

PREVALENCE OF POTENTIALLY INAPPROPRIATE MEDICATION (PIM)
AND FACTORS ASSOCIATED WITH PIM IN ELDERLY OUTPATIENT
PRESCRIPTIONS AT A DISTRICT HOSPITAL IN THE SOUTHERN REGION OF
THAILAND.

Mr.Tanavij Pannoi

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บทคัดย่อและแฟ้มข้อมูลฉบับเต็มของวิทยานิพนธ์ตั้งแต่ปีการศึกษา 2554 ที่ได้รับสิทธิอันสงวนลิขสิทธิ์ (CUIR)
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ความชุกของการใช้ยาที่มีแนวโน้มไม่เหมาะสม และปัจจัยที่สัมพันธ์ต่อการใช้ยาที่มีแนวโน้มไม่
เหมาะสมจากการประเมินใบสั่งยาของผู้ป่วยนอกสูงอายุ ณ โรงพยาบาลชุมชนแห่งหนึ่งทางภาคใต้
ของประเทศไทย

นายชนะวิชัย ปานน้อย

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สาขาวิชาสาธาณสุขศาสตร์

วิทยาลัยวิทยาศาสตร์สาธาณสุข จุฬาลงกรณ์มหาวิทยาลัย

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 THAILAND.

By MR. TANAVIJ PANNOI

Field of Study Public Health

Thesis Advisor Alessio Panza, M.D, M.Com.H, DTMH

Thesis Co-advisor Robert Sedgwick Chapman, M.D. (Harvard Univ.),
 M.P.H.

Accepted by the Faculty of Science, Chulalongkorn University
in Partial Fulfillment of the Requirements for the Master's Degree

.....Dean of the College of Public Health Sciences
(Professor Surasak Taneepanichskul, M.D.)

THESIS COMMITTEE

.....Chairman
(Associate Professor Ratana Somrongthong, Ph.D)

.....Thesis Advisor
(Alessio Panza, M.D, M.Com.H, DTMH)

.....Thesis Co-advisor
(Robert Sedgwick Chapman, M.D.(Harvard Univ.), M.P.H.)

.....External Examiner
(Nithima Sumpradit, Ph.D)

ชนะเลิศ ปานน้อย : ความชุกของการใช้ยาที่มีแนวโน้มไม่เหมาะสม และปัจจัยที่สัมพันธ์ต่อการใช้ยาที่มีแนวโน้มไม่เหมาะสมจากการประเมินใบสั่งยาของผู้ป่วยนอกสูงอายุ ณ โรงพยาบาลชุมชนแห่งหนึ่งทางภาคใต้ของประเทศไทย.
(PREVALENCE OF POTENTIALLY INAPPROPRIATE MEDICATION (PIM) AND FACTORS ASSOCIATED WITH PIM IN ELDERLY OUTPATIENT PRESCRIPTIONS AT A DISTRICT HOSPITAL IN THE SOUTHERN REGION OF THAILAND) อ.ที่ปรึกษาวิทยานิพนธ์หลัก: นพ. อะเลสซิโอ พัลซ่า, อ. ที่ปรึกษาวิทยานิพนธ์ร่วม:
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การศึกษานี้มีวัตถุประสงค์เพื่อหาความชุกและอธิบายปัจจัยที่สัมพันธ์เกี่ยวกับการใช้ยาที่มีแนวโน้มไม่เหมาะสมในผู้ป่วยสูงอายุ ณ โรงพยาบาลชุมชนแห่งหนึ่งทางภาคใต้ของประเทศไทยเป็นการศึกษาเป็นแบบตัดขวาง(Cross-sectional study) โดยใช้ข้อมูลใบสั่งยาเฉพาะผู้ป่วยนอกที่มีการสั่งใช้ในระหว่างวันที่ 1 ตุลาคม 2554 ถึง 30 กันยายน 2555 จำนวนผู้ป่วยนอกที่ถูกสุ่มคัดเลือกอย่างเป็นระบบทั้งหมด 430 คน โดยผู้ป่วยนอกอายุ 65 ปีขึ้นไปและได้รับยาจากแผนกผู้ป่วยนอกจากโรงพยาบาลอย่างน้อย 1 รายการในช่วงเวลาดังกล่าว และมีจำนวนใบสั่งยาของผู้ป่วยที่ได้รับการคัดเลือกเหล่านี้ในช่วงเวลาดังกล่าวทั้งหมด 2,128 ใบ. เครื่องมือที่ใช้ในการประเมินการใช้ยาที่มีแนวโน้มไม่เหมาะสม คือ เกณฑ์มาตรฐาน Beers 2012

ผลการศึกษาพบว่าความชุกของของใบสั่งยาที่มีการใช้ยาที่มีแนวโน้มไม่เหมาะสมคิดเป็นร้อยละ 28 ของจำนวนใบสั่งยาทั้งหมด ปัจจัยที่มีผลต่อการการใช้ยาที่มีแนวโน้มไม่เหมาะสมอย่างมีนัยสำคัญทางสถิติ คือ จำนวนรายการยาตั้งแต่ 5 รายการขึ้นไป ($p < 0.001$) อายุของผู้ป่วย ($OR = 1.018$, $p = 0.040$, $CI = 1.001 - 1.035$) และผู้ที่มีการใช้บริการในแผนกผู้ป่วยนอกของโรงพยาบาลมีแนวโน้มที่จะได้รับยาที่มีแนวโน้มไม่เหมาะสมต่ำกว่าผู้ป่วยในกลุ่มเปรียบเทียบซึ่งใช้บริการ 1-3 ครั้ง (4-6 ครั้ง และ ≥ 7 ครั้ง : $OR = 0.581$ [$95\%CI = 0.408 - 0.828$], $p = 0.003$ และ $OR = 0.704$ [$95\%CI = 0.526 - 0.943$], $p = 0.019$ ตามลำดับ) อย่างไรก็ตามไม่พบว่า ปัจจัยที่เกี่ยวข้องกับ เพศของผู้ป่วย จำนวนโรคที่ได้รับการวินิจฉัย ประเภทของสิทธิผู้ประกันตนของผู้ป่วยจำนวนครั้งการเข้ารักษาพยาบาลในหอผู้ป่วยใน รวมถึง เพศอายุ อายุการทำงาน และประเภทของผู้สั่งใช้ยามีความสัมพันธ์ต่อการใช้ยาที่มีแนวโน้มไม่เหมาะสมสำหรับผู้ป่วยสูงอายุในการศึกษานี้

