สำนักงานวิทยทรัพยากร
จุฬาลงกรณ์มหาวิทยาลัย

Chapter IV

Results

This chapter comprised three main parts according to study objectives including (1) developing computer adaptive assessment tool (CAAT), (2) validating CAAT for two high cost drug use (HCD) evaluation (Atorvastatin and Rosiglitazone),and (3) evaluating of their use by developed CAAT and their alternatives in terms of rational utilization and drug spending.

I: Computer adaptive assessment tool (CAAT) development

Drug use evaluation (DUE) has been done in hospitals for many years to improve quality of care and efficiency of resource use by using Conventional DUE method. Currently, a lot of drugs require DUE. Conventional DUE method couldn't respond enough because of its limitation. More resources including human, time, materials are needed for Conventional DUE even though many hospitals have electronic database for important information record. Furthermore, the results of drug use evaluation might not be updated enough for policy makers in decision making. Because CAAT can reduce some limitation of Conventional DUE especially resources use. Thus, CAAT should be developed for evaluating or monitoring drug use. In addition, update monitoring of drug use can be done by using CAAT. However, quality of developed CAAT is also important.

To develop qualified CAAT for high cost drug (HCD) use monitoring, there are two major parts that should be concerned;

1.1 Development of CAAT Algorithm for high HCD use evaluation

To develop algorithm for HCD use evaluation, five steps were included as follow,

1.1.1 CAAT guidelines development

1.1.2 Selecting key variables

1.1.3 Setting cut point of key variables

1.1.4 Time frame requirement

1.1.5 Algorithm of HCD use evaluation by CAAT

1.1.5.1 Algorithm of Atorvastatin use evaluation

1.1.5.2 Algorithm of Rosiglitazone use evaluation

1.2 Database management

This part is composed of 3 steps as followed

1.2.1 Data extraction

1.2.2 Data linkage

1.2.3 Data completeness

1.1 Development of CAAT algorithm for HCD use evaluation

Purposes of CAAT algorithm for HCD use evaluation development were to get an easy to understand and follow DUE with appropriate guidelines and to get results that are similar to that of using Conventional method as much as possible. To develop CAAT algorithm, these following five steps should be conducted.

1.1.1 CAAT guidelines development

This step is aimed to get the suitable guidelines for CAAT to evaluate HCD use. Literature review and expert review about the interest HCD use guidelines were conducted. For literature review, researches and articles related to HCD use were reviewed. Documents should include guidelines from many levels, such as international standard guidelines, national recommended guidelines etc. Consistent criteria for the guidelines should be obtained to be used as the principal criteria. Expert reviews were necessary to get their opinion about the appropriate criteria or guidelines in clinical practice. However, expert reviews had to concern some variables, especially for those variables which effect measurement of the use of study drugs. Main criteria obtained from literature and expert reviews should be consistent. It led to key variables which would be used for DUE. For example, main criteria for CAAT guidelines for rational initiating Atorvastatin use evaluation review from literature and experts were the same, the use of Atorvastatin should be initiated after Simvastatin use and LDL-cholesterol check.. Thus, key variables from this guidelines would be Simvastatin use date , LDL-cholesterol check date, and Atorvastatin use date. For CGD's guidelines, which was more specific, type of CHD prevention and LDL-cholesterol level were required for Atorvastatin use. Therefore, more key variables, such as diseases related to CHD prevention were needed.

1.1.2 Selecting key variables

This step is aimed to select key variables and variables related to reviewed guidelines in CAAT guidelines development step those available in database. It must be realized that the more key variables availability in the database, the more quality of CAAT there is. However, some key variables might not be available in the database. The researcher had to find the proxy variables that reflects those key variables as much as possible. For example, diseases related to CHD prevention which were variables related to the evaluation guidelines of this study, were retrieved from ICD-10 database. But it was argued that some of those diseases might not be recorded in the database. To make this data more complete, drugs related to those diseases that had been dispensed for the studied period of time would be retrieved. It was assumed that a patient had the disease of interest if those drugs related to the disease were available in the dispensing database.

Because some variables related to the developed guidelines might not be recorded in database or incompletly recorded, these variables have to be assumed properly. If it's possible, sampling of some database records, then compare them with the patients records whether those variables of interest were available in patient records or not. It was useful for adjusting the validity of CAAT guidelines.

1.1.3 Setting cut point of key variables

This step is aimed to set the appropriate cut point of key variables that might be similar to the standard guidelines and meet the acceptance of the clinician. Some value or criteria cut point of key variables that were determined from literature review might not be enough for the acceptant of prescribers in real practice. Experts opinions had to be employed for the appropriateness of cut point criteria or value. If there were some differences at this point, the researcher might select the general one as the principle. However, the researcher should evaluate drug use follow guidelines according to the other different cut points too. It might be useful for the decision makers to improve the policy of drug use in the future.

1.1.4 Time frame requirement

This step is aimed to specify the period of time that is suitable for data collection related to drug use evaluation guidelines. Specifying the duration of time might be related to the general standard guidelines or real practice depending on

the phase of DUE implementation. During the beginning phase of retrospective drug use evaluation, the time duration for data collection might be related to real practice. In this study, time duration for retrospective data collection of patients' histories of drug use, diseases, and laboratory checks related to the guidelines were one year from first use dates of Atorvastatin and Rosiglitazone.

1.1.5 Algorithm of HCD use evaluation by CAAT

This step is aimed to set an easy to understand algorithm for HCD use evaluation by CAAT. The algorithm is contained of key variables and their cut point. A good algorithm should run step by step with clear explanation and direction to each step. It will help the evaluators or auditors ensure their evaluating results and save their time. A complex algorithm might cause some problems in evaluation process and more errors of evaluating results.

Atorvastatin and Rosiglitazone were the examples used to demonstrate the development of CAAT guidelines for high cost drug use evaluation.

1.1.5.1 Algorithm of Atorvastatin use evaluation

Concerning CAAT guidelines development for Atorvastatin use evaluation for new CSMBS outpatients, documents of standard treatment or clinical practice guidelines, research and articles related to Atorvastatin use were reviewed. Based on 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) LDL-cholesterol was identified as the primary target of cholesterol lowering therapy to reduce risk of CHD. For the clinical guidelines of Atorvastatin use, the guidelines of National Institute for Clinical Excellence (NICE)-2006, Pharmaceutical Benefit Scheme (PBS) list of Australia, 20004 National essential drug list of Thailand, and Comptroler's General Department (CGD) were revealed. There were consistence findings that Atorvastatin was not recommended as the first line drug for statins therapy. Atorvastatin would be used after the maximum recommended dose of Simvastatin did not achieve target LDL-cholesterol level. About the maximum dose of Simvastatin, NICE guidelines had recommended 20mg or 40 mg daily for secondary prevention. CGD guidelines had recommended 40 mg daily continuous use for at least 3 months for both primary and secondary prevention. For expert review of the guidelines for Atorvastatin use, CGD'S guidelines was applied. Because CGD's

guidelines had done by clinical experts committee for monitoring Atorvastatin use in CSMBS patients.

According to the findings above, CGD's guidelines was applied to be used as the guidelines for CAAT to evaluate the rational use of Atorvastatin initiated in CSMBS outpatients. To evaluate rationale use of Atorvastatin, two aspects were assessed. Evaluating of rational use of Atorvastatin based on pattern analysis was the first evaluation aspect. Rationale use of Atorvastatin evaluated based on specific guidelines was the second aspect.

Rational use of Atorvastatin evaluated in terms of pattern analysis before starting Atorvastatin use was followed by the first part of algorithm in Figure4.1. The step of Simvastatin use followed by LDL-cholesterol checking before initiating the use of Atorvastatin was evaluated. According to this guidelines, 4 patterns of Atorvastatin use were classified. The patterns were

SLA : Simvastatin use ⟶ LDL-cholesterol check ⟶ Atorvastatin use

SA : Simvastatin use ⟶ Atorvastatin use

LA : LDL-cholesterol check ⟶ Atorvastatin use

A : Atorvastatin use

Patients who initiated Atorvastatin followed by SLA pattern were rational drug use evaluated. Others, patients who started Atorvastatin followed by SA, LA, and A patterns were irrationale drug use evaluated.

Rational use of Atorvastatin evaluation based on specific guidelines was the second aspect of the evaluation. It was the next step of Atorvastatin use pattern evaluation. For this aspect, types of CHD prevention had effect on require target LDL-cholesterol level. The types of CHD prevention was categorized into 2 categories, primary and secondary prevention. To identify the type of CHD prevention , CHD diseases equivalent and number of CHD major risk factors were important data. CHD major risk factors, such as cigarette smoking and family history of premature CHD, were not usually documented, resulting in a number of risk factors could not be analyzed. Therefore, the researcher assumed that patients who were diagnosed CHD or CHD equivalent were in secondary prevention category .The rest of the patients were assumed in the primary prevention category with CHD major risk factors $\geq$ 2. Thus, the specific guidelines was used to evaluate the rational use of Atorvastatin in patients who initiated Atorvastatin use following SLA pattern were as follows,

- For primary prevention category, Atorvastatin would be used after patients had received Simvastatin continuously with maximum dose to 40 mg at least 3 months, but LDL-cholesterol did not achieve ≤ 130 mg/dl.

- For secondary prevention category, Atorvastatin would be used after patients had received Simvastatin continuously with maximum dose to 40 mg at least 3 months, but LDL-cholesterol did not achieve ≤ 100 mg/dl .

