EFFICIENCY AND COST-EFFECTIVENESS OF DYSLIPIDEMIA SCREENING METHODS AMONG WORKERS IN BANGKOK

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Abstract. Dyslipidemia is now a worldwide health problem. Secondary prevention in the form of early detection of dyslipidemia and risk modification via drug and non-drug procedures, particularly among the high-risk group, is thus imperative. The objective of this study was to determine the sensitivity and specificity, cost, and cost-effectiveness of dyslipidemia screening methods which were proposed by the Royal Thai Medical Association (RTMA), the United States National Cholesterol Education Program (NCEP), British Hyperlipidemia Association (BHA), and our modified screening instrument (MSI). A cross-sectional descriptive study was conducted among 2,000 workers aged ≥ 35 years taking annual health examination from a university hospital during July- September, 2008. Sensitivity and specificity of the screening methods were analyzed using the universal serum lipid testing as the gold standard. Their total and unit costs, and cost-effectiveness were then calculated. Overall, the sensitivities for detecting any type of serum lipid abnormalities ranged between 29.9-99.4 %, while the specificities ranged between 0.5-74.1%. The total costs per 1,000 people screened ranged between THB 88,742 - 184,750. No screening method was obviously more cost-effective when using the cost per case detected of the universal blood test as the reference.

Key words: dyslipidemia, cost-effectiveness, screening instruments

INTRODUCTION

Dyslipidemia is a term refer to a number of lipid disorders including high serum total cholesterol (TC) and triglyceride (TG), elevated low-density lipoprotein cholesterol (LDL-C), and low high-density lipoprotein cholesterol (HDL-C) as its major categories. It is a serious and costly health problem worldwide (Smith, 2007). World Health Organization estimated that this condition accounted for 18 % of ischemic heart disease(IHD) and 56 % of stroke and more than 4 million deaths per year (World Health Organization, 2002). It is closely related to diet and physical inactivity, which are amendable to lifestyle modification. Lipid lowering agents were also effective in managing dyslipidemia and reducing morbidity and mortality due to the IHD and stroke in the long run (Eaton, 2005). Secondary prevention in the form of early detection of dyslipidemia and risk modification via drug and non-drug procedures, particularly among the

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high-risk group, is thus imperative.

Recent surveys showed the burden of dyslipidemia among Thai population is high. The overall prevalence rates of high serum TC and TG among Thai adults during the last 10 years were 31 - 72% and 20 - 43 %, respectively, while those prevalence rates for high LDL and low HDL were 11 - 67% and 4 - 14%, respectively (Nillakupt *et al*, 2005; Pongchaiyakul and Pratipanawatr, 2005; Porapakkam and Bunyaratanabhun 2006; Lohsoonthorn *et al*, 2007). Proportion of adults with >35 years of age and eligible for lipid lowering agents ranged between 23-64% (Patel *et al*, 2005). Variation in the reported prevalence was due to differences in the characteristics of the surveyed populations and criteria for abnormal serum lipid levels. Adults at working age group were at the highest risk for these abnormalities, particularly for those who were 30 years old or older (Porapakkam and Bunyaratanabhun, 2006).

A number of dyslipidemia screening methods have been proposed. These included those proposed by the United States National Cholesterol Education Program (NCEP)(Expert Panel on Detection EaToHBiA, 2001), the British Hyperlipidemia Association(Hutchison *et al*, 1998), and the Royal Thai Medical Association (The Royal Thai Medical Association, 2001). However, their performance–specifically among Thai population–has never been determined. In this study we thus sought to determine the performance (sensitivity and specificity), unit cost, and cost-effectiveness of the above mentioned dyslipidemia screening methods among a group of Thai adults who were 35-59 years of age.

MATERIALS AND METHODS

Study population

As the serum lipid examination is generally offered only for those who were 35 years old or older, our study population were healthy workers who were 35-59 years of age and had participated in the annual physical examination which was provided by King Chulalongkorn Hospital during July-September, 2008. Those with history of pre-existing dyslipidemia or taking lipid lowering agent were excluded. Of the overall 2,557 eligible workers, 2,000 participated in the present study (with the response rate of 78.2%). The study protocol was approved by the Ethics Committee of the Faculty of Medicine, Chulalongkorn University. Informed consent was obtained from each participant before the data collection.