สาขาวิชา.....สาขารณสุขศาสตร์.....ลายมือชื่อนิติ.....
ปีการศึกษา.....2556.....ลายมือชื่อ อ.ที่ปรึกษาวิทยานิพนธ์หลัก.....
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PANZA, M.D, M.Com.H, DTMH., CO-ADVISOR: ROBERT
SEDGWICK CHAPMAN M.D. (Harvard Univ.), M.P.H., 111 pp.

The aims of study are to know the prevalence of, and to describe factors associated with prescribing PIM at a district hospital in the south of Thailand. In this cross-sectional study, the elderly patients were a ≥ 65 -year outpatient and had at least 1 prescribed medication from the hospital. Overall patients were 430 with 2,128 prescriptions. 2012 Beers criteria were applied to detect PIM. Prevalence of PIM was calculated by their total prescriptions. Prescription, patient, and prescriber characteristics associated with PIM were analyzed by logistic regression.

Results showed that 28% of total prescriptions had at least 1 PIM. There was the more likelihood of PIM prescription at outpatient department increased significantly when that prescription comprised of more than 5 medications ($p < 0.001$). The positive association between age of participant and the presence of PIM prescription was observed (OR=1.018, $p = 0.040$, CI=1.001-1.035). Interestingly, the elderly outpatients who had more frequent outpatient visits had less PIM prescription as compared to reference group, who had 1-3 visits. (4-6 vs. ≥ 7 : OR = 0.581 [95%CI=0.408-0.828], $p=0.003$ vs. OR=0.704 [95%CI=0.526-0.943], $p=0.019$) No statistically significant association between the presence of PIM and patient's gender, number of diagnoses, Types of health insurance schemes, hospitalizations, prescriber's gender, ages, types of prescriber and length of prescriber's years work was observed.

Field of Study : Public Health

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Student's Signature.....

Advisor's Signature.....

Co-advisor's Signature.....

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LIST OF ABBREVIATIONS

BZDs	Benzodiazepines
COX	Cyclooxygenase
CSMBS	Civil Servant Medical Benefit Scheme
GP	General Practitioner
ICD-10	International Classification of Diagnosis code version 10
NCD	Non-communicable disease
NSAIDs	Non-steroidal Anti-inflammatory Drugs
PIM	Potentially Inappropriate Medication
SP	Specialists in medicine
SSS	Social Security Scheme
TCAs	Tri-cyclic Antidepressants
UHC	Universal Health Coverage Insurance

CHAPTER I

INTRODUCTION

The first chapter introduces the situation of elderly population, health issues among the older persons, potentially inappropriate medication (PIM) use in the elderly and its associated factors and outcomes, including the rationale of this study. Besides that, this chapter addresses research questions of study, research hypothesis, objectives of the study, conceptual framework and operational definitions.

1.1 Background

Elderly population tends to rise rapidly around the world. An estimated 524 million people, who were over 65 years or 8 per cent of the global populations, are projected to 1.5 billion or to nearly 3-folds, representing 16 per cent of world's population by 2050. Moreover, the most rapidly increase of aging populations is in less developed countries, which is estimated to increase more than 250 per cent, compared with a 71 per cent increase in developed countries.(National Institute of Aging & Health, 2011) In Thailand, Thai older persons have also been at a rapid growth of the elderly population, which was at 11.9 per cent in 2010. It is projected to increase to 25 per cent in 2030, when Thailand completely becomes an “aged society.” (Chunharas et al., 2011)

The dramatic increase in average life expectancy is notably a part of decline of high to low fertility; a steady increase in life expectancy at birth and at older ages; and a shift in leading causes of death from infectious and parasite diseases to non - communicable and chronic diseases (NCD) or conditions.(National Institute of Aging & Health, 2011)

Regarding the trend of NCD, the percentage of women with moderate or severe hypertension in those developing countries has an upward trend. Those hypertensive women, who were not adequately addressed, are going to have progression to cerebrovascular and cardiovascular diseases that require costly medical treatments.(National Institute of Aging & Health, 2011)

In Thailand, similarly, the recent population structure has indicated a trend toward an aging society because of advanced medical care that allows for better diagnosis, treatments, as well as proper self-care, exercise, and nutrition. Although

Thai people live longer, they are also suffering with NCD; in 2010, statistically, 31.7 per cent of the elderly had high blood pressure, 13.3 per cent for diabetes, 7.0 per cent for heart diseases, 1.6 per cent for cerebrovascular disease, 2.5 per cent for stroke, and 0.5 per cent for cancer. Undoubtedly, those NCDs increase the utilization of healthcare resources; 6.2 outpatients visits per elderly person per year compared to 2.8 visits by working-age group; and 3 times in inpatient admission higher than working-age group.