Patients whose initiating Atorvastatin use followed the above guidelines were rational evaluated, as shown in the second part of algorithm of Atorvastatin use by CAAT in Figure 4.1

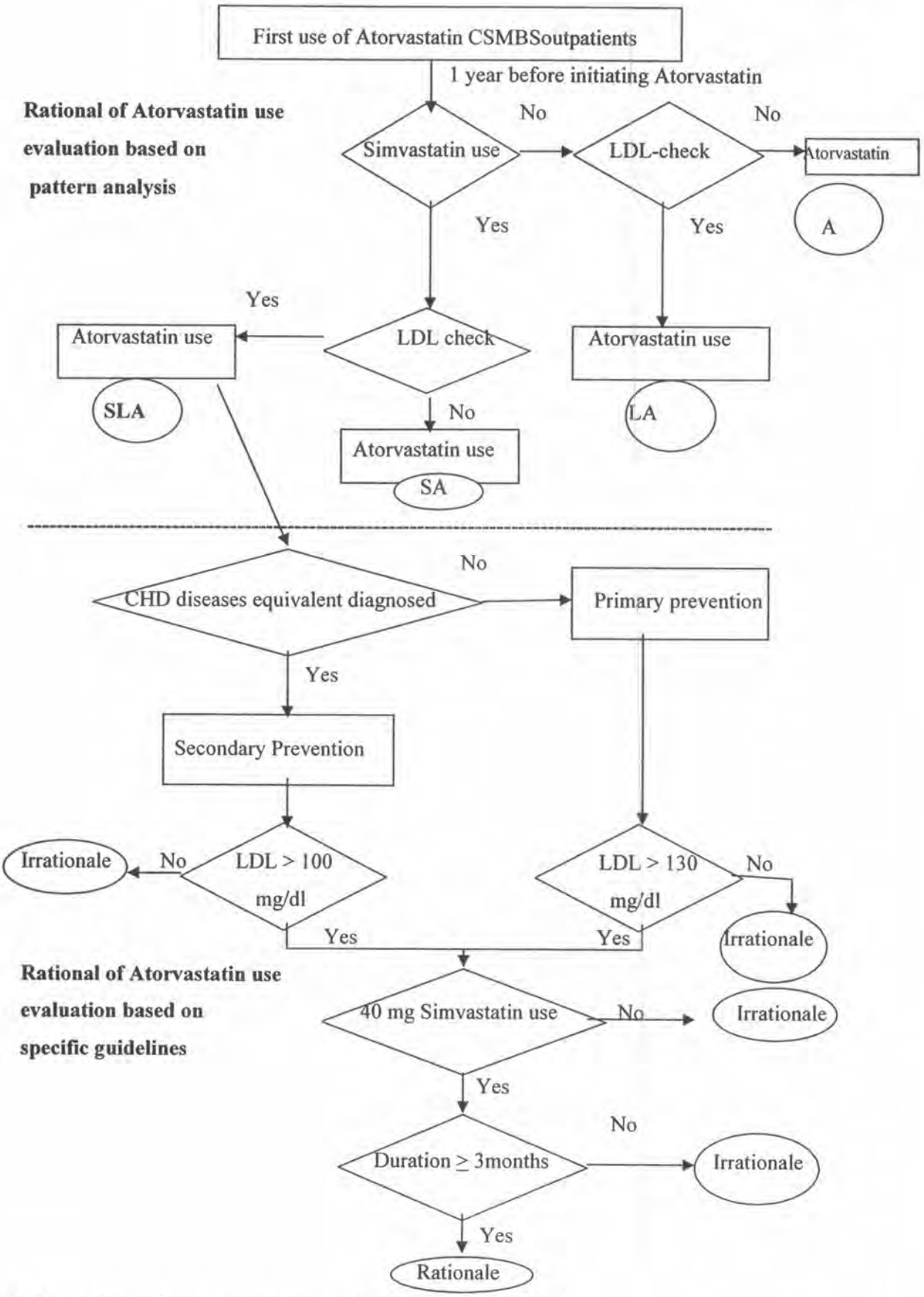


Figure 4.1 : Algorithm of the evaluation of Atorvastatin use

1.1.5.2 Development of CAAT guidelines for Rosiglitazone use evaluation

Concerning CAAT guidelines development for evaluation of the first use of Rosiglitazone in CSMBS outpatients, documents of Standard of Medical Care in Diabetes in 2007 of American Diabetes Association (ADA), a consensus statement from the American Diabetes Association and the European Association for the Study of Diabetes (EASD), Global Guidelinesd for Type 2 Diabetes, Guidance on the use of Rosiglitazone for Type2 Diabetes Mellitus (NICE technology appraisal guidance no. 9 [2000]), National Prescribing Service Limited for Rational Assessment of Drug and Research (NPS RADAR) on the authority required for Rosiglitazone for type 2 diabetes, 2004 National Essential Drug List of Thailand, and Diabetes Association of Thailand were revealed. Most of them have agreed that HbA1C level was the target variable of diabetic drugs' therapy for adequate controlling blood glucose concentration. The level of HbA1C to indicate adequately controlled blood glucose concentration varied from 6.5% to 7.5%. However, most of revealed document defined HbA1C <7% as adequate blood glucose control. The response of each initiation or dose increase of glucose-lowering drugs after 3-6 months should be monitored. For initiating the use of Rosiglitazone, the consistence findings showed that Rosiglitazoen was not recommended as the first line drug for controlling plasma glucose in type 2 diabetes patients. Rosiglitazone should be combined as dual oral therapy with Metformin or a sulfonylurea in patients whose blood glucose concentration was inadequately controlled. Rosiglitazone was also used when combination therapy with Metformin and a sulfonylurea was contra-indicated. In addition, NPS RADAR allowed using Rosigltazone as triple oral therapy with maximally tolerated dose of Metformin and a sulfonylurea. Experts review about the guidelines of Rosiglitazone use did not done. However, main indicators (HbA1C level, glucose-lowering drug use before Rosiglitazone initiated) required to evaluate the rational use of Rosiglitazone had been found in the Thai documents were not different from the majority of international documentations.

According to the findings above, the CAAT guidelines to evaluate the first use of Rosiglitazone in CSMBS outpatients was created. To evaluate the use of Rosiglitazone, two aspects were assessed. Rational use of Rosiglitazone were evaluated based on pattern analysis and based on specific guidelines.

Patterns of Rosiglitazone use were evaluated following the first part of algorithm of evaluation of Rosiglitazone use in Figure4.2. The step of Metformin use, HbA1C checking before initiating Rosiglitazone were evaluated. According to the guidelines, 4 patterns of Rosiglitazone use were classified. The patterns were

MHR : Metformin use → HbA1C checking → Rosiglitazone use

MR : Metformin use → Rosiglitazone use

HR : HbA1C check → Rosiglitazone use

R : Rosiglitazone use

Patients who initiated Rosiglitazone use following MHR pattern were rational drug use evaluated. Patients who started the use of Rosiglitazone following MR, HR, and R patterns were irrational drug use evaluated.

Rational use of Rosiglitazone evaluation based on specific guidelines was the second aspect of the evaluation. Patients in MHR pattern were recruited. For this aspect, duration of the use of Metformin had to be considered. Patients who had used Metformin continuously at least 3 months and HbA1C checked was $\geq$ 7% before initiating Rosiglitazone were rational evaluated as shown in the second part of the algorithm in Figure 4.2

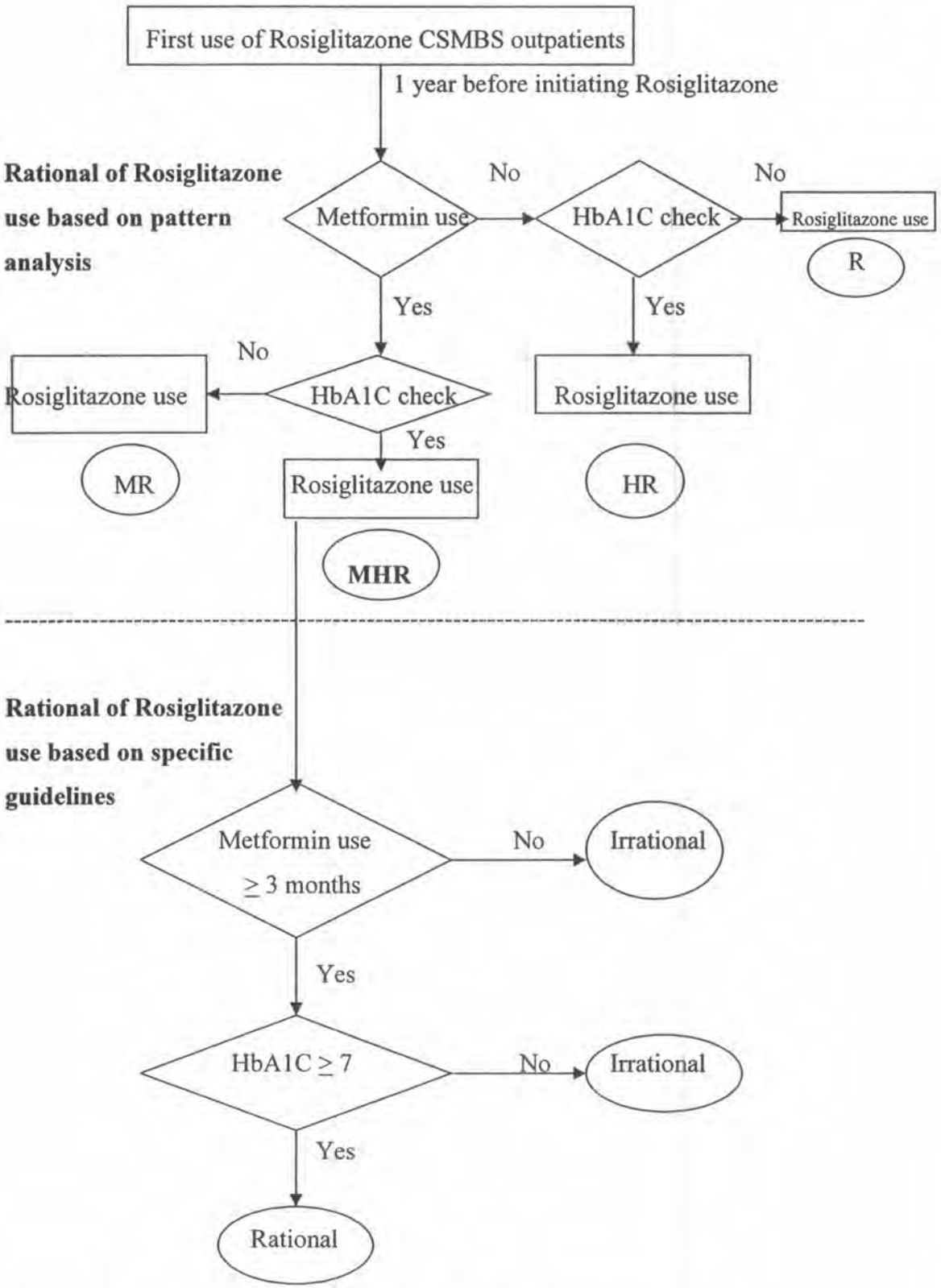


Figure 4.2 : Algorithm of the evaluation of Rosiglitazone use

1.2 Database management

The aims of database management was to extract data related to developed CAAT guidelines from database, to link data among database, and to prepare sets of data for analysis process. Troubles of data management process depended on the database use in the study. Separate database system management made more troubles and consumes much time more than integrated database system management. In this study, data needed for CAAT development were documented in three separate databases including Dispense database for drug prescribing data , HOMC database for ICD-10 , and LIS database for laboratory record.

