

## CHAPTER III

### METHODOLOGY

#### Research Design

This study was a retrospective research during November 2002 to December 2002 in orthopedic outpatient clinic at Lerdsin Hospital.

#### Subjects

Data from orthopedic outpatient prescriptions and OPD Card having specific COX II inhibitors and NSAIDs was collected.

#### Inclusion Criteria

All orthopedic outpatient prescriptions visited during November 2002 to December 2002.

#### Instrument

Data collection form was used to be instrument of this study. The data collection form is shown in Appendix A.

#### Sample Sizes

$$\text{From } n = \frac{Z^2_{\alpha/2} PQ}{e^2}$$

n = Number of samples

$Z_{\alpha/2}$  = Z score of  $\alpha/2$

P = Proportion of population

Q = 1 - P

e = Error of proportion approximation

From our pilot study at Rajavithi Hospital, we collected 38 prescriptions. There were 16 prescriptions of high risk group, and 22 prescriptions of low risk group.

From pilot study, data was modified into equation,

$$\begin{aligned} P &= \text{Proportion of high risk group} \\ &= 16/38 \\ &= 0.42 \\ Q &= 1 - P \\ &= 1 - 0.42 \\ &= 0.58 \end{aligned}$$

At 95% Confident Interval,  $\alpha = 0.05$ ,  $Z_{\alpha/2} = Z_{0.05/2} = 1.96$

$$e = 0.05$$

$$\begin{aligned} \text{Therefore } n &= \frac{Z_{\alpha/2}^2 PQ}{e^2} \\ &= \frac{1.96^2 * 0.42 * 0.58}{(0.05)^2} \\ &= 374.3 \quad \text{prescriptions} \\ &\approx 375 \quad \text{prescriptions} \end{aligned}$$

Based upon the pilot study, 55 prescriptions were collected. However, of all the 55 prescriptions, only 38 prescriptions had the OPD cards at Medical Record Department. Therefore, to achieve the total of 375 prescriptions, 542 prescriptions were collected.

We planned to collect 542 prescriptions of specific COX II inhibitors and 542 prescriptions of NSAIDs during the time of the study. Of the 542 prescriptions, 271 prescriptions of specific COX II inhibitors were collected in November 2002 and 271 prescriptions of specific COX II inhibitors were collected in December 2002. In the same manner, NSAIDs were collected as same as specific COX II inhibitors prescriptions. To collect specific COX II inhibitors prescriptions in each month, a proportion of celecoxib and rofecoxib prescriptions were used. By the same way, proportion of all NSAIDs prescriptions in each month was reported as Appendix B.

## Setting

Data were collected from Lerdsin Hospital, the special Institute of Orthopedics. There were 21 orthopedists (data from administrative department in July1, 2002). There were approximately 2,000 orthopedic outpatients per month based on computerized patient records.

## Data Collection Procedures

Data collection procedure was shown in Figure 3.1. The process was described as follows:

1. HN and name of orthopedic outpatients were searched by computerized patient records. To select the prescriptions, computerized simple random sampling (SRS) was used.

2. Specific data from all prescriptions and OPD Card were recorded into data collection form. These data included patients' characteristics, patients' history, and physicians prescribing as follows:

- 2.1 Patients' characteristics.

- 2.1.1 Age

- 2.1.2 Gender

- 2.1.3 Marital Status

- 2.1.4 Religion

- 2.1.5 Nationality

- 2.1.6 Occupation

- 2.1.7 Payment status

- 2.2 Patients' histories

- 2.2.1 Clinical history of gastrointestinal and gastroduodenal symptoms.

- 2.2.2 Concomitant use of medications.

- 2.2.3 Presence of serious co-morbidities.

- 2.2.4 Prolonged used of maximum recommended doses of standard NSAIDs.