Because most elderly populations have aged-related physiological changes, the presence of NCD, and consume types and numbers of prescribed and non-prescribed medicines, they are all at risk for medication-related problems (MRP)--improper drug selection, sub-therapeutic dosage, failure to receive drugs, over dosage, adverse drug reactions, drug interactions, and drug use without indication. (Hepler. & Strand, 1990) Besides that older persons have alterations in pharmacokinetic processes (absorption, distribution, first-pass metabolism, and excretion) that lead to lower effectiveness of some drugs, and can also contribute to increase risk of adverse drug events. Accordingly, inappropriate prescribing or inappropriate medication may occur if prescribers do not consider these conditions. (Guaraldo, Cano, Damasceno, & Rozenfeld, 2011)

To prevent those MRP among elderly, potentially inappropriate medication (PIM) should be assessed by process or outcomes measures. These measures are screening tools, which are mainly divided into 2 categories--explicit or criterion-based measures (e.g. Improved Prescribing in the elderly tool (IPET), Screening Tool of Older Persons (STOPP), and the Beers' criteria) and implicit or judgment-based measures (e.g. Medication Appropriateness Index (MAI)). This study focuses only on explicit criteria, namely, Beers criteria. The Beers criteria were initiated by Beers and colleagues in 1990. The criteria were revised in 1997 and 2003 and the latest revision of Beers' list of medications was published in 2012. (The American Geriatrics Society, 2012)

Beers criteria were selected to be a screening tool of PIM to determine inappropriate prescription that firstly were used in nursing home in United States and later use widely in all healthcare settings. The Beers criteria 2012 comprise of list of high-risk drugs, which should not be taken or taken with cautions in older patients.

The list of drugs in Beers list is evidently associated with adverse events; numerous research studies have employed the Beers criteria to evaluate PIM prescribing and ADE in out- and in-patient setting.(Page II, Linnebur, Bryant, & Ruscin, 2010)

In this study, the unconditional list of 2012 Beers criteria are used purposively to determine PIM prescribing in elderly outpatients because of their easy applicability to computerized administrative databases in outpatient compared to other explicit tools. The feasibility of Beers criteria in detecting PIM were evaluated and published in international researches that used Beers as a screening tool of PIM. (Page II et al., 2010)

The review of several studies worldwide shows that the prevalence of PIM among elderly is ranged from 11.5 per cent to 62.5 per cent. The use of PIM is high among community-dwelling elderly and rural hospitals, emergency departments and associated with significant factors, such as, female sex, advanced age, the number of drugs prescribed, characteristics of the prescribers and number of in-patients and outpatient service use, .(Guaraldo et al., 2011; Chen et al., 2009; Tamblyn, 1996; Dong et al., 1999) Explicitly, comorbidity exposes to a large number of medications, which were prescribed from many general practitioners and specialists. (Page II et al., 2010)

In Thailand, only one article was found by Winit-Watjana that set the criteria in terms of prescribing and monitoring medication use in older patients and proposed the term “high-risk medication”, instead of PIM.(Winit-Watjana, Sakulrat, & Kespichayawattana, 2008).The study classified the medications into 4 levels; 1=drug should be avoided; 2=drug rarely appropriate; 3=drug with some indication with patients; and 4=unclassified.

Another second article reports a cross-sectional descriptive, community based study of PIM using Winit-Watjana criteria in Central Thailand. The prevalence of high-risk medication use in the community was 18.7 per cent, which most of those were level 3.(Tharvornwattanayong, Anothayanon, Reungsakul, Sriphiromrak, & Chomjan, 2011)

1.2 Rationale of Study

While there are international studies on factors related to PIM, to the author’s knowledge, there are no studies of PIM with regard to 2012 Beers criteria and studies of PIM at Thai district hospitals., a study of PIM used in Thai older at district hospital

is essential. Within the services offered by a district hospital, the outpatient services are the more likely to have problems of PIM as a result of increased elderly outpatient visits and worldwide time constraints associated with provision of outpatients of services. Therefore, a study of prevalence and factors associated with PIM use among elderly Thai outpatients is required.

1.3 Research Questions of Study

1. What is the prevalence of PIM measured by the 2012 Beers criteria among elderly outpatients at a district hospital in the south of Thailand?
2. What are the frequencies of PIM, categorized by pharmacological categories, diagnosis (matching each PIM to diagnoses), and classified indication, and measured by the 2012 Beers criteria among elderly outpatients at a district hospital in the south of Thailand?
3. What are the factors associated with prescribing PIM measured by the 2012 Beers criteria among elderly outpatients at a district hospital in the south of Thailand?

1.4 Objectives of the Study

The general objective of the study is to contribute to the improvement of outpatient service quality by a more rational use of medication in elderly to promote “social justice” for the elderly seeking out patient-service without creating any legal problem to the prescribers.

Specific Objectives

1. To know the prevalence of PIM measured by the 2012 Beers criteria among elderly outpatients at a district hospital in the south of Thailand.
2. To know the frequencies and percentages of prescribing 2012 Beers' PIM, disaggregated by pharmacological categories, diagnosis (matching each PIM to diagnoses), and classified indication, among elderly outpatients at a district hospital in the south of Thailand
3. To describe factors associated with prescribing PIM measured by the 2012 Beers criteria among elderly outpatients at a district hospital in the south of Thailand.

1.5 Research Hypothesis

1. The prevalence of PIM used in elderly outpatients measured by 2012 Beers criteria at the district hospital in the south of Thailand is similar to that reported worldwide. (Guaraldo et al. (Guaraldo et al., 2011))

2. The PIMs used in central nervous system and cardiovascular diseases are the most frequently prescribed to the elderly outpatients in the study hospital.