For the database management process, there was some information that should be taken concern, as follow;

1.2.1 Data extraction: The objective of this step is to extract variables and data related to CAAT guidelines from database completely. Burdens of data extraction depends on three main factors, the type of database system used whether each database was separate system or integrate in one system, algorithm of data extraction, and different recording code in the same variable. For integrated database system, all data and variables of interest were extracted together. In contrast to separate database system, necessary data were extracted from each database system. For separate database system, sometimes other software programs were needed in order to transform database before beginning data extraction. Concerning algorithm of data extraction, it should have preliminary run with some samples to check whether it worked or not before extracting all needed data. Repeating data was also one important problems of data extraction in both types of database. The researcher must check during doing data extraction.

1.2.2 Data linkage: This step aimed to make data relation among database to prepare set of data for analysis. Data linkage was used in every step of data management process. Primary key variables were essential for linking. HN was an important primary key variable use for linking among table of data in the database. Primary key variables in data linking process must be the same in terms of type, form, and value or content. Direction of linking must be concerned. Because the results might be different when different direction was made. For example, the results extracted from the direction of linking HN from Table a to Table b might be different from the direction of linking HN from Table b to Table a.

1.2.3 Data completeness: This step is aimed to make unique variables name and type of data for each variables of dataset for CAAT analysis. In this step, the researcher faced with the problems of different types or codes of data recorded in database. Some variables having different codes needed to be recoded in the same new variables codes for the analysis process.

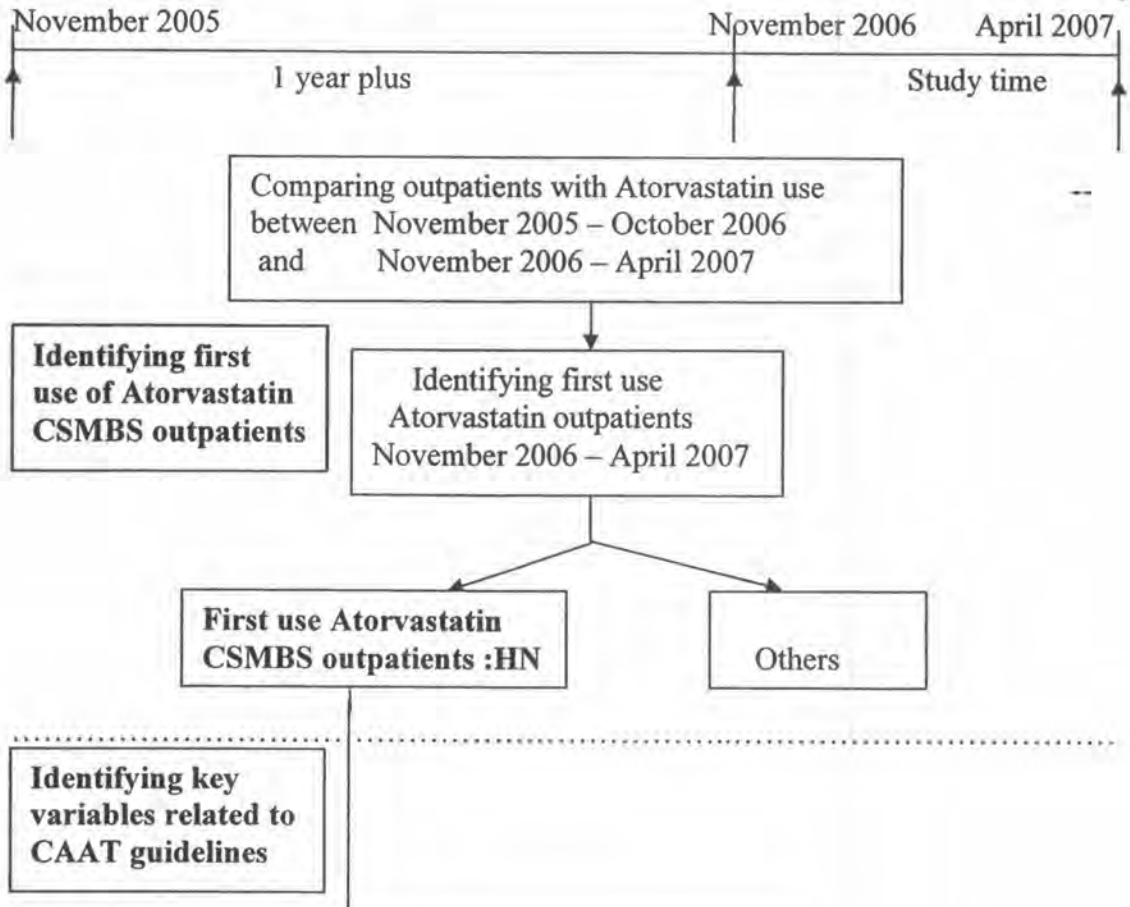
To prepare set of data for the rational use of HCD analysis by using CAAT, data management of Atorvastatin and Rosiglitazone were demonstrated. These following steps were done.

1. Identifying first use of Atorvastatin / Rosiglitazone in CSMBS outpatients and key variables related to CAAT guidelines
2. Data management to obtain key variables

a.) Data management for Atorvastatin use evaluation

1.) Identifying first use of Atorvastatin in CSMBS outpatients and key variables related to CAAT guidelines

To identify first use of Atorvastatin in CSMBS outpatients and key variables related to CAAT guidelines, the results were shown in Figure 4.3.



Key variables	
Study patient	HN
Date	LDL –cholesterol check date
	First Atorvastatin use date
	Simvastatin use date
Lipid level	LDL-cholesterol level
Drug dose	Simvastatin dose/day
	Atorvastatin dose/day
Duration of drug use	Duration of Simvastatin use
Disease diagnosis	Diseases related to CAAT guidelines

Figure 4.3 : Identifying first use of Atorvastatin in CSMBS outpatients and key variables related to CAAT guidelines

2) Data management to obtain key variables

Key variables for rational Atorvastatin use analysis were retrieved directly from main variables or indirectly from proxy variables related to the CAAT guidelines in the database. All of these variables were extracted from the database as shown in Table 4.1.

Table 4.1: Variables extracted from database for Atorvastatin use evaluation

Variables	Definition of variables
All database	
(1) HN	New Atorvastatin use CSMBS outpatients
Dispensing database	
(2) Atorvastatin use date	First date of Atorvastatin use
(3) Simvastatin use date	Date of Simvastatin use in the study time plus 1 year before
(4) Atorvastatin dose	Dose of Atorvastatin per time
(5) Frequency of Atorvastatin use	Frequency of Atorvastatin use in one day
(6) Quantity of Atorvastatin	Number of Atorvastatin dispensed
(7) Simvastatin dose	Dose of Simvastatin use per time
(8) Frequency of Simvastatin use	Frequency of Simvastatin use in one day
(9) Quantity of Simvastatin	Number of Simvastatin dispensed
(10) Related drugs	Drug dispense related to interest diseases
(11) Related drug date	Dispensing date of drugs related to interest diseases in the study time plus 1 year before
(12) Patient type	Outpatient or Inpatient
ICD-10 database	
(13) Related disease diagnosed date	Related diseases diagnosed date in study time plus 1 year before
(14) Related disease diagnosed	Diseases related to the CAAT guidelines
(15) Birth date	Birth date of study patients
(16) Sex	Sex of study patients
Laboratory database	
(17) LDL check date	Date of LDL-cholesterol check in the study time plus 1 year before
(18) LDL level	LDL-cholesterol level
(19) Cholesterol check date	Date of Total cholesterol check in the study time plus 1 year before
(20) Cholesterol level	Total- cholesterol level
(21) HDL check date	Date of HDL-cholesterol check in the study time plus 1 year before
(22) HDL level	HDL-cholesterol level
(23) Triglyceride check date	Date of Triglyceride check in the study time plus 1 year before
(24) Triglyceride level	Triglyceride level

All variables extracted from database were processed to obtain the key variables as outputs according to the CAAT guidelines for the rational Atorvastatin use evaluation as shown in Table 4.2.