Data collection

After an overnight fast, the participants underwent anthropometric measurements and blood samples. Weight, height, and blood pressure (in the sitting position) were measured by staff nurses. Serum lipid levels including the TC, TG, and HDL-C were measured in a standardized manner at the biomedical laboratory of the hospital. LDL-C level was determined by Friedewald's formula for those with the TG level not exceed 400 mg/dl (Friedewald *et al*, 1972).

Diagnostic criteria of dyslipidemia in this study were (1) TC > 200 mg/dl, (2) TG > 150 mg/dl, (3) HDL < 40 mg/dl, (4) LDL > 100 mg/dl, (5) TC/HDL ratio > 4.5, and (6) LDL/HDL ratio > 3.0 (Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults, 2001).

Screening method

Dyslipidemia screening methods included in this study were screening questionnaires based on the guidelines or recommendations of the Royal Thai Medical Association (RTMA) *(Method 1)*(The Royal Thai Medical Association, 2001), the

United States National Cholesterol Education Program (NCEP) *(Method 2)*(Expert Panel on Detection EaToHBCiA, 2001), and British Hyperlipidemia Association (BHA) *(Method 3)* (Hutchison *et al*, 1998). We also developed another screening questionnaire–modified screening instrument (MSI)–basing on the above three guidelines or recommendations combined with the additional information of dyslipidemia risk factors which were not included in the above three guidelines or recommendations *(Method 4)*. Those subjects whose scores exceeded the pre-determined cut-off points for each of these screening questionnaires then proceeded with laboratory test for serum lipid level. Detail information about of four screening questionnaires, as well as the total scores and cut-off points for positive screening results was presented in Table1.

Analytical procedures

Performance of screening strategies. Universal serum lipid testing for all study subjects were used as gold standard in the examination of the performance of each screening method. Receiver Operating Characteristic Curves (ROC) and Area under Curves (AUC) were used to find out the best point of each screening method (Fletcher *et al*, 1996). We measured the effectiveness of a screening method by the proportion of those with dyslipidemia who were identified by the screening method (sensitivity) and the proportion of those without dyslipidemia and have negative result from screening method (specificity). Numbers of missed dyslipidemia cases (false negative cases) per 1,000 subjects screened were also determined. All these analyses were conducted separately for each type of outcome (namely high TC, high TG, low HDL, high LDL, TC/HDL ratio > 4.5, and LDL/HDL ratio > 3.0).

Unit cost and cost-effectiveness analyses

The health economical analysis was conducted from the societal perspective. We included both medical and non medical costs of each screening method. Medical cost included laboratory testing, personnel time, and other medical costs (*eg*, costs of mailing and copying) (Zhang *et al*, 2003). Non-medical costs included transportation to a health care provider and worker's time spent travelling and receiving tests. The total direct cost for each method was calculated as a sum of the cost associated with various resources (*eg*, physician time, laboratory tests) used. The cost of each resource was the product of the following three components: number of physical units used to screen one person, the unit value of the resource, and the number of workers screened. The resources used and their unit values by screening are presented by Table 3.

The cost of a laboratory test was based on the experience at the Out-Patient Department of King Chulalongkorn Hospital (Charuruks *et al*, 2004). The cost of physician, nurse, and secretary time was calculated from total salaries including welfare expenditure (The National Health Association of Thailand, 2009). Transportation costs to the hospital were obtained from the literature (Department of Land Transport, 2008). Patients' time was obtained from the Ministry of Labor (Ministry of Labor, 2008). All costs were expressed in Thai baht for the year 2008.

Unit cost was determined by dividing the total cost of each screening method by the number of screened subjects, while the cost of identifying one case (or cost-effectiveness) was calculated as the total cost of a screening method divided by the total number of case identified. All these calculations were based on 1,000 subjects screened.

Table 1
Screening criteria used in the four dyslipidemia screening questionnaires.