3. Older age, female sex, number of medications, multiple diagnoses, outpatient visits, health insurance schemes, inpatient admissions and characteristics of prescribers are hypothesized as significant factors associated with PIM prescriptions measured by 2012 Beers criteria at a district hospital in the south of Thailand

1.6 Conceptual Framework

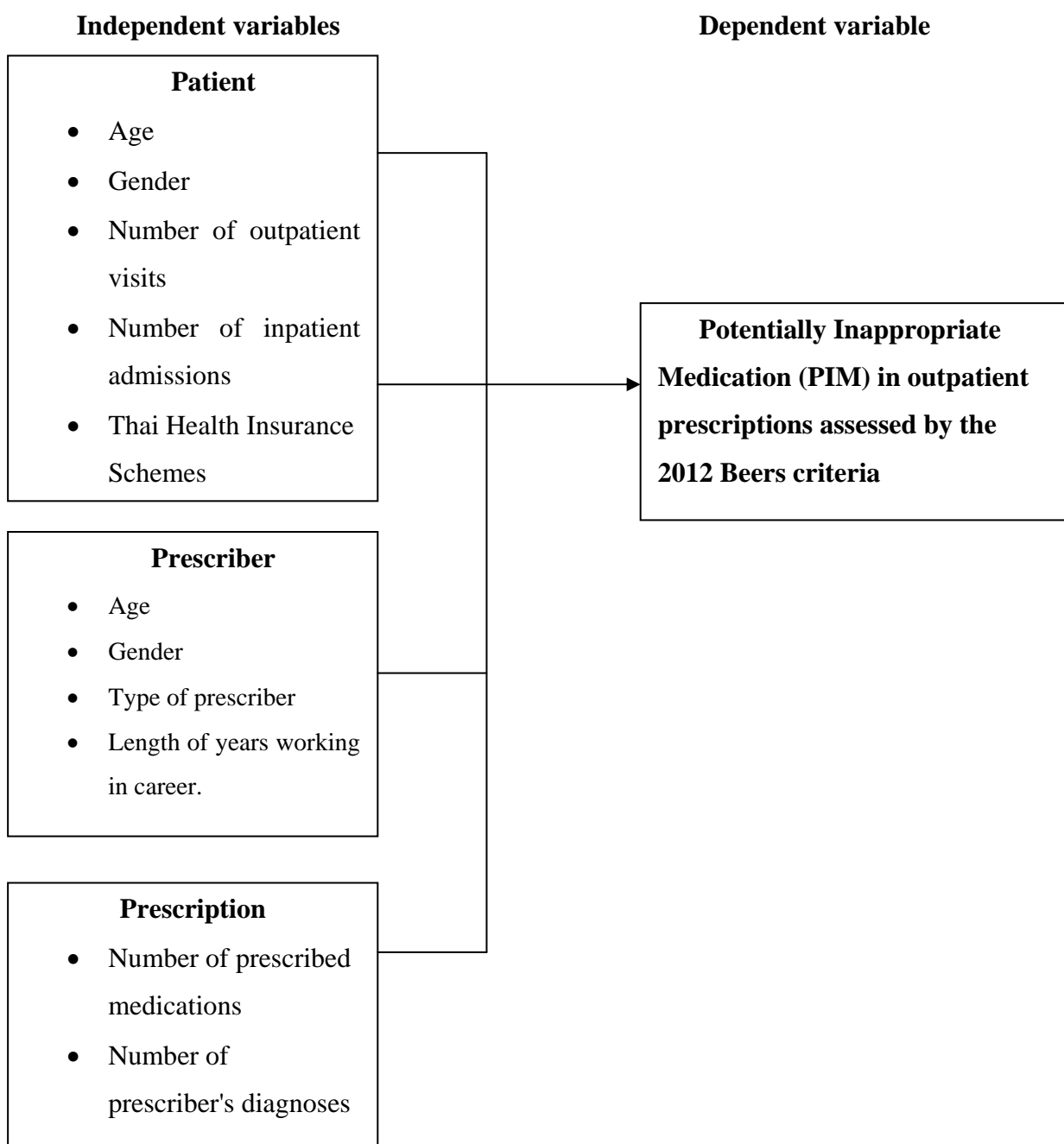


Figure 1.1: Conceptual Framework

1.7 Operational Definitions

1.7.1 Prescribed medication

Prescribed medication in the study is defined as any medications, which were ordered by physicians and prescribed to elderly patients at outpatient department of the study hospital. The number of prescribed medications is calculated by the record of pharmacy codes of medications, which are available in the study hospital. To compare results among the ranges of number of medications, the number of prescribed medications is categorized for 5 intervals--1-4, 5-7, 8-10, 11-14, and more than or equal 15 items.

1.7.2 Patient's age

To compare to other international PIM studies, the elderly age is defined as 65 years old or more. (World Health Organization [WHO], 2003) The age is calculated in number of years from the last complete birthday to the date of September Thirtieth, 2012. In order to compare results among age groups, age is categorized for 65-69, 70-74, 75-79, and 80 or more years old.

1.7.3 Gender (patient and prescriber)

Gender is a dichotomous, dummy variable coded "1" for male and 0 for female in the study.

1.7.4 Number of prescriber's diagnosis

Prescriber's diagnosis is defined as diseases or symptoms that prescribers assigned in the electronic medical record of each outpatient and converted those diagnoses into the group of diseases or symptoms with regard to International Statistical Classification of Diseases and related health problems version 10 Thai Modification (ICD-10-TM). In this study, ICD codes were grouped as stated below.

A00-B99	Certain infectious and parasitic diseases
C00-D48	Neoplasms
D50-D89	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism
E00-E90	Endocrine, nutritional and metabolic diseases
F00-F99	Mental and behavioural disorders
G00-G99	Diseases of the nervous system
H00-H59	Diseases of the eye and adnexa

H60-H95	Diseases of the ear and mastoid process
I00-I99	Diseases of the circulatory system
J00-J99	Diseases of the respiratory system
K00-K93	Diseases of the digestive system
L00-L99	Diseases of the skin and subcutaneous tissue
M00-M99	Diseases of the musculoskeletal system and connective tissue
N00-N99	Diseases of the genitourinary system
O00-O99	Pregnancy, childbirth and the puerperium
P00-P96	Certain conditions originating in the perinatal period
Q00-Q99	Congenital malformations, deformations and chromosomal abnormalities
R00-R99	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified
S00-T98	Injury, poisoning and certain other consequences of external causes
V01-Y98	External causes of morbidity and mortality
Z00-Z99	Factors influencing health status and contact with health services
U00-U89	Codes for special purposes
UM	Unmatched-code with any PIM list

Number of prescriber's diagnoses is calculated by the existence of ICD codes in each outpatient's prescription. To compare results among the ranges of number of prescriber's diagnoses, the variable is ranged into 3 groups-- 1-2, 3-4 and 5 or more codes.