Table 4.2: Input Process Output table for Atorvastatin use evaluation

Input variables	Process	Outputs
(1)HN (2) Atorvastatin use date, (17) LDL check date, (18) LDL level,) (19) Cholesterol check date, (20)Cholesterol level, (21) HDL check date, (22) HDL level, (23)Triglyceride check date, (24)Triglyceride level	1. Data linkage 2. Direct extraction of LDL- cholesterol level 3. Calculation of LDL-cholesterol level from (20),(22),and (24) for those patients whose LDL-cholesterol check were not available	Possible LDL-cholesterol level and LDL-cholesterol check date of each patient for data analysis process
(1) HN all new CSMBS patients , (2) Atorvastatin use date, (3) Simvastatin use date, LDL-cholesterol level*and LDL-cholesterol check date from outputs part above	1.Data linkage 2.Sequential analysis of these three dates of each patient	Pattern of Atorvastatin use (SLA, SA, LA, and A patterns) for each patient
(1) HN of patients in SLA pattern, (2) Atorvastatin use date, (10) Related drugs, (11) Related drugs'date ,(13) Related disease diagnosed date, (14) Related disease diagnosed	1. Data linkage 2.Diseases related to CAAT guidelines analysis	Diseases related to CAAT guidelines for evaluation of the use of Atorvastatin of each patient to identify type of CHD prevention

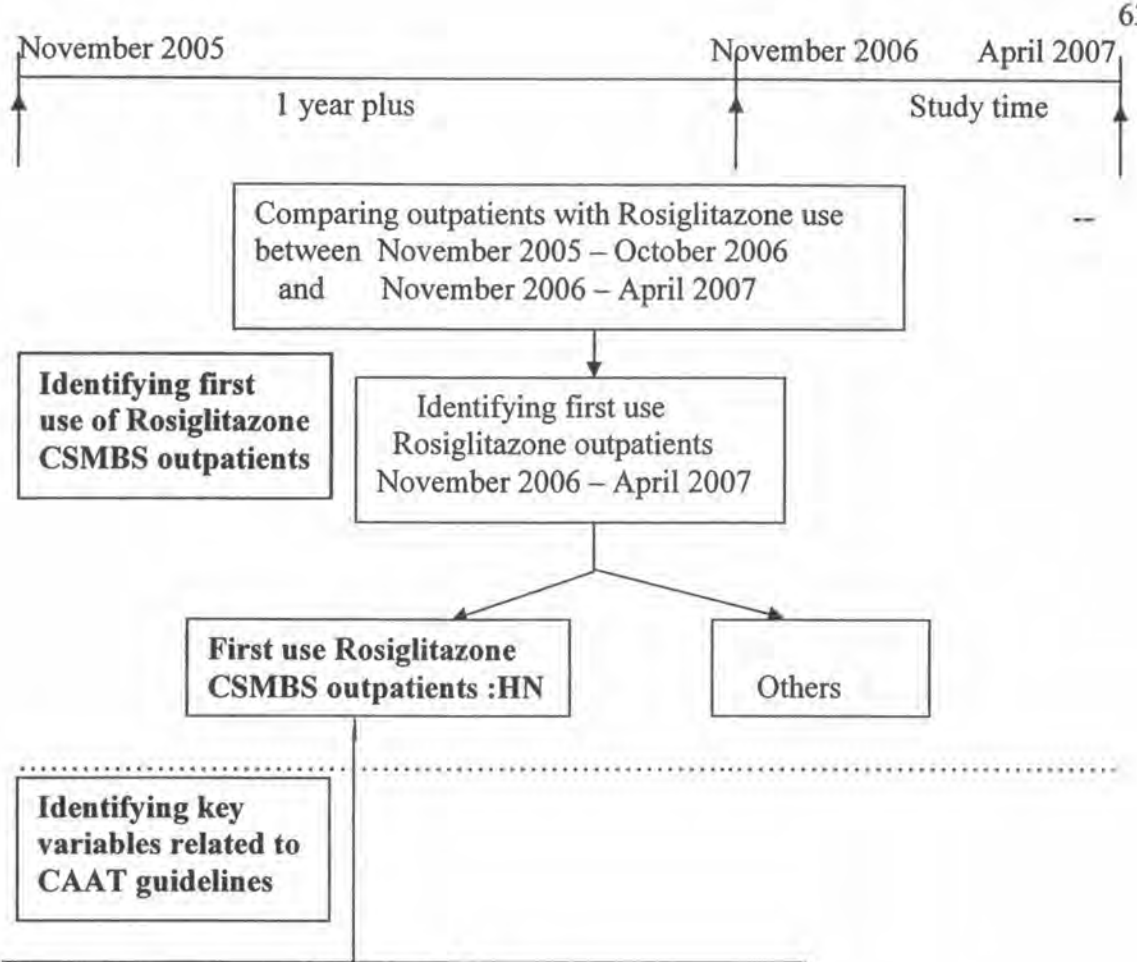
Table 4.2: Input Process Output table for Atorvastatin use evaluation (cont.)

Input variables	Process	Outputs
(1)HN of patient in SLA pattern, (2) Atorvastatin use date, (3) Simvastatin use date, (4) Atorvastatin dose, (5) Frequency of Atorvastatin use, (6) Quantity of Atorvastatin, (7) Simvastatin dose, (8) Frequency of Simvastatin use, (9) Quantity of Simvastatin, (12) Patient type	1. Data linkage 2. Calculation of Simvastatin dose/day 3. Calculation of Atorvastatin dose/day 4. Calculation of duration of Simvastatin use	Simvastatin dose/day Atorvastatin dose/day Duration of Simvastatin use
All output variables in SLA pattern	Data completeness	Set of data for rational Atorvastatin use analysis based on specific guidelines

b.) Data management for Rosiglitazone use evaluation

1.) Identifying first use of Rosiglitazone in CSMBS outpatients and key variables related to CAAT guidelines

To identify first use of Rosiglitazone in CSMBS outpatients and key variables related to CAAT guidelines, the results are shown in Figure 4.4.



Key variables	
Study patient	HN
Date	HbA1C check date
	First Rosiglitazone use date
	Metformin use date
HbA1C level	HbA1C level
Drug dose	Metformin dose/day
	Rosiglitazone dose/day
Duration of drug use	Duration of Metformin use

Figure 4.4 : Identifying first use of Rosiglitazone in CSMBS outpatients and key variables related to CAAT guidelines

2) Data management to obtain key variables

Key variables for rational Rosiglitazone use analysis were retrieved directly from main variables or indirectly from proxy variables related to the CAAT guidelines. All of these variables were extracted from the database as shown in Table 4.3.

Table 4.3: Variables extracted from database for Rosiglitazone use evaluation

Variables	Definition of variables
All database	
(1) HN	New Rosiglitazone use CSMBS outpatients
Dispensing database	
(2) Rosiglitazone use date	First date of Rosiglitazone use
(3) Metformin use date	Date of Metformin use in the study time plus 1 year before
(4) Rosiglitazone dose	Dose of Rosiglitazone use per time
(5) Frequency of Rosiglitazone use	Frequency of Rosiglitazone use in one day
(6) Quantity of Rosiglitazone use	Number of Rosiglitazone dispensed
(7) Metformin dose	Dose of Metformin use per time
(8) Frequency of Metformin use	Frequency of Metformin use in one day
(9) Quantity of Metformin use	Number of Metformin dispensed
(10) Related drugs	Drug dispense related to interest diseases
(11) Related drug date	Dispensing date of drugs related to interest diseases in the study time plus 1 year before
(12) Patient type	Outpatient or Inpatient
ICD-10 database	
(13) Disease of interest diagnosed date	Interest diseases diagnosed date in study time plus 1 year before
(14) Disease of interest diagnosed	Interest diseases
(15) Birth date	Birth date of study patients
(16) Sex	Sex of study patients
Laboratory database	
(17) HbA1C check date	Date of HbA1C check in the study time plus 1 year before
(18) HbA1C level	HbA1C level

All variables extracted from database were processed to get the target variables according to the CAAT guidelines for the rational Atorvastatin use evaluation as shown in Table 4.4.

Table 4.4: Input Process Output table for Rosiglitazone use evaluation

Input variables	Process	Outputs
(1) HN all new CSMBS patients , (2) Rosiglitazone use date, (3) Metformin use date, (17) HbA1C checkdate	1.Data linkage 2.Sequential analysis of the three dates of each patient	Pattern of Atorvastatin use (MHR, MR, HR, and R patterns) for each patient
(1)HN of patient in MHR pattern, (2) Rosiglitazone use date, (3) Metformin use date, (4) Rosiglitazone dose, (5) Frequency of Rosiglitazone use, (6) Quantity of Rosiglitazone use, (7) Metformin dose, (8) Frequency of Metformin use, (9) Quantity of Metformin use, (12) Patient type	1. Data linkage 2. Calculation of Metformin dose/day 3. Calculation of Rosiglitazone dose/day 4. Calculation of duration of Metformin use	Metformin dose/day Rosiglitazone dose/day Duration of Rosiglitazone use
All output variables in MHR pattern	Data completeness	Set of data for rational Rosiglitazone use analysis based on specific guidelines

II: Validating CAAT

CAAT validation was aimed to determine the effectiveness of CAAT for HCD use monitoring. Conventional DUE was used as standard method. For CAAT, sets of data and developed CAAT guidelines for Atorvastatin and Rosiglitazone evaluations in Part I were used. Concerning Conventional DUE method, data collection forms were used to collect data from outpatient records. Some data, such as LDL-cholesterol were collected from LIS database case by case. DUE guidelines which were used for both drugs used for Conventional DUE method were the same as DUE guidelines that were also used for CAAT. Sensitivity, specificity, and accuracy of CAAT were analyzed. Acceptable sensitivity, specificity and accuracy were $\geq$ 80%.

2.1 Validating CAAT for Atorvastatin use evaluation

To validate CAAT for Atorvastatin use evaluation, 148 samples of first use of Atorvastatin in CSMB outpatients between November 2006 and April 2007 from Hospital 1 (HOSP1) were recruited. Rational use of Atorvastatin were evaluated by CAAT and Conventional methods based on pattern of Atorvastatin use analysis and based on specific guidelines.

Regarding the evaluation of Atorvastatin use based on pattern analysis by using CAAT and Conventional DUE method, the results are shown in Table 4.5.

Conventional DUE guidelines was as same as CAAT guidelines. The number of patients initiating Atorvastatin followed by SLA and LA pattern when evaluated by Conventional method were more than the number of patients started Atovastatin following the same patterns evaluated by CAAT 3 and 8 cases respectively. In contrast, the number of patients initiating Atorvastatin followed by SA and A pattern when evaluated by CAAT were more than the number of patients that started Atovastatin following the same patterns evaluated by Conventional method 3 and 8 cases respectively. These differences were affected from date of laboratory checked which were recorded in database and in the patient records. When comparing set of data from database against the data from patient records, it was found that number of patients who had date of laboratory checked collected from patient records were more than number of patients who had these data from database. It was possible that patients really had laboratory checked date as same as laboratory checked date documented in laboratory database, but they visited hospital to see doctors the day after laboratory

checked date. Thus, the laboratory result would be recorded in the patient records on the visiting date in stead of real laboratory checked date. Another reason that caused the difference of laboratory checked date was patients might have laboratory checked outside hospital. Thus, laboratory results would be recorded in only patient records. This differences had main effect on the pattern analysis for rational use of Atorvastatin evaluation . In addition, the differences of laboratory checked date in patients' records and database had major effect not only on the accuracy but also the sensitivity of CAAT. Patients initiating the use of Atorvastatin followed by LA pattern were the highest.