Risk factors	Definition	Screening method			
		RMAT(1)	NCEP(2)	BHA(3)	MSI(4)
Personal characteristics					
Gender and age (years)	Male ≥ 35, Female≥ 45	+	-	-	+
Body mass index (BMI)	≥ 25 kg/m^2	+	-	-	+
Waist (cm)	Male ≥ 90, Female ≥ 80	+	-	-	+
Blood pressure	≥ 140/90 mmHg	+	-	-	+
Family history					
Death from stroke		+	+	+	+
Death from coronary heart disease, angina, or myocardial infarction	Parent < 60 yr; Sibling-male < 55, female< 65 yr	+	+	_	+
Hyperlipidemia		+	_	_	+
Personal disease history					
Angina, stroke, myocardial infarction		+	+	+	+
Left ventricular hypertrophy (LVH)		-	-	-	+
Type 2 diabetes		+	+	+	+
Hypertension		+	+	+	+
Chronic renal failure or nephritic syndrome		-	-	-	+
Health behavior					
Exercise		-	-	-	+
Cigarette smoking		+	+	+	+
Alcohol drinking		-	-	-	+
Food consumption					
Frequent high lipid diet consumption		-	-	-	+
Urban residence		+	-	-	+
Cut-off point					
Total cholesterol (TC)		≥ 3	≥ 3	≥ 1	≥ 5
Triglyceride (TG)		≥ 4	≥ 2	≥ 2	≥ 7
HDL cholesterol		≥ 3	≥ 1	≥ 1	≥ 7
LDL cholesterol		≥ 3	≥ 1	≥ 2	≥ 5
TC/HDL > 4.5		≥ 3	≥ 1	≥ 1	≥ 5
LDL/HDL > 3.0		≥ 3	≥ 1	≥ 1	≥ 5
Total score		11	6	7	24

RMAT, Royal Medical Association of Thailand; NCEP, National Cholesterol Education Program; BHA, British Hyperlipidemia Association; MSI, Modified Screening Instrument

Sensitivity analysis

We examined two factors that may have important effects on study outcomes. These factors were changing of prevalence and changing of laboratory cost. As the prevalence of high serum lipid level among urban workers increased gradually so we studied sensitivity analysis at 3.3, 5, 7 and 10% of prevalence. According to economic uncertainty, the cost of laboratory testing should be higher than THB 58 (present cost) so we studied sensitivity

Table 2
Performance of 4 screening methods for serum lipid abnormalities.

Screening method	Sensitivity (%)	Specificity (%)	AUC	Outcome per 1,000 persons screened		
				TP (No. of cases)	FP (No. of cases)(	FN No. of cases)
Cholesterol > 200 mg/dl						
Method 1	73.9	33.0	0.545	368	336	130
Method 2	30.2	70.9	0.507	150	146	348
Method 3	58.9	45.9	0.522	293	146	205
Method 4	99.4	0.5	0.521	495	499	3
Universal blood test				498	-	-
Triglyceride > 150 mg/dl						
Method 1	85.3	32.9	0.639	154	550	27
Method 2	46.3	74.1	0.562	83	213	97
Method 3	77.8	48.2	0.659	141	424	40
Method 4	99.4	0.5	0.586	179	815	2
Universal blood test				181	-	-
HDL < 40 mg/dl						
Method 1	85.1	31.3	0.621	89	616	18
Method 2	45.2	72.2	0.588	47	251	57
Method 3	82.2	46.5	0.655	85	480	19
Method 4	99.0	0.5	0.554	102	892	2
Universal blood test				104	-	-
LDL > 100 mg/dl						
Method 1	71.8	34.3	0.538	550	154	216
Method 2	29.9	71.3	0.506	229	67	537
Method 3	58.0	48.4	0.534	444	121	322
Method 4	99.5	0.6	0.530	762	232	4
Universal blood test				766	-	-
TC/HDL > 4.5						
Method 1	82.4	33.2	0.615	189	515	40
Method 2	39.7	73.4	0.568	91	205	138
Method 3	75.8	49.8	0.634	174	391	56
Method 4	99.3	0.5	0.568	227	767	2
Universal blood test				229	-	-
LDL/HDL > 3.0						
Method 1	79.7	32.1	0.591	167	537	43
Method 2	37.5	72.5	0.552	79	217	131
Method 3	73.3	47.9	0.610	154	412	56
Method 4	99.3	0.5	0.552	208	786	1
Universal blood test				209	-	-