1.7.5 Number of outpatient visits

Outpatient visit is calculated by the number of visits among those elderly patients who attended outpatient department during the Thai fiscal year 2012 (October 1, 2011-September 30, 2012). It was divided into 3 groups--1-3, 4-6, and more than or equal 7 visits.

1.7.6 Number of inpatient admissions

Inpatient admission is a continuous variable defined as the number of inpatient admissions in inpatient department classified by service status during the Thai fiscal year 2012 (October 1, 2011-September 30, 2012) among the elderly outpatients in the study. It was categorized only as 0 and ≥ 1 visit in order to test difference between PIM and non-PIM with regard to inpatient admission status.

1.7.7 Thai Health Insurance Schemes

Thai Health Insurance Schemes are nominal variable defined by the years 2000 Universal Health Coverage (UHC), coded "0", Social Security Scheme (SSS), coded "34", Civil Servant Medical Benefit Scheme (CSMBS), coded "23", Disability Fund (DF), coded "64", and other schemes, which were self-payment, coded "10", Car accident insurance (CAR), coded "12", and Employees' workplace fund (WF), coded "21". In order to reverse multicollinearity among independent variables, however, this variable was categorized for only 2 interested major groups--UHC and non-UHC--in the analysis of inferential statistic.

1.7.8 Prescriber's age

Prescriber's age is collected and expressed as last completed birthday during the Thai fiscal year 2012. The prescriber's age was categorized by 20-28, 29-37, 38-46, and 47-55 in descriptive analysis and the analysis of inferential statistic with Chi-square. However, the ages were converted into continuous in binary logistic regression analysis in order to reverse multicollinearity among independent variables.

1.7.9 Type of Prescriber

Type of prescriber is a nominal variable defined as a degree of prescriber with regard to any specializations during the Thai fiscal year 2012. This variable is categorized as general practitioner (GP) coded "1", specialist (SP) coded "2", nurses coded "3", and others (dentist, traditional medicine, pharmacy technician) coded "4".

1.7.10 Length of years working in career.

Length of years working in career is defined as the duration of working experience of prescribers since graduated from undergraduate degree of medicine, nurse and other professions until September, 2012. In order to compare those results among ages, the ranges are categorized as of 0-3, 4-10, 11-20, and 21 or more in descriptive analysis and the analysis of inferential statistic with Chi-square. However,

the ages were converted into continuous in binary logistic regression analysis in order to reverse multicollinearity among independent variables.

1.7.11 Potentially inappropriate medication (PIM)

Potentially inappropriate medication (PIM) is defined by the 2012 American Geriatrics Society, (AGS) Beers criteria (see appendix A). The 25 medications of PIM are adopted that classes to avoid in older adults. (The American Geriatrics Society, 2012) The unconditionally list of PIMs are referred to medications, which were generally considered inappropriate under all circumstances, regardless of the consideration of particular diseases in each elderly patient or specific dosage form of prescribed medications. (Rigler, Perera, Jachna, Shireman, & Eng, 2004)

In this study, under- or over- prescription is not considered as PIM in accordance with 2012 Beers criteria. Any patients receiving any of PIM drugs are classified as PIM users and receiving none of PIM drugs are classified as nonusers.

The cases of prescribing PIM for every patients were defined as a dichotomous variable, coded "1" for PIM and "0" for non-PIM.

CHAPTER II

REVIEW OF LITERATURE

The literature review aims to identify articles and related documents that addressed the relevant theories and concepts in elderly health and medication use in the elderly. First of all, definition of elderly population is introduced and current situations of elderly population were summarized in both international and national levels. Elderly population health is also reported that elaborates the stem of medication problems among the elderly. Secondly, the part of elderly medication use reviews pharmacodynamic, pharmacokinetic changes and medication related problems in elderly. Lastly, potentially inappropriate medication (PIM) use among elderly is evidently emphasized with its definition, prevalence, associated factors, and health outcomes. The last topic is also dedicated for screening tools of PIM from country and cross-country experiences.

2.1 Elderly population

2.1.1 Definition of elderly population

The evidence of the conventional definition of Elderly is unknown. Admittedly, the term 'elderly' is defined a chronological age of 65 years old or older; those from 65 through 74 years old are referred to as 'early elderly'; and, those over 75 years old as 'late elderly'. (Orimo et al., 2006) Most developed world countries have accepted the chronological age of 65 years as a definition of "elderly" or "older person." As opposed to United Nations (UN), there is no standard numerical criterion to define older person. At this moment, UN agreed cutoff is over 60 years as its definition. (WHO, 2003) Likewise UN definition, the Thai elderly population refers to any Thai nationals registered under the Thai civil registration who are 60 years of age and over. (Ministry of Social Development and Human Security, 2003)

2.1.2 Situations of elderly population

Regarding the growth of global elderly, the number of over 65-year people is estimated to grow from 524 million in 2010 to 1.5 billion in 2050 that will increase rapidly in developing countries. Thus, the number of older people in less developed countries will increase more than 250 percent, compared with a 71 per cent increase

in developed countries. This remarkable phenomenon is caused by declines in fertility and improvements in longevity associated with the improvement of health care provisions. In accordance with the fewer children entering the population and people living longer, older people are increasing in the proportion of total population. Most developed nations have had their changes of age structures of population that people aged 65 or older increase from 7 percent to 14 percent in decades. In contrast, many less developed countries have more rapid increase in the number and percentage of older people, often within a single generation. (National Institute of Aging & Health, 2011)