Table 4.5 : Comparison of Conventional method and CAAT for Atorvastatin use evaluation based on pattern analysis

CAAT	Conventional method				
	A	LA	SA	SLA	Total
A	38	8	0	0	46
LA	0	71	0	0	71
SA	0	0	15	3	18
SLA	0	0	0	13	13
Total	38	79	15	16	148

A : Pattern of patients initiating Atorvastatin use without Simvastatin use and LDL-cholesterol check before.

LA : Pattern of patients had LDL-cholesterol checked before initiating the use of Atorvastatin

SA : Pattern of patients had used Simvastatin before initiating the use of Atorvastatin

SLA : Pattern of patients had used Simvastatin followed by LDL-cholesterol checked before initiating the use of Atorvastatin

As shown in Table 4.6, patients initiating the use of Atorvastatin followed by SLA pattern were the group that was rational. When it was evaluated by Conventional method, there were 16 cases (10.8%). When it was evaluated by CAAT, there were 13 cases (8.8%).

Using Conventional method as a standard reference, the sensitivity, specificity, and accuracy of CAAT for Atorvastatin use evaluation were 81.3%,100% and 98 %respectively.

Table 4.6 : Comparison of Conventional method and CAAT for rational Atorvastatin use evaluation based on pattern analysis

CAAT	Conventional method		
	Rationale	Irrationale	Total
Rationale	13	0	13
Irationale	3	132	135
Total	16	132	148

To evaluate rational Atorvastatin use based on specific guidelines by Conventional method and CAAT, only patients in SLA pattern were evaluated. Rational Atorvastatin use evaluation must meet all criteria of the specific guidelines which include LDL-cholesterol-level which Atorvastatin use required according to type of CHD prevention (LDL-cholesterol >130 mg/ml) for primary prevention and > 100 mg/ml for secondary prevention, duration of continuous Simvastatin use (≥ 3months) with maximum dose of Simvastation use (40 mg).

Based on the specific guidelines above, most of the patients initiating Atorvastatin use following SLA pattern met criteria of LDL-cholesteral level according to the type of CHD prevention and duration of Simvastatin use (10 out of 16 for Conventional method, and 8 out of 13 for CAAT). None of the patients evaluated by both methods had use Simvastatin 40 mg. Thus, based on specific guidelines, all patients following the SLA pattern were irrationally evaluated by both Conventional method and CAAT.

Because there was irrationally evaluated by using both Conventional method which is used as the reference standard, the sensitivity of CAAT couldn't be calculated. The specificity and accuracy of CAAT for Atorvastatin use evaluation in this study was 100%.

2.2 Validating CAAT for Rosiglitazone use evaluation

To validate CAAT for Rosiglitazone use evaluation, 74 CSMBS outpatients initiating the use of Rosiglitazone between November 2006 and April 2007 from Hospital 1 (HOSP1) were recruited. Rational use of Rosiglitazone were evaluated by CAAT and Conventional methods based on pattern of Rosiglitazone use analysis and based on specific guidelines.

Regarding the evaluation of Rosiglitazone use based on pattern analysis by using CAAT and using Conventional method, results are shown in Table 4.7.

Patients initiating Rosiglitazone followed by the MHR pattern evaluated by Conventional method were 3 cases more than patients started Rosiglitazone followed the same patterns assessed by CAAT. Patients initiating Rosiglitazone followed MR pattern were the highest.

Table 4.7 : Comparison of Conventional method and CAAT for Rosiglitazone use evaluation based on pattern analysis

CAAT	Conventional method				
	R	HR	MR	MHR	Total
R	6	0	0	0	6
HR	0	5	0	1	6
MR	0	0	46	2	48
MHR	0	0	0	14	14
Total	6	5	46	17	74

R : Pattern of patients initiating Rosiglitazone use without Metformin use and HbA1C check before.

HR :Pattern of patients who had HbA1C checked before initiating the use of Rosiglitazone

MR : Pattern of patients who had used Metformin before initiating the use of Rosiglitazone

MHR : Pattern of patients who had used Metformin followed by HbA1C checked before initiating the use of Rosiglitazone

As shown in Table 4.8, the number of rational use of Rosiglitazone evaluated by Conventional method were 17 cases (23.8%). The number of rational use of Rosiglitazone evaluated by CAAT were 14 cases (18.9%).

Using Conventional method as a standard reference, the sensitivity, specificity, and accuracy of CAAT CAAT for Rosiglitazone use evaluation were 82.3%, 100% and 95.9 %respectively.

Table 4.8 : Comparison of Conventional method and CAAT for rational use of Rosiglitazone evaluation based on pattern analysis

CAAT	Conventional method		
	Rationale	Irrationale	Total
Rationale	14	0	14
Irationale	3	57	60
Total	17	57	74

To evaluate rational Rosiglitazone use based on specific guidelines by using Conventional method and CAAT, only patients in MHR pattern were recruited. Rational Rosiglitazone use evaluation must meet all criteria of the specific guidelines which includes the continuous use of Metformin at least 3 months and the HbA1C level is $\geq$ 7%.

According to the specific guidelines above, all patients in MHR pattern met HbA1C criteria but the duration of Metformin use before initiating Rosiglitazone was different among these patients. There were 14 out of 17 cases for Conventional method, and 12 out of 14 cases for the CAAT method which met this criteria.. Thus, based on the specific guidelines, 14 and 12 patients following MHR pattern were rational, evaluated by using Conventional method and CAAT respectively as shown in Table 4.9.

Using the Conventional method as a standard reference, the sensitivity, specificity, and accuracy of CAAT for Rosiglitazone use evaluation were 85.7%, 100% and 97.3 % respectively.

Table 4.9 : Comparison of Conventional method and CAAT for rational use of Rosiglitazone evaluation based on specific guidelines

CAAT	Conventional method		
	Rationale	Irrationale	Total
Rationale	12	0	12
Irrational	2	60	62
Total	14	60	74

According to the results of the study of this part, it should be concluded that CAAT can be used to monitor high cost drug use in the hospitals. It could be used in stead of Conventional DUE method because CAAT had high validity with more than 80 % of sensitivity, specificity, and accuracy when compared with Conventional method. In addition, it was more efficient than manual.

Part III : Evaluation of studied high cost drug use by using developed CAAT

CAAT was used to evaluate the use of Atorvastatin and Rosiglitazone in four and two regional hospitals respectively in terms of rational utilization and their spending.

To evaluate rational use of these two drugs, the evaluation started with pattern analysis followed by rational evaluation using specific guidelines.

3.1 Evaluation of the use of Atorvastatin in four regional hospitals

To evaluate the use of Atorvastatin in this study, all first use of Atorvastatin in CSMBS outpatients between November 2006 and April 2007 of four regional hospitals were recruited. 307 (52.6%) from hospital 1 (Hosp1), 175 (30.0%) from hospital 2 (Hosp2), 56 (9.6%) from hospital 3 (Hosp.3) , and 46 cases (7.9%) from hospital 4 (Hosp.4). General information of patients were in Appendix D.

Concerning pattern of the use of Atorvastatin evaluation in all of patients of the 4 hospitals, results are shown in Figure 4.5.

Thirteen percent of all patients in four hospitals initiating Atorvastatin use followed SLA pattern which was rationale evaluated based on rational use pattern analysis. Eighty seven percent of patients including 44.3%, 29.5%, and 13.2% followed LA, A, and SA patterns respectively were irrationaly Atorvastatin use evaluated.

Comparing the evaluation of patterns of the use of Atorvastatin in patients following SLA pattern among four hospitals with the total cases of each hospital, it varied from 10.1 to 17.9%. The highest magnitude was in Hosp.3. Most of irrational use evaluated in each hospital were following LA and A patterns. It was noticed that the highest percentage of irrational use evaluated in most hospitals, except Hosp.4, followed LA pattern.

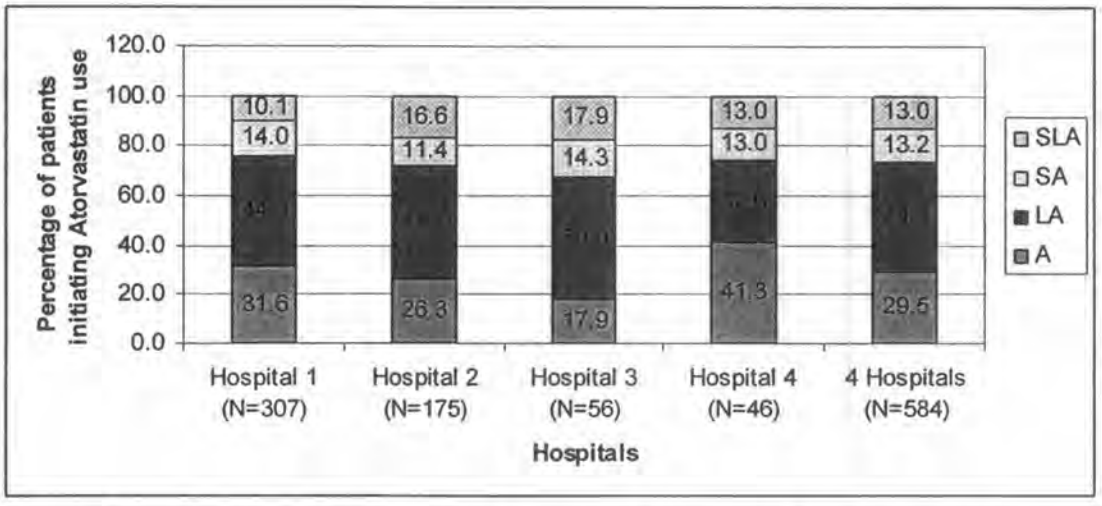


Figure 4.5 : Evaluation of patterns of the use of first use of Atorvastatin in CSMBS outpatients in four hospitals

The overall Atorvastatin expenditure for all studied patients between November 2006 to April 2007 was 2,990.1 thousand baht. It included the spending of Hospl, Hosp.2, Hosp.3, and Hosp.4, the exact number arel,537 , 897.0, 343.1, and 212.9 thousand or 51.4%, 30.0%, 11.5, and 7.1% of 4 hospitals' Atorvastatin spending respectively.