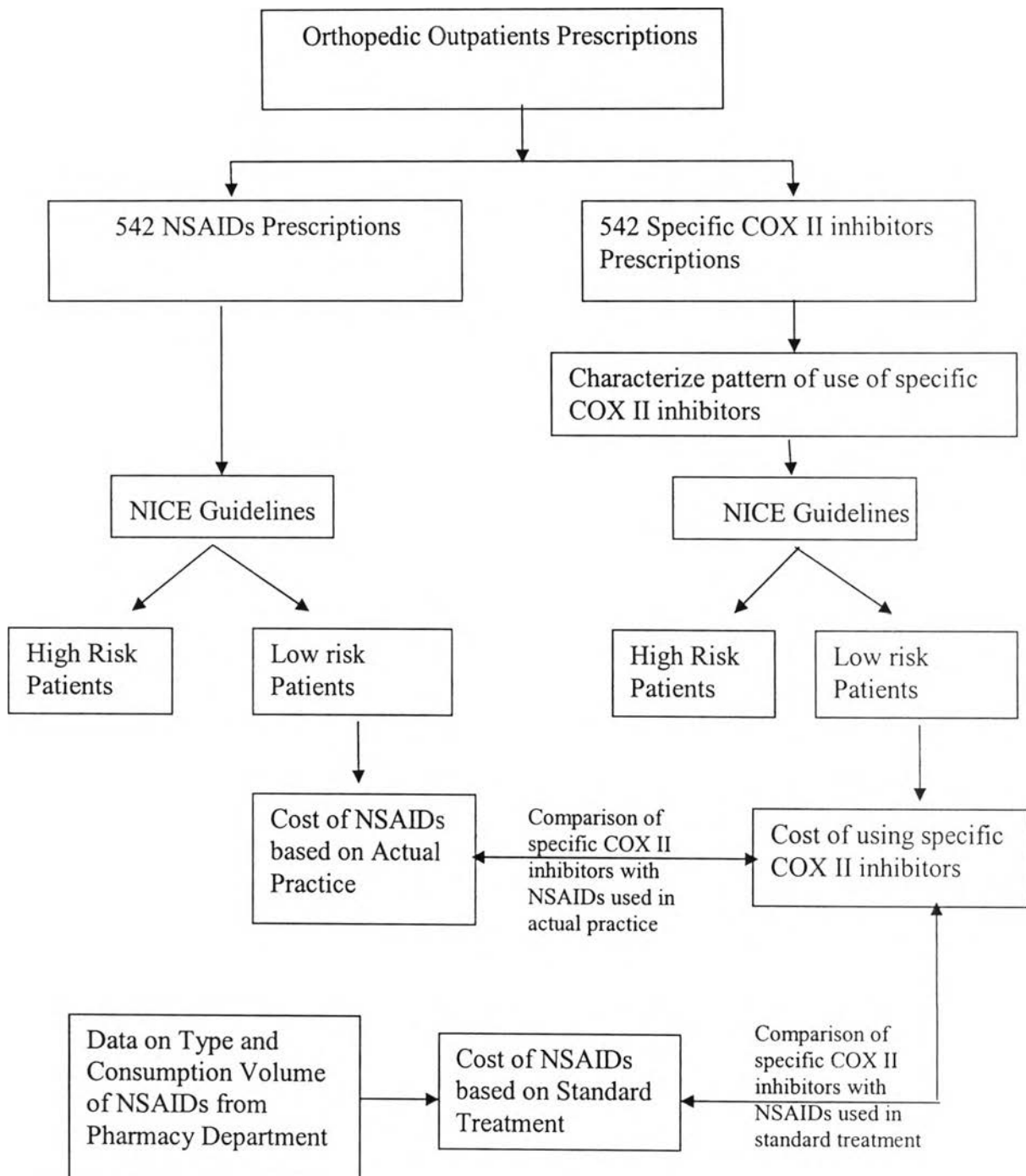


Figure 3.1: Flow of data collection procedure.

### 2.3 Physicians prescribing

2.3.1 Type of diseases or indications for specific COX II inhibitors and NSAIDs use.

2.3.2 Therapy duration of specific COX II inhibitors and NSAIDs use.

2.3.3 Regimen of specific COX II inhibitors and NSAIDs use.

2.4 If there were problems based on data collected, the researcher followed these criteria;

2.4.1 If there was no symptom, indication or disease appearing in OPD Card, the researcher assumed that the patients do not have any symptom.

2.4.2 If the payment status of patients was not identify or unclear, the researcher asked Medical Record officer.

2.4.3 If the researcher could not read the information physician prescribing, the researcher asked the pharmacist in pharmacy department. If the pharmacist could not answer, the researcher asked physician who prescribe.

3. Patients were classified into two groups: 1) those at high risk for GI adverse events and 2) those in a low risk group. The criteria to determine whether high risk or low risk was used based on NICE guideline (2).

Criteria for High Risk groups were as follows;

3.1 Age of 65 years and over;

3.2 Previous clinical history of gastroduodenal ulcer, gastrointestinal bleeding or gastroduodenal perforation;

3.3 Concomitant use of medications that are known to increase the likelihood of upper GI adverse events e.g. steroids and anti-coagulants;

3.4 Presence of serious co-morbidity, such as cardio-vascular disease, renal or hepatic impairment, diabetes and hypertension;

3.5 Requirement for the prolonged use of maximum recommended doses of standard NSAIDs.

#### 4. Drug costs would be calculated and compared as follows:

##### 4.1 Low risk group cost in actual practice;

4.1.1 Calculation of cost of specific COX II inhibitors in actual practice:

- Total cost, average cost per prescriptions and average cost per day of specific COX II inhibitors in low risk groups would be calculated based on actual practice.