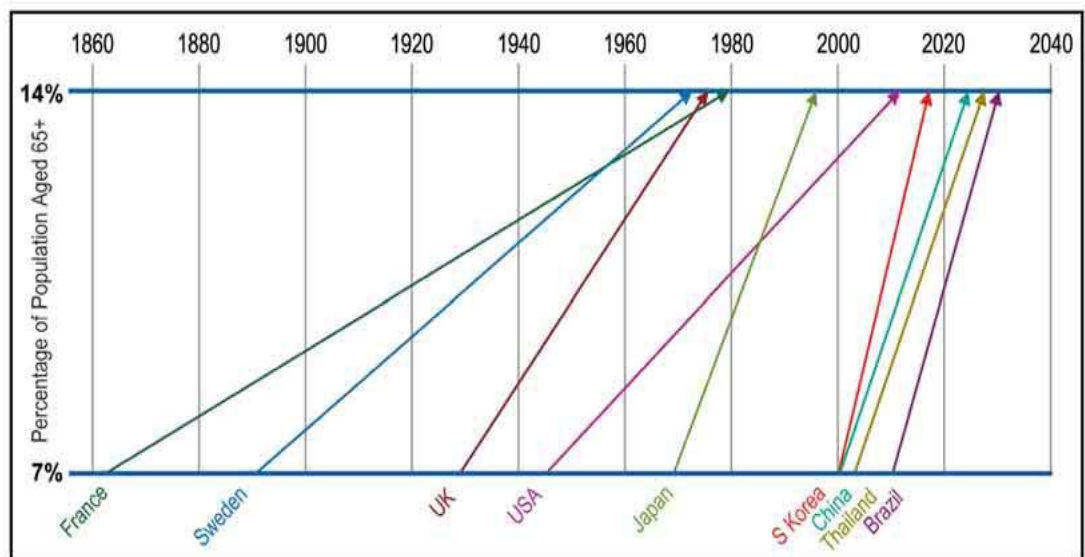


Figure 2.1: The Speed of Population Aging (by Kinsella K, He W. *An Aging World: 2008*. Washington, DC: National Institute on Aging and U.S. Census Bureau, 2009; Cited in Global Health and Aging.)

Thailand is a country of aging society as documented in 2010, when the proportion of over 60-year population increased to over 10 per cent out of the total population as seen in table 2.1. The proportion of older people started to grow rapidly during the year 1980 - 2000, which raised from 6.3 per cent in 1980 to 9.5 per cent in 2000. The projection of population during 2010 to 2030 shows that the proportion will rise from 11.9 per cent in 2010 to 25 per cent in 2030, or a two fold increase.

Likewise the projection of growth among international elderly populations, Thai population will reach approximately 17 million in the next 20 years. (Chunharas et al., 2011)

Table 2.1: Size and trends of the elderly population, 1960-2030

Year	Total Population	Number of population aged 60 and above	Percentage of population aged 60 and above	Median age (year)
1960	26,257,916	1,506,000	5.4	18.4
1970	34,397,371	1,680,900	4.9	17.8
1980	44,824,540	2,912,000	6.3	19.9
1990	54,509,500	4,014,000	7.4	25.1
2000	60,916,441	5,792,970	9.5	29.2
2010	67,313,000	8,011,000	11.9	33.9
2020	70,100,000	12,272,000	17.5	38.5
2030	70,829,000	17,763,000	25.1	43.1

Source: Situation of the Thai Elderly in 2010 (Chunharas et al., 2011)

In table 2.2, the study of demographic shifts in 3 age groups of over 65, 70, and 80 indicates that older people have increased rapidly their numbers in the next 30 years. The elderly do not only grows rapidly among people aged over 60 years, but also in the late elderly group aged 80 years and over.(Chunharas et al., 2011)

Table 2.2: Number of the elderly population classified by age groups, 2000-2030
(unit: 1,000 persons)

Age group	2000	2010	2020	2030
60-64 years	5,887	8,011	12,272	17,783
65-69 years	3,871	5,389	8,048	12,705
70-80 years	2,321	3,391	4,913	8,204
80 years and over	593	804	1,348	2,155

Source: Situation of the Thai Elderly in 2010 (Chunharas et al., 2011)

In 2006 and 2010, the distribution of elderly population across residential and regional areas illustrates a greater density of the elderly in the rural than the municipal areas. The proportion of elderly living in the municipal areas raised from 30 per cent in 2006 to 35 per cent in 2010. The pattern of elderly distribution across regions were not much different between 2006 and 2010; the highest concentration in the northeast (32 per cent), followed by central (25 per cent), north (20 per cent), south (13 per cent), and Bangkok (9 per cent) respectively.

Table 2.3: Characteristics of over 60-year elderly population during 2006 to 2010

Characteristics	2006 (%)	2010 (%)
Gender		
Male	44.67	44.39
Female	55.33	55.61
Age		
60-69 years	55.21	55.2
70-79 years	32.66	32
80 years and over	12.13	12.8
Residential areas		
Municipal	29.99	35
Non-municipal	70.01	65
Regions		
Bangkok	8.90	9.24
Central	25.11	25.3
North	20.76	20.2
Northeast	31.74	32.14
South	13.49	13.12

Source: Situation of the Thai Elderly in 2010 (Chunharas et al., 2011)

2.1.3 Elderly population health

An implication of long-life expectancy of population over the past century, which led to the remarkable growth of older people, is a shift in the leading causes of disease and death. In the early 20th century, the major health threats were infectious and parasitic diseases that mostly affected the lives of infants and children. Currently, non-communicable diseases (NCDs) affect older population health and becomes the greatest burden on global health, in particular, chronic-non communicable diseases (CNCDs) because of changes in lifestyle, diets as well as aging.(National Institute of Aging & Health, 2011)