Spending of Atorvastatin for 76 patients (13% of all patients) following SLA pattern (rational pattern evaluated), were 764.5 thousand bath (15% of 4hospitals's spending). Eighty five percent of all expenditure (2,225.6 thousand bath) were the spending of Atorvastatin use for 508 patients (87% of all patients) following LA, SA, and A patterns. High spending on irrational Atorvastatin use might have been affected from the policy of the hospitals for the weak control on rational Atorvastatin use. In addition, Atorvastatin was mainly prescribed for CSMBS patients who can reimburse all of their drug payment. Thus, government hospitals get this income for cross subsidy of people holding other health insurances with capped budgets. Another reason was the prescribers usually prefer using more potent new drug like Atorvastatin to generic old drug lik Simvastatin. Resulting from the prescribers' preference to using new drugs and the weak control over HCD use, irrational use is trended to be high. The highest irrational expense of Atorvastatin use was in LA pattern with 43.9% of overall spending (1,312.8 thousand baht) for 259 patients (44.3% of all patients).

Comparing the expenditure of rational Atorvastatin use with its total expenditure of each hospital, it varied from 11.1% to 24.9%. Hosp.3 showed the highest percentage

with 24.9% but Hosp.1 reported the lowest percentage of rational Atorvastatin use expenditure with 11.1% as showed in Figure 4.6

Among irrational Atorvastatin use patterns , the highest spending were an LA and A patterns respectively. It was found in most hospitals, except Hosp.4. More than 40% of total Atorvastatin expenditure of each hospital were spent for patients initiating Atorvastatin following LA pattern.

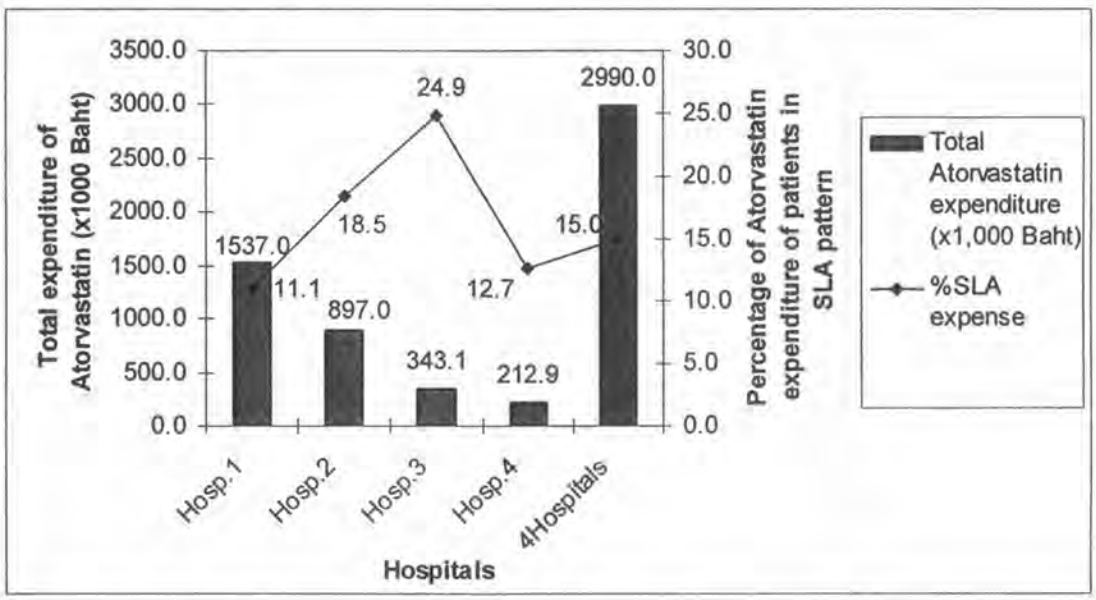


Figure 4.6 : Total expenditure of Atorvastatin and percentage of Atorvastatin use in patients in SLA pattern

Concerning excess spending of irrational use of Atorvastatin, the quantitiy of Atorvastatin use in LA, SA, and A pattern were analyzed. Based on the assumption that these patients might get high dose Simvastatin. Thus, 4 tablet of generic Simvastatin 10 mg. were used to substitute 1 tablet of Atorvastatin. To calculate the cost of Simvastatin, the highest price of generic Simvastatin 10 mg, at 1.50 baht /tablet, was used. Therefore, the formulation of cost of Simvastatin use for Atorvastatin substitution analysis was as follow,

Expenditure of Simvastatin substituted for irrational Atorvastatin use

= Number of irrational use of Atorvastatin tablet x 6

Thus, Excess expenditure of irrational use of Atorvastatin

= All expenditure of irrational– Expenditure of Simvastatin substitute

Atorvastatin use for all irrational Atorvastatin use

Calculation of expenditure of Simvastatin substituted for 50,693 tablet of Atorvastatin use in LA, SA, and A pattens of 4 hospitals was only 304.1 thousand baht.

Cost wasted because of irrational use of Atorvastatin was 2, 237.5 thousand baht for 508 new CSMBS outpatients during a 6 months spending , as shown in Figure 4.7. It should be assumed that the average of cost waste of irrational use of Atorvastatin = 8,809 bath/patient/year.

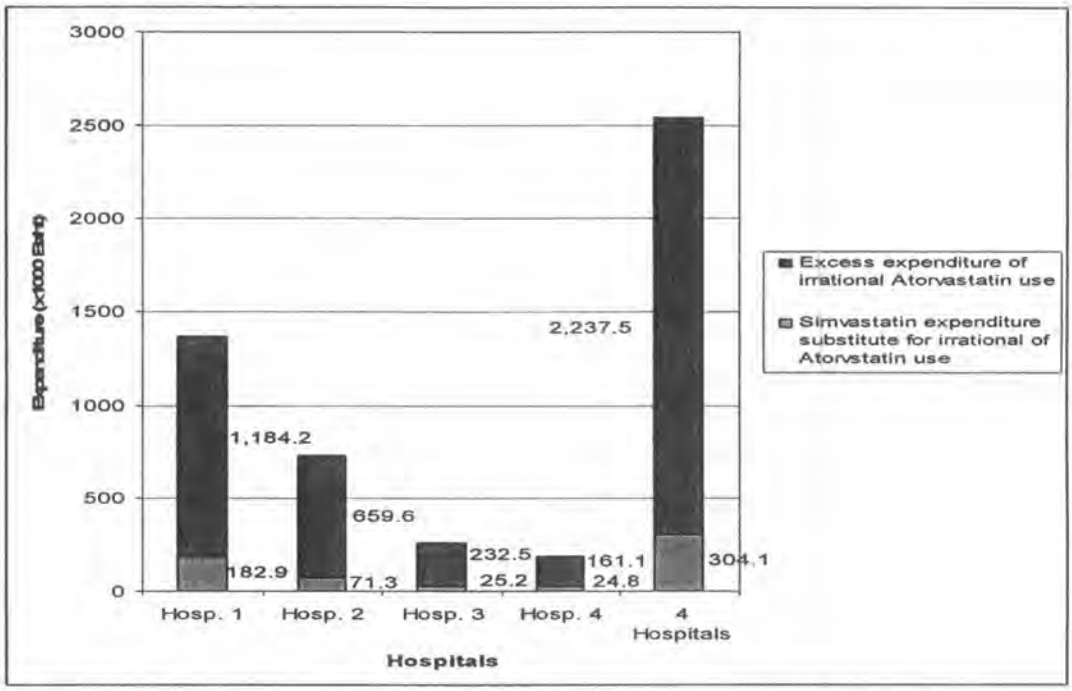


Figure 4.7 : Simvastatin expenditure substitute for irrational use of Atorvastatin expenditure and excess expenditure of irrational Atorvastatin use based on pattern analysis of the use of Atorvastatin

Concerning evaluation of rational Atorvastatin use in patients based on specific guidelines, 76 patients who initiatiated Atorvastatin following SLA pattern were recruited, as results are reported in Table 4.10.

Classifying patients following SLA pattern according to the type of CHD prevention, 24 (31.6%) patients were in primary CHD prevention group and 52 (68.4%) patients were in secondary CHD prevention group.

According to rational Atorvastatin use evaluated in primary CHD prevention type of patients, Atovastatin would be used on patients who had been using Simvastatin 40 mg continuously for at least three months and LDL-cholesterol level more than 130 mg/dl. Only 1 patients (1.3%) was rational evaluated of Atorvastatin use based on specific guidelines.

According to rational Atorvastatin use evaluated in secondary CHD prevention type of patients, Atovastatin would be used on patients who had been using Simvastatin

40 mg continuously for at least three months and LDL-cholesterol level more than 100 mg/dl. Only 1 patient (1.3%) was rational evaluated of Atorvastatin use based on specific guidelines.

Based on specific guidelines above, only 2 patients (2.6%) of all patients following SLA pattern initiating the use of Atorvastatin were rational. Evaluating of Atorvastatin use based on the specific guidelines in 584 patients, only 2 patients (0.3%) were rational evaluated, one case being in Hosp.4 and the other in Hosp.2.

Table 4. 10 : Number and percentage of rational Atorvastatin use in patients initiating Atrovastatin follow SLA pattern based on specific guidelines

Type of CHD prevention	Atorvastatin use evaluation	Patients initiating Atorvastatin use followed SLA pattern (N = 76)	
		Number	Percentage
Primary prevention	Rationale	1	1.3
	Irrationale	23	30.3
Secondary prevention	Rationale	1	1.3
	Irrationale	51	67.1

Based on the evaluation by specific guideline, the expenditure of rational use was 0.3 % (8,730 baht).

3.2 Evaluation of the pharmaceutical spending of first use of lipid regulating drugs of CSMBS outpatients during November 2006 and April 2007 in four regional hospitals.

Lipid regulating drugs reported in this study were the drugs initiated in CSMBS outpatients during November 2006 and April 2007 in four regional hospitals. Results of the evaluation of lipid regulating drugs' use of new CSMBS outpatients are shown in Figure 4.8.