4.1.2 Comparison of specific COX II inhibitors with NSAIDs use in actual practice:

- Total cost, average cost per prescriptions and average cost per day of NSAIDs use in low risk groups based on actual practice would be calculated.
- Cost waste was calculated. Cost waste is average cost per day of specific COX II inhibitors minus average cost per day of NSAIDs and multiplied by mean duration of specific COX II inhibitors use and multiplied by number of patients who received specific COX II inhibitors.

##### 4.2 Low risk group cost in standard treatment;

4.2.1. Comparison of specific COX II inhibitors with standard treatment of NSAIDs use :

- To compare with standard treatment of NSAIDs use, data of NSAIDs consumption volume was collected from the pharmacy department. Types of NSAIDs were selected based on the three highest rank of consumption volume.
- Cost of NSAIDs use were calculated based on type of NSAIDs selected and average cost per day of NSAIDs. This was the defined daily dose (DDD) (49) of standard treatment of such drugs multiplied by acquisition cost.

- Cost waste was to average cost per day of specific COX II inhibitors minus average cost per day of selected three NSAIDs and multiplied by mean duration of specific COX II inhibitors use and multiplied by number of patients of specific COX II inhibitors use in low risk group.

#### 4.3 High risk group cost in actual practice

4.3.1 Calculation of cost of specific COX II inhibitors in actual practice:

- Total cost, average cost per prescriptions and average cost per day of specific COX II inhibitors in high risk groups would be calculated based on actual practice.

4.3.2 Comparison of NSAIDs with specific COX II inhibitors use in actual practice:

- Total cost, average cost per prescriptions and average cost per day of NSAIDs use in high risk groups based on actual practice would be calculated.
- Additional cost of specific COX II inhibitors compared with NSAIDs in high risk

#### 5. Equation for calculation

5.1 Low risk group cost in actual practice:

5.1.1 All specific COX II inhibitors and all NSAIDs of low risk could be used this formula. Average cost per prescription equal total cost divided by number of prescription as following formula:

$$\text{Average Cost Per Prescription} = \frac{\text{Total Cost}}{\text{Number of Prescriptions}}$$

5.1.2 All specific COX II inhibitors and all NSAIDs of low risk could be used this formula to calculate average cost per day as in the following formula:

$$\text{Average Cost Per Day} = \frac{\text{Average Cost Per Prescription}}{\text{Mean Duration of therapy}}$$

5.1.3 Cost waste of celecoxib in low risk group was calculated as in the following formula:

$$\text{Cost Waste}_{\text{Celecoxib}} = (C_{\text{Celecoxib}} - C_{\text{NSAIDs}}) * D_{\text{Celecoxib}} * N_{\text{Celecoxib}}$$

; Total Cost Waste<sub>Celecoxib</sub> was total cost waste of celecoxib when physicians prescribed celecoxib in low risk group.

$C_{\text{Celecoxib}}$  was average cost per day of celecoxib in low risk group.

$C_{\text{NSAIDs}}$  was average cost per day of NSAIDs in low risk group.

$D_{\text{Celecoxib}}$  was mean duration of celecoxib use in low risk group.

$N_{\text{Celecoxib}}$  was number of patients of celecoxib use in low risk group.

5.1.4 Cost waste of rofecoxib in low risk group was calculated as following formula:

$$\text{Cost Waste}_{\text{Rofecoxib}} = (C_{\text{Rofecoxib}} - C_{\text{NSAIDs}}) * D_{\text{Rofecoxib}} * N_{\text{Rofecoxib}}$$

; Total Cost Waste<sub>Rofecoxib</sub> was total cost waste of rofecoxib when physicians prescribed rofecoxib in low risk group.

$C_{\text{Rofecoxib}}$  was average cost per day of rofecoxib in low risk group.

$C_{\text{NSAIDs}}$  was average cost per day of NSAIDs in low risk group.

$D_{\text{Rofecoxib}}$  was mean duration of rofecoxib use in low risk group.

$N_{\text{Rofecoxib}}$  was number of patients of rofecoxib use in low risk group.

5.1.5 Total cost waste of specific COX II inhibitors use in low risk equal cost waste of celecoxib use plus cost waste of rofecoxib use in low risk. Total cost waste of specific COX II inhibitors was calculated as following formula:

$$\text{Total Cost Waste}_{\text{Specific COX II inhibitors}} = \text{Cost Waste}_{\text{Celecoxib}} + \text{Cost Waste}_{\text{Rofecoxib}}$$



## 5.2 Low risk group cost in standard treatment:

5.2.1 Three selected NSAIDs were calculated to average cost per day for standard treatment as following formula:

$$\text{Average Cost Per Day} = \text{Defined Daily Doses} * \text{Acquisition Cost}$$

5.2.2 Cost waste of celecoxib in low risk group was calculated as following formula:

$$\text{Cost Waste}_{\text{Celecoxib}} = (C_{\text{Celecoxib}} - C_{\text{NS1 or NS2 or NS3}}) * D_{\text{Celecoxib}} * N_{\text{Celecoxib}}$$

; Total Cost Waste<sub>Celecoxib</sub> was total cost waste of celecoxib when physicians prescribed celecoxib in low risk group.