AUC, area under the curve; TP, true positive; FP, false positive; FN, false negative
Method 1: screening method according to the recommendation of the Royal Medical Association of Thailand (RMAT); Method 2: screening method according to the recommendation of the United States National Cholesterol Education Program (NCEP); Method 3: screening method according to the recommendation of the British Hyperlipidemia Association (BHA); Method 4: Modified Screening Instrument (MSI)

Table 3
Resources used and unit values for dyslipidemia screening per 1,000 persons.

Cost categories	Resources uses					Unit cost (Baht)
	Method 1	Method 2	Method 3	Method 4	Method 5	
Direct medical cost						
Screening questionnaire	1,000	1,000	1,000	1,000	0	THB 1/test
Physician time (1/4 h)	[a]704x70	[a]296x70	[a]565x70	[a]994x70	1,000x70	THB 284/h
Nurse time (1/6 h)	1,000x28	1,000x28	1,000x28	1,000x28	1,000x28	THB 170/h
Secretary time (1/12 h)	1,000x3.75	1,000x3.75	1,000x3.75	1,000x3.75	1,000x3.75	THB 45/h
Laboratory test[a]	704x58	296x58	565x58	994x58	1,000x58	THB 8/test
Other direct costs (1 mail)	[a]704x5	[a]296x5	[a]565x5	[a]994x5	1,000x5	THB/mail
Non-medical cost						
Patients' time						
High score persons (4h)	[b]30x4 h	[b]16x4 h	[b]29x4 h	[b]33x4 h	1,000x4 h	THB 25/h
Low score persons (2h)	[c]674x2 h	[c]280x2 h	[c]336x2 h	[c]961x2 h	0	THB 25/h
Transportation cost (1 trip)	1,000x16	1,000x16	1,000x16	1,000x16	1,000x16	THB 16/trip
Total direct medical cost	126,382	72,118	107,895	164,952	164,750	
Total non-medical cost	17,468	16,624	16,788	18,054	20,000	
Total cost (baht)	143,850	88,742	124,683	183,006	184,750	

[a]Total number of those with positive result from screening questionnaire; [b] number of true positive case of each screening method; [c] number of false positive case of each screening method
Method 1: screening method according to the recommendation of the Royal Medical Association of Thailand (RMAT); Method 2: screening method according to the recommendation of the United States National Cholesterol Education Program (NCEP); Method 3: screening method according to the recommendation of the British Hyperlipidemia Association (BHA); Method 4: Modified Screening Instrument (MSI); Method 5: Universal serum lipid screening

analysis at THB 100 and THB 190 which based on Medicare Reimbursement rates of Ministry of Finance.

RESULTS

Performance and effectiveness of the screening strategy

Overall, Method 4 had highest sensitivities (99%) for detecting any type of serum lipid abnormalities, followed by Method 1(sensitivities=72-85%) and Method 3 (59-82%). Method 2 had the lowest sensitivities (30-46%). The reverse was however true for the specificities of the screening methods, that is, methods with highest sensitivities had lowest specificities (Table 2). The pattern of true and false positivity also followed the pattern of sensitivity. Numbers of true and false positive cases were highest for Methods 4, 1, and 3, respectively, and lowest for Method 2. In contrary, false negativity correlated with the degree of specificity of screening method. Numbers of false negative cases were highest for Methods 2, 3, and 1, and lowest for Method 4.

When using area under the ROC curve (AUC) as the measure of screening performance, Method 3 (AUC=0.522-0.659) generally had the highest performance, followed by Method 1 (AUC=0.538-0.621),

Table 4
Cost-effectiveness of dyslipidemia screening methods.