3,508 patients were recruited in this study. Eighty three percent (N=2,919) of patients were first use of statins including Simvastatin 45% (N=1,579), Rosuvastatin 21.6% (N=756), and Atorvastatin 6.6% (N=584). Thirteen percent (N=453) of patients were first use of fibric acids, Nicotinic acid, Ezitimide, and Cholestyramine.

Concerning the spending of drugs used in the patients during studied time, the total drugs' was were 7,497.1 thousand baht. Eighty eight percent (6,595.9 thousand baht) was for Statins use. Among statins drurgs, Rosuvastatin consumed the highest expense with 44.8% (3,356.6 thousand baht) of overall lipid regulating drug spending. The spending of Atorvastatin was 39.9% (2,990 thousand baht), and only 3.3% (249.3 thousand baht) spent for Simvastatin.

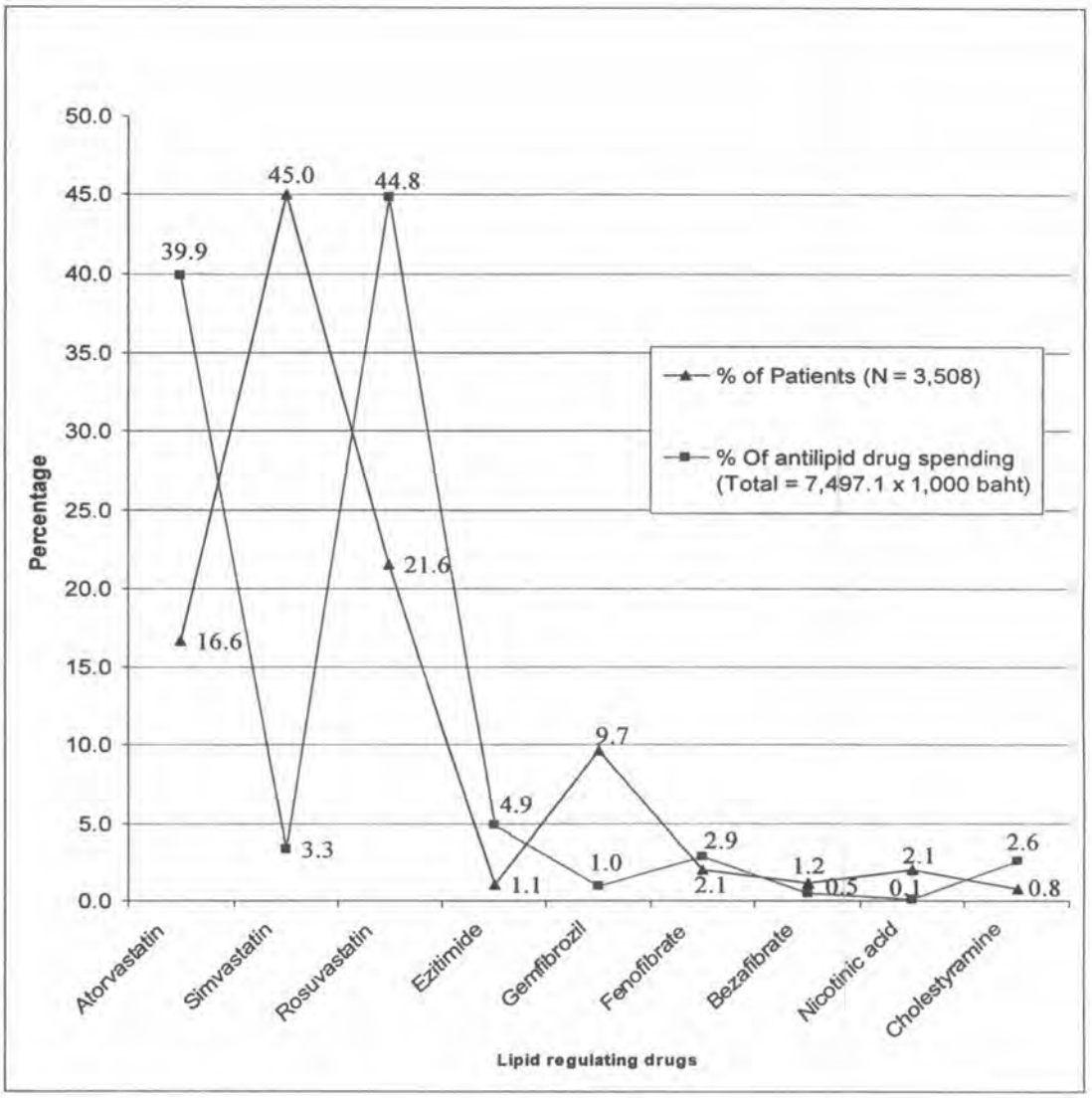


Figure 4.8 : Lipid regulating drugs used in new CSMBS outpatients during November 2006 and April 2007

Concerning lipid regulating drugs use among four hospitals, Atorvastatin, Rosuvastatin, Simvastatin, and other lipid drugs were analyzed in terms of percentage of patients and their spending on these drugs. The results are reported in Table 4.11.

The number of patients who initiated the use of lipid drug regulation among hospitals, there were 1,208, 1183, 684, 433 patients in Hosp.1-4 respectively.

Simvastatin has the highest proportion of patients in all four hospitals. Hosp.4 and Hosp.1 had patients who initiated Simvastatin with very high proportion at 71.6% and 60.5% of patients in each hospital respectively. Comparing the proportion of Rosuvastatin use ,three hospitals except Hosp4 were higher than the proportion of Atorvastatin.

In most of the hospitals, Rosuvastatin and Atorvastatin consumed much higher proportion of expenditure than Simvastatin spending proportion in most hospitals. Comparing proportion of Simvastatin spending among the hospitals, Hosp.4 had the highest proportion with 20% of overall lipid spending of its hospital. It was 16.7, 6.25, and 2.8 times greater when compare with the proportion of Simvastatin spending in Hosp.1, Hosp.2 and Hosp.3 respectively.

Table 4.11 : Lipid regulating drug use initiated in CSMBS patients among four hospitals

Hospitals	Simvastatin	Atorvastatin	Rosuvastatin	Others*
New CSMBS outpatients : n (%)				
Hosp.1 (N=1208)	428 (35.4)	307 (25.4)	361 (29.9)	112 (9.3)
Hosp.2 (N=1183)	427 (36.1)	175 (14.8)	317 (26.8)	264 (22.3)
Hosp.3 (N=684)	414 (60.5)	56 (8.2)	73 (10.7)	141 (20.6)
Hosp.4 (N=433)	310 (71.6)	46 (10.6)	5 (1.2)	72 (16.6)
Lipid regulation drug spending .....x1000 B (%)				
Hosp.1 (Total =3,692.6x1,000B)	43.3 (1.2)	1,537.0(41.6)	1,733.7(47.0)	378.6(10.3)
Hosp.2 (Total=2,700.7x1,000B)	87.2 (3.2)	896.9(33.2)	1,256.2(46.5)	460.4(17.0)
Hosp.3 (Total= 796.2x1,000B)	57.2 (7.2)	343.2 (43.1)	350.7 (44.0)	45.1 (5.7)
Hosp.4 (Total= 307.6x1,000B)	61.1 (20.0)	212.9 (69.2)	16.0 (5.2)	17.1 (5.6)

- Fibric acids group + Ezitimide + Nicotinic acid + Cholestyramine
-

3.3 Evaluation of the use of Rosiglitazone in two regional hospitals

To evaluate the use of Rosiglitazone of this study, all new CSMBS outpatients initiating Rosiglitazone between November 2006 and April 2007 of two regional hospitals were included. There were 87 patients, being 80 (92.0%) and 7 cases (8.0%) in Hosp.1 and Hosp.2 respectively. General information of the patients are in Appendix E.

Concerning pattern of the use of Rosiglitazone evaluation in patients of the hospitals, results were shown in Table 4.12.

Evaluation of Rosiglitazone use based on pattern analysis found that 17.2% of all patients initiating Rosiglitazone use following MHR pattern that was rationale evaluated. Patients starting Rosiglitazone following MR, HR, and R patterns were irrational use evaluated with 63.2%, 8.0%, and 11.5% respectively.

Only 17.2% of patients from 2 hospitals were in MHR pattern. All of them were in Hosp.1. Most of irrational use patients were following MR and R patterns.

Concerning the spending of Rosiglitazone use in all patients among patterns, spending of Rosiglitazone use in 15 patients following MHR pattern were 94.5 thousand bath (15.3% of two hospitals' spending). Eighty five percent of all expenditure (522.5 thousand bath) were irrational Rosiglitazone use for 72% patients. The highest of irrational expense of Rosiglitazone use was in MR pattern with 65.8% (406.1 thousand baht).

Table 4.12 : Frequency of CSMBS outpatients in any pattern of initiating Rosiglitazone use and their spending

Hospitals	Pattern of first Rosiglitazone use in CSMBS outpatients			
	MHR	MR	HR	R
Patients: % (n)				
Hosp.1 (N=80)	18.8 (15)	63.8 (51)	8.8 (7)	8.8 (7)
Hosp.2 (N=7)	0.0	57.1 (4)	0.0	42.9 (3)
2 Hospitals (N=87)	17.2 (15)	63.2(55)	8 (7)	11.5 (10)
Expenditure: % (...x1.000 Baht)				
Hosp.1 (Total = 551.6)	17.1 (94.5)	66.1 (364.4)	9.2 (50,7)	7.6 (42.0)
Hosp.2 (Total = 65.4)	0 (0)	63.7 (41.7)	0 (0)	36.3 (23.7)
2 Hospitals (Total= 617.0)	15.3 (94.5)	65.8 (406.1)	8.2 (50.7)	10.7 (65.7)

Concerning evaluation of rational Rosiglitazone use in patients based on specific guidelines, patients initiating Rosiglitazone following MHR pattern were recruited. Patients who had used Metformin continuously for at least 3 months and HbA1C $\geq$ 7% and were rational evaluated. Fifteen patients who initiated Rosiglitazone followed MHR pattern would be analyzed as results are reported in Table 4.13.