The potential economic and societal costs of NCDs rise sharply with ages and affect economic growth. A World Health Organization analyzed among 23 low- and middle-income countries estimated the economic losses from three major NCDs (heart disease, stroke, and diabetes). The estimated data show that the potential economic losses from 3 types of NCDs in these countries will be US\$83 billion between 2006 and 2015. Therefore, reducing severe disability from NCDs and those related-health conditions is a key to holding down health and social costs.(National Institute of Aging & Health, 2011)

Potentially increasing health burden of older population in developing countries is a major concern because generations of children and young adults, who grew up in poverty and ill health in those countries, will be evidently entering old age in coming decades. With continuing declines in mortality rates among older people, the proportion of over 80-year elderly is rising significantly, and more people are living past 100 years.(National Institute of Aging & Health, 2011)

In Thailand, physical deterioration, which causes the impaired functions of physiological systems and immune systems, is commonly a high risk of health problems among the Thai elderly. As well as international situation, the majority of older Thai people suffer from NCDs. In 2007, the survey of elderly in Thailand by the National Statistical Office reported that 31.7 per cent of the elderly suffered from high blood pressure, 13.3 per cent of diabetes, 7.0 per cent of heart disease, 1.6 per cent of cerebro-vascular disease, and 2.5 per cent of stroke, and 0.5 per cent of cancer. Compared to their male counterpart, a higher proportion of elderly women was found to suffer from those diseases, excluding stroke.(Chunharas et al., 2011)

With regard to the distribution of those NCDs among residences, almost three times of older people living in non-municipal areas suffered from these diseases more than those living in municipal areas. People living in the northeastern part of Thailand suffered the highest ratio of 33.6 per cent. The second highest proportion was those in central Thailand (23.9 per cent), while, those living in Bangkok suffered the lowest ratio of 9.2 per cent.(Chunharas et al., 2011)

Having said that, the Thai population structure has become an aging society as a result of advanced medical care, which provides better diagnosis, treatments, as well as self-care, physical exercise, and good nutrition. The administration of Thai healthcare services for older people is divided into 3 major categories.(Chunharas et al., 2011)

Firstly, disease prevention and health promotion are managed by an elderly team or club and trained healthcare volunteers in the individual villages. A basic disease screening service program is mainly administered by local public community health center, along with other healthcare services under Ministry of Public Health in terms of medical devices. In many local areas, there are also participation from public and private hospitals in giving health education to the older persons.(Chunharas et al., 2011)

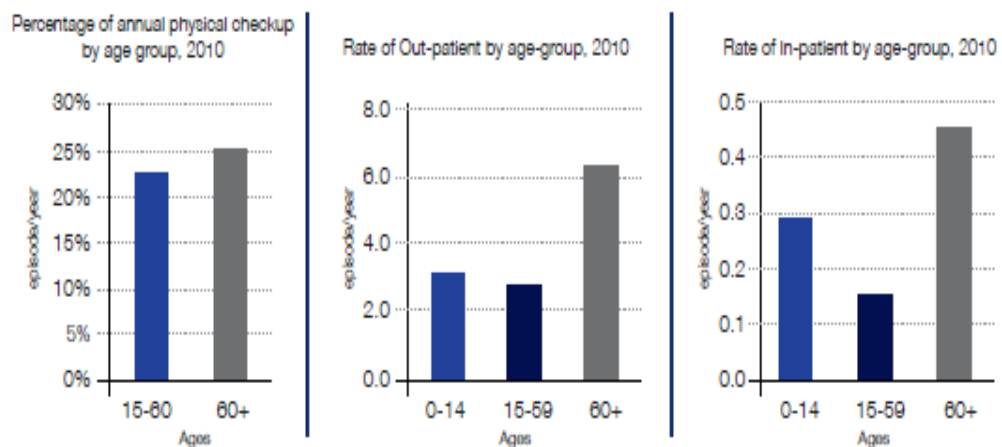
Secondly, geriatric health treatment and rehabilitation services are offered mainly by public healthcare settings. Provincial and district hospital initially establish an elderly clinic to provide specialized care and services. A home health care project is responsible by a multidisciplinary team and volunteers to provide healthcare services to elderly chronic patients who recently return home from hospital. Rehabilitation work receives supports from all involved entities.(Chunharas et al., 2011)

Thirdly, long-term care for the elderly is offered to dependent older people, who have deteriorated body function, chronic illness conditions, or disability. The service focuses on facilitation of daily life, housing, and other living necessities in aspects of home care and institutional care, community care, and any cares in unusual circumstances.(Chunharas et al., 2011)

In 2010, Thavorn Skulpanich et al. assessed performance of health care for elderly and concluded that older people can gain access to health services compared

to other age groups. Nevertheless, screening for chronic diseases, such as, diabetes and high blood pressure during the pre-stage of disease remains low, though, a great number of the elderly were at risk of those chronic diseases and the associated symptoms. In addition, the rate of the older ages for in-and outpatients was the highest among other age groups, which were 6.2 visits per person per year for outpatient services compared to 3.3 visits by other age groups, as well as, 0.23 visits per person per year in in-patients services, which were 2 times higher than those in other aged group (see figure 2.2). (Sakunpanich, 2011)