Type of dyslipidemia	Cost per case detected (baht/case)				
	Method 1	Method 2	Method 3	Method 4	Universal blood test
TC>200 mg/dl	391	592	426	370	371
TG>150 mg/dl	934	1,069	884	1,022	1,021
HDL < 40 mg/dl	1,616	1,888	1,467	1,794	1,776
LDL >100 mg/dl	262	388	281	240	241
TC/HDL> 4.5	761	975	717	806	807
LDL/HDL> 3.0	861	861	810	880	884

Method 1: screening method according to the recommendation of the Royal Medical Association of Thailand (RMAT); Method 2: screening method according to the recommendation of the United States National Cholesterol Education Program (NCEP); Method 3: screening method according to the recommendation of the British Hyperlipidemia Association (BHA); Method 4: Modified Screening Instrument (MSI)

while Method 2 had the lowest performance (AUC=0.506-0.588) (Table 2).

Cost and cost-effectiveness of screening methods

The total costs (direct medical and direct non-medical costs) per 1,000 people screened according to screening method ranged between THB 88,742 - 184,750, whereas the direct medical costs ranged between THB 72,118 - 164,952 (81-90% of total cost) (Table 3). Laboratory testing contributed to the highest cost (28-32%). Method 4 had the highest cost, followed by Methods 1 and 3, while Method 2 had the lowest cost.

Using the cost per case detected of the universal blood test as the reference, the cost-effectiveness analytical results of the screening methods were mixed. Overall, the costs per case detected for Methods 3 and 1 were lower than those for the universal blood test in the detection of TG>150 mg/dl, HDL < 40 mg/dl, TC/HDL> 4.5, and LDL/HDL> 3.0. The reverse was true for the detection of TC>200 mg/dl and LDL>100 mg/dl (Table 4). Concerning Methods 2 and 4, their costs per case detected were comparable or even higher than those for the universal blood test.

Sensitivity analysis

Sensitivity analysis by varying the dyslipidemia prevalence showed that when the prevalence increases the cost-effectiveness of all screening methods increases and approaches each other, while the cost-effectiveness decreases when the laboratory cost increases. However, the relative cost-effectiveness among different screening methods was not changed from former analytical results (details not shown).

DISCUSSION

We evaluated the performance, cost, and cost-effectiveness of four screening methods in detecting abnormal serum lipid level by using the universal serum lipid test as the gold standard. The results were mixed and no screening method showed prominent superiority over the

other methods or the universal serum testing. Method 3 (proposed by British Hyperlipidemia Association) seemed to be the most cost effective, it however showed higher cost-effectiveness over the universal serum lipid test only when the outcomes were hypertriglyceridemia (TG>150 mg/dl), TC/HDL> 4.5, and LDL/HDL> 3.0.

The US National Cholesterol Education Program (NCEP) and the British Hyperlipidemia Association (BHA) recommended selective screening of serum cholesterol for the adults with established cardiovascular risk factors (such as high BMI, high blood pressure, presence of diabetes, personal and family histories of CVD, cigarette smoking, and unhealthy diet) (Hutchison *et al*, 1998; Expert Panel on Detection EaToHBCiA, 2001), while the Royal Medical Association of Thailand recommended such approach only for men ≥35 years and women ≥45 years of age (The Royal Thai Medical Association, 2001). Our study results showed that such approaches were not cost-effective in detecting dyslipidemia among our study population. These were due to their relatively low specificities and the consequently high false positivities had resulted in the high total costs of screening. Furthermore, as the prevalence rates of various subtypes of dyslipidemia among this population were quite high, insufficient sensitivities of these screening methods had resulted in high numbers of missed or undetected dyslipidemia cases (false negative cases). All these disadvantages make these screening methods far less than satisfactory for the utilization among Thai adults. An innovative and more effective dyslipidemia screening approach is then needed.

However, as the prevalence of abnormal serum lipid levels were quite high and their long-term consequences are serious, screening program for these conditions are urgently needed. In the current situation where no effective screening method existed, universal serum lipid test or the screening method according to the US Preventive Task Force (which suggested that serum cholesterol should be implemented among all men with 35 and women with 45 years old or older) might be temporally implemented (Agency for Healthcare Research and Quality, 2008).

