอดเลือดหัวใจที่พบเรียงจากมากไปหาน้อยได้แก่ เกณฑ์อายุ พบร้อยละ 78, ความดันโลหิตสูงร้อยละ 69.8, เบาหวานร้อยละ 43.6, สูบบุหรี่ร้อยละ 24.6 และประวัติครอบครัวเป็น โรคหลอดเลือดหัวใจร้อยละ 6.9 ในกลุ่มที่ศึกษาพบผู้ป่วยอ้วน (ค่าดัชนีมวลกายมากกว่าหรือเท่ากับ 25 กิโลกรัม/เมตร<sup>2</sup>) คิดเป็นร้อยละ 53.8, ผู้ป่วยที่เคยมีประวัติทางโรคหลอดเลือดแดงแข็งและตีบตัน (atherosclerotic diseases) มีจำนวน ร้อยละ 28, กลุ่มยาที่แพทย์สั่งจ่ายมากที่สุดคือ สแตตินร้อยละ 64 ตามด้วยกลุ่มไฟเบรทร้อยละ 25, การรักษาบรรลุ เป้าหมายโดยรวมคิดเป็นร้อยละ 46.5 โดยกลุ่มผู้ป่วยโรคหลอดเลือดหัวใจและเทียบเท่า กลุ่มผู้ป่วยความเสี่ยงสูง และกลุ่มผู้ป่วยความเสี่ยงต่ำบรรลุเป้าหมายในการรักษา คิดเป็นร้อยละ 34.6, 56.4 และ 76.8 ตามลำดับ บัจจัยที่ ทำให้บรรลุเป้าหมายในการรักษาสูงขึ้นอย่างมีนัยสำคัญทางสถิติคือ กลุ่มผู้ป่วยความเสี่ยงต่ำ การรักษาโดยแพทย์ ผู้เซี่ยวชาญเฉพาะทาง และการได้รับยาสแตติน

**สรุป**: การศึกษานี้แสดงให้เห็นว่าสแตตินเป็นยาที่ใช้ควบคุมระดับไขมันในเลือดมากกว่ายากลุ่มอื่น กลุ่มผู้ป่วย โรคหลอดเลือดหัวใจ และเทียบเท่าเป็นกลุ่มที่บรรลุเป้าหมายในการลด LDL-C น้อยสุด ส่วนปัจจัยที่มีผลต่อการบรรลุ เป้าหมายในการลดระดับ LDL-C ในเลือดคือ ผู้ป่วยที่มีความเสี่ยงต่ำ การดูแลโดยแพทย์ผู้เชี่ยวชาญเฉพาะทาง และการรักษาด้วยสแตติน