$C_{\text{Celecoxib}}$  was average cost per day of celecoxib in low risk group.

$C_{\text{NS1}}$  was average cost per day of first NSAIDs in low risk group.

$C_{\text{NS2}}$  was average cost per day of second NSAIDs in low risk group.

$C_{\text{NS3}}$  was average cost per day of third NSAIDs in low risk group.

$D_{\text{Celecoxib}}$  was mean duration of celecoxib use in low risk group.

$N_{\text{Celecoxib}}$  was number of patients of celecoxib use in low risk group

5.2.3 Cost waste of rofecoxib in low risk group was calculated as following formula:

$$\text{Cost Waste}_{\text{Rofecoxib}} = (C_{\text{Rofecoxib}} - C_{\text{NS1 or NS2 or NS3}}) * D_{\text{Rofecoxib}} * N_{\text{Rofecoxib}}$$

; Total Cost Waste<sub>Rofecoxib</sub> was total cost waste of rofecoxib when physicians prescribed celecoxib in low risk group.

$C_{\text{Rofecoxib}}$  was average cost per day of rofecoxib in low risk group.

$C_{\text{NS1}}$  was average cost per day of first NSAIDs in low risk group.

$C_{\text{NS2}}$  was average cost per day of second NSAIDs in low risk group.

$C_{\text{NS3}}$  was average cost per day of third NSAIDs in low risk group.

$D_{\text{Rofecoxib}}$  was mean duration of rofecoxib use in low risk group.

$N_{\text{Rofecoxib}}$  was number of patients of rofecoxib use in low risk group

5.2.4 Total cost waste of specific COX II inhibitors versus NSAIDs<sub>1</sub>, NSAIDs<sub>2</sub> and NSAIDs<sub>3</sub> was calculated in the following formula:

$$\text{Total Cost Waste}_{\text{Specific COX II inhibitors vs NS}} = \text{Total Cost Waste}_{\text{Celecoxib vs NS}} + \text{Total Cost Waste}_{\text{Rofecoxib vs NS}}$$

; Total Cost Waste<sub>Specific COX II inhibitors vs NS</sub> was total cost waste of celecoxib use when physician prescribed NSAIDs plus total cost waste of rofecoxib use when physician prescribed NSAIDs.

### 5.3 High risk group cost in actual practice:

Assuming that a patient at high risk should received specific COX II inhibitor instead of NSAIDs.

5.3.1 Additional cost of NSAIDs compared with celecoxib in high risk group as following formula:

$$\text{Additional Cost}_{\text{NSAIDsVS Celecoxib}} = (C_{\text{celecoxib}} - C_{\text{NSAIDs}}) * D_{\text{NSAIDs}} * N_{\text{NSAIDs}}$$

; Additional cost<sub>NSAIDs VS Celecoxib</sub> was total additional cost of NSAIDs when physicians prescribed NSAIDs in high risk group comparing specific COX II inhibitors. Physician should prescribed specific COX II inhibitors in high risk group.

$C_{\text{Celecoxib}}$  was average cost per day of celecoxib in high risk group.

$C_{\text{NSAIDs}}$  was average cost per day of NSAIDs in high risk group.

$D_{\text{NSAIDs}}$  was mean duration of NSAIDs use in high risk group.

$N_{\text{NSAIDs}}$  was number of patients of NSAIDs use in high risk group.

5.3.2 Additional cost of NSAIDs compared with rofecoxib in high risk group as following formula:

$$\text{Additional cost}_{\text{NSAIDsVS Rofecoxib}} = (C_{\text{Rofecoxib}} - C_{\text{NSAIDs}}) * D_{\text{NSAIDs}} * N_{\text{NSAIDs}}$$

; Additional cost<sub>NSAIDsVS Rofecoxib</sub> was total additional cost of NSAIDs when physicians prescribed NSAIDs in high risk group versus specific COX II inhibitors. Physician should prescribed specific COX II inhibitors in high risk group.

$C_{\text{Rofecoxib}}$  was average cost per day of rofecoxib in high risk group.

$C_{\text{NSAIDs}}$  was average cost per day of NSAIDs in high risk group.

$D_{\text{NSAIDs}}$  was mean duration of NSAIDs use in high risk group.

$N_{\text{NSAIDs}}$  was number of patients of NSAIDs use in high risk group.

### **Data analysis**

SPSS was used for analyzing the data. Data on patients' characteristics, patients' history, physicians prescribing, total cost waste and additional cost were descriptively analyzed.