Some limitations of this study need mentioning. First, as our study population included only those who were 35 years of age or older, the study results were then unable to apply for the dyslipidemia screening among those below this age-group. Second, LDL-C level in this study was calculated by using Friedewald's formula, therefore only those who had TG ≤ 400 mg/dl were enrolled. The resulted might then have had limited applicability for those who had TG >400 mg/dl. Finally, our study was for one-time screening, its findings about the screening performance, cost and cost-effectiveness might not have well reflected those for long-term screening.

In conclusion, abnormal serum lipid screening methods available nowadays were still not effective or cost-effective in detecting those with dyslipidemia among Thai adults. In the present situation with high prevalence of these conditions among the population, the innovation of more effective and cost-effective screening method is urgently needed.

REFERENCES

Agency for Healthcare Research and Quality (AHRQ). Guide to clinical preventive services, 2008. Rockville, MD: AHRQ, 2008. [Cited 2009 Mar 6]. Available from: URL: http://www.ahrq.gov/clin

Charuruks N, Chamnanpai S, Seublinvog T. Cost analysis of laboratory tests: a study of the Central Laboratory of King Chulalongkorn Memorial Hospital. *J Med Assoc Thai* 2004; 87: 955-63.

Department of Land Transport. Transportation fee [Online]. 2008. [Cited 2009 Mar 6]. Available from: URL: http:// www.mol.go.thic/pocketgd.htm

Eaton CB. Hyperlipidemia. *Prim Care* 2005; 32: 1027-55.

Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. 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.

Fletcher R, Fletcher S, Wagner E. Clinical epidemiology: the essentials. 3rd ed. Baltimore: Williams & Wilkins, 1996.

Friedewald WT, Levy RI, Fredrickson DS. Estimation of the concentration of low-density lipoprotein cholesterol in plasma, without use of the preparative ultracentrifuge. *Clin Chem* 1972; 18: 499-502.

Hutchison B, Birch S, Evans CE, *et al*. Screening for hypercholesterolaemia in primary care: randomised controlled trial of postal questionnaire appraising risk of coronary heart disease. *BMJ* 1998; 316: 1208-13.

Lohsoonthorn V, Lertmaharit S, Williams MA. Prevalence of metabolic syndrome among professional and office workers in Bangkok, Thailand. *J Med Assoc Thai* 2007; 90: 1908-15.

Ministry of Labor. Minimum wage 2008. [Cited 2009 Mar 6]. Available from: URL: http:// www.dlt.go.th

Nillakupt K, Nathalang O, Arnutti P, *et al*. Dyslipidemia in Thai rural adults. *J Med Assoc Thai* 2005; 88: 824-8.

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.

Pongchaiyakul C, Pratipanawatr T. Prevalence of dyslipidemia in rural Thai adults: an epidemiologic study in Khon Kaen province. *J Med Assoc Thai* 2005; 88: 1092-7.

Porapakkam Y, Bunyaratanabhun P. The third national health examination survey 2003-2004. Bangkok: Veteran's Affairs Organization Printing Company, 2006.

Smith DG. Epidemiology of dyslipidemia and economic burden on the healthcare system [Review]. *Am J Manag Care* 2007; 13 (3 suppl)): s69-s71.

The National Health Association of Thailand. Public Health Calendar, 2552 BE. Bangkok: Sahaprachapanich Printing Co, 2009.

The Royal Thai Medical Association. Screening for high serum lipid level. In: Suntorntham S, ed. Evidence-based Clinical Practice Guideline: periodic health examination and maintenance in Thailand. Bangkok: Mohchaoban, 2001: 132-43.

World Health Organization (WHO). Quantifying selected major risks to health. In: The World Health Report 2002-Reducing Risks, Promoting Healthy Life. Geneva: WHO, 2002: 47-97.

Zhang P, Engelgau MM, Valdez R, Benjamin SM, Cadwell B, Narayan KM. Costs of screening for pre-diabetes among US adults: a comparison of different screening strategies. *Diabetes Care* 2003; 26: 2536-42.