According to the specific guidelines, 80.0% (n = 12) of patients following MHR pattern were rational evaluated of Rosiglitazone use. However, there was only 13.8 % (12out of 87 cases) of overall patients who were initiating Rosiglitazone rationally. All rational cases were in Hosp.1.

Table 4.13 : Number and percentage of rational use of Rosiglitazone of patients initiating Rosiglitazone use followed MHR pattern based on specific guidelines

Rosiglitazone use evaluation	Patients initiating Atorvastatin use followed MHR pattern (N = 15)	
	Number	Percentage
Rationale	12	79.9
Irrationale	3	20.1

The expenditure of Rosiglitazone use in studied patients according to rational evaluation following specific guidelines was 12.1 % (7.5 thousand baht) of the overall spending of Rosiglitazone.

3.3 Evaluation of the pharmaceutical spending of newly use ofAnti-diabetic drugs of CSMBS outpatients during November 2006 and April 2007 in four regional hospitals.

Anti-diabetic drugs reported in this study are the drugs that were initiated use in the CSMBS outpatients during November 2006 and April 2007 in four regional hospitals. Results of the evaluation of first use of anti-diabetic drug in CSMBS outpatients are shown in Figure 4.9.

The number of first use of anti-diabetic in CSMBS outpatients of this study were 2,200 cases. The patients initiating the use of sulfonylureas drug group were the highest magnitude with 39.8 % (n = 876) of all patients. Thirty two percent (n = 698) of all patients were initiated the use of Metformin. Patients initiated the use of Thiazolidinedione drug group were 9.5 % including 4% of Rosiglitazone and 5.5 % of Pioglitazone. Glagine insulin was initiated by about 4.6% (n = 102) of all studied patients.

Concerning spending of diabetic drugs' used in the studied patients during studied time, the total drugs' expense was 3,024.7 thousand baht. Thiazolidinedione group consumed 41.5 % (1,255.8 thousand baht) of all spending. That of which included the spending of Rosiglitazone and Pioglitazone with 20.4% (617.1 thousand baht) and 21.1% (638.7 thousand baht) respectively. Sulfonylureas drugs consumed 19.7 % (595.7 thousand baht) of all expenditure. The spending of insulin Glagine was 20.3% (614.7 thousand baht) of all expense.

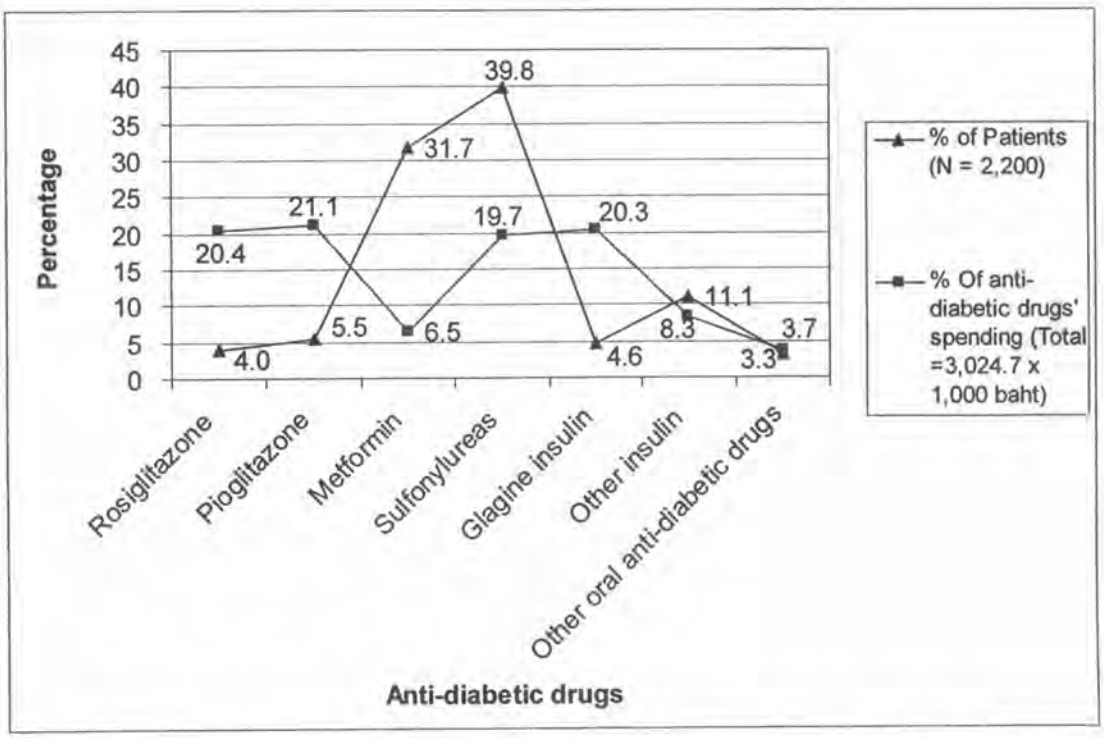


Figure 4.9 : Anti-diabetic drugs use in new CSMBS outpatients of four studied hospitals during November 2006 and April 2007

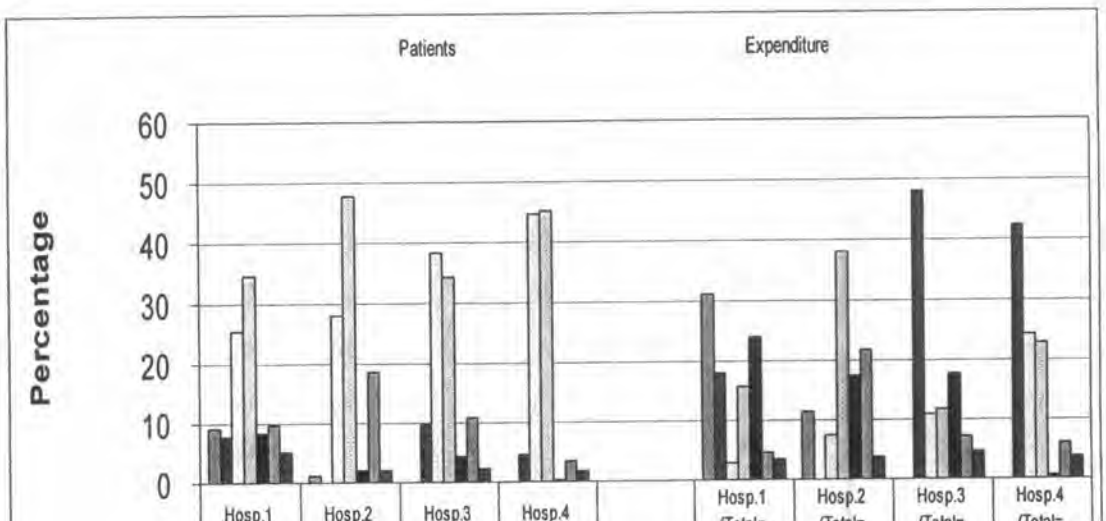
Concerning anti-diabetic drugs use among four hospitals, Rosiglitazone, Pioglitazone, Metformin, Sulfonylureas, Glagine insulin, other oral diabetics drugs, and other insulin were analyzed in terms of percentage of patients and their spending of each hospitals. Results are reported in Figure 4.10.

The number of patients who initiated the use of anti-diabetic drugs were 865 in Hosp.1, 561 in Hosp.2, 376 in Hosp.3 and 398 in Hosp 4.

Sulfonylureas initiation had the highest proportion of patients in most hospitals. The next was the proportion of patients initiating the use of Metformin. Proportion of new Metformin use were 25.3%, 28.0%, 38.3%, and 44.7% in Hosp.1, Hosp.2, Hosp.3, and Hosp.4 respectively. About the proportion of patients initiating thiazolidinedione drugs among hospitals, Hosp.1 had the highest magnitude with 16.8%. Hosp.2 had the lowest percentage of patients who started thiazolidinedione drug group with 1.2%. There were 18.7 % of patients in Hosp.2 initiating other insulin, being greater than other hospitals by about 2-6 times. The highest proportion of patients initiating Glagine insulin was in Hosp.1 with 8.4% and the lowest proportion was in Hosp.4 with 0.3%.

Concerning the spending of each anti-diabetic drugs use among hospitals, there were some differences among the highest spending. Most hospitals had highest

spending on thiazolidinedione (Rosiglitazone and/or Pioglitazone) group at 49.3%, 48.0%, and 42.3% in Hosp.1, Hosp.3, and Hosp.4 respectively. On the other hand, Hosp.2 spent the highest expenditure on sulfonylureas drugs at 38.0%, followed by other insulin at 21.8%. Considering the expenditure on Metformin use, Hosp.4 showed the highest percentage with 24.4%. The next were 10.8%, 7.5%, and 3.0% of all expense of Hosp.3, Hosp.2, and Hosp.1 respectively. Regarding the spending on Glagine insulin, Hosp.1 reported the highest percentage, 24.1%, when compare with other hospitals. Proportion of insulin Glagine expenditure of Hosp.2 and Hosp.3 were alike with 17%. Hosp.4 reported the lowest proportion of insulin Glagine expenditure, 0.5%.



	Hosp.1 (N=865)	Hosp.2 (N=561)	Hosp.3 (N=376)	Hosp.4 (N=398)		Hosp.1 (Total= 1766.3x1000	Hosp.2 (Total= 572.0x1,000B	Hosp.3 (Total= 493.3x1,000B	Hosp.4 (Total= 192.5x1,000B
Rosiglitazone	9.2	1.2	0.0	0.0		31.2	11.4	0.0	0.0
Pioglitazone	7.6	0.0	9.8	4.5		18.1	0.0	48.0	42.3
Metformin	25.3	28.0	38.3	44.7		3.0	7.5	10.8	24.4
Sulfonylureas	34.6	47.8	34.3	45.2		15.6	38.0	11.8	22.9
Glagine insulin	8.4	2.1	4.3	0.3		24.1	17.5	17.8	0.5
Other insulin	9.7	18.7	10.9	3.5		4.5	21.8	7.1	6.1
Other oral diabetic drugs	5.1	2.1	2.4	1.8		3.4	3.7	4.5	3.7

Figure 4.10 : Anti-diabetic drugs use initiated in CSMBS patients among four studied hospitals in terms of percentage of patients and their spending