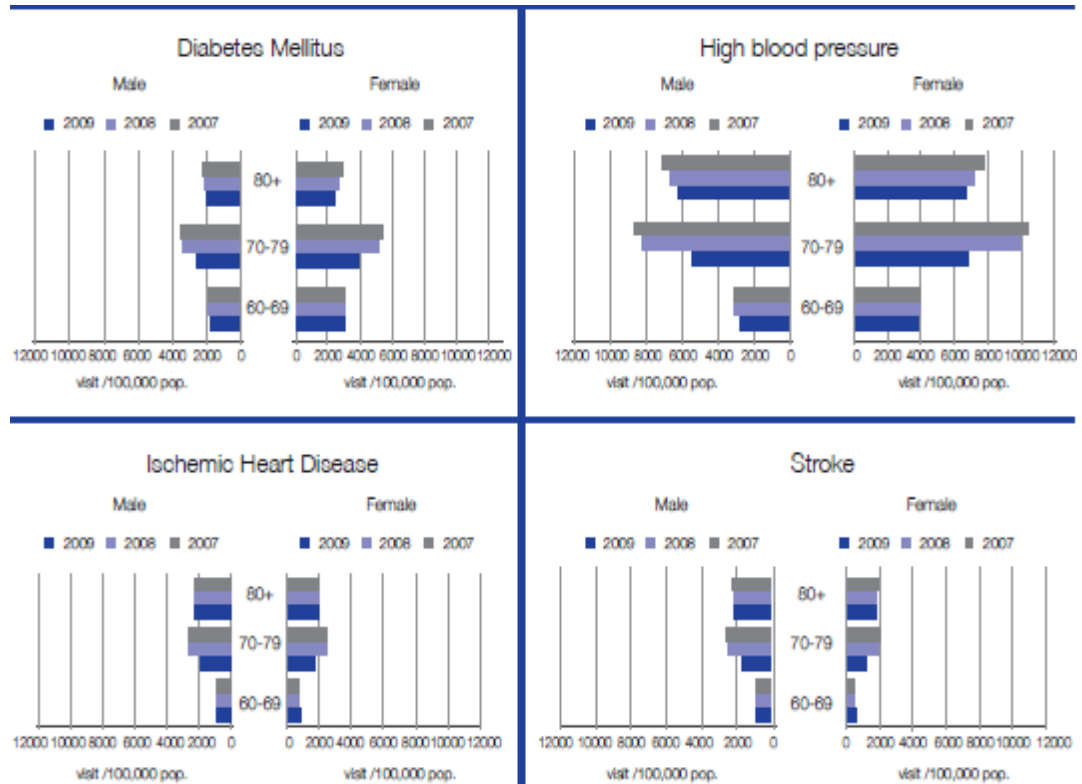
Figure 2.2: Access to health services by older people, compared to other age group



Source: Database on 2010 outpatients from the Government Office Welfare, Social Security fund, and National Health Security Fund (Chunharas et al., 2011)

Compare to the utilization rate of outpatients among age groups in 2008, additionally, the rate of utilization of health service among older age group in 2009 increased considerably rather than other age groups. However, the in-patient service rate was similar in both years. In 2009, the major chronic diseases among elderly were diabetes and hypertension, which would be progress to ischemic heart disease and stroke, and the number of those diseases among the old populations ages 70-79 illustrated in figure 2.3. (Sakunpanich, 2011)

Figure 2.3: Numbers and types of elderly patients, divided by 4 major chronic diseases in individual age groups



Source: Database on 2010 outpatients from the Government Office Welfare, Social Security fund, and National Health Security Fund (Chunharas et al., 2011)

2.2 Medication Use in elderly population

As the result of rapid growth of aging populations, it causes an increasing demand for medications in order to delay and/or treat those chronic diseases, and to improve quality of life. Inevitably, the increased number of medication used in those elderly patients attributes the medication-related problems.

2.2.1 Pharmacokinetic and Pharmacodynamic changes in the elderly

Increasing ages associates with pharmacokinetic and pharmacodynamic changes with impaired homeostatic mechanisms and the effect of coexisting diseases. These changes also contribute to a significant increase of hypersensitivity in particular medications, including a corresponding increase in the incidence of adverse drug reactions (ADRs). (Hughes, 1998)

Pharmacokinetic changes are explained throughout 4 pathways--absorption, distribution, metabolism, and excretion. In absorption, the elderly are likely to have a local acid concentration (pH) change, which is probably caused by a long-term infection of *H. Pylori*, or hypochlorhydria with the use of acid-suppressive drugs, such as, proton-pump inhibitors or H₂-receptor antagonist drugs. In addition, gastric motility is slow down with age due to region- specific loss of neurons. Impaired gastric emptying is caused by diseases, such as diabetes mellitus, depression, hypothyroidism, chronic renal failure, by the use of anticholinergic drugs, in particular, antidepressants with anticholinergic effect, metoclopramide, opioid analgesics or calcium antagonist. Moreover, the impact of dietary food, age- related diseases and drugs on gastric motility also causes the change of absorption pathway.(Bumgartner, 2008)

Changes in body composition, such as, an increase in body fat, a decrease in lean body mass and in total body water, result in reduce volume of distribution of water soluble drugs, e.g. digoxin is increased initial drug concentration, and increased volume of distribution of lipid soluble drugs, e.g. benzodiazepines are increased elimination half-life, and prolonged effect. Therefore, both drugs may require reduction in dose and/or dose interval. Distribution of drugs is also affected by plasma-protein binding; with highly plasma protein bound drugs tending to have a low volume of distribution. In contrast, Drugs whose reduced protein binding in elderly people, such as, warfarin, tolbutamine, phenytoin, and salicylic acid, may result in adverse reactions.(Hughes, 1998)

Drug metabolism is essential for the elimination of drugs from the body, as well as, for termination of biological activity and active drugs. Evidently, genetic, environmental and other patient- specific parameters have a greater clinical importance concerning hepatic metabolism than the aging process itself.(Bumgartner, 2008) However, drug metabolism, in particular, first-pass metabolism of drugs, such as, propranolol, verapamil, metoclopramide, opioids, is probably reduced in the elderly.(Hughes, 1998)

Older people have a number of renal changes that there are approximately 30 to 40 per cent reductions in overall renal function in age 90. This results in reduced excretion of digoxin, which is mainly excreted via filtration at the kidney, and

penicillin, which is actively secreted by renal tubules. Prescriber who concerns these issues may consider reducing dose of both drugs for older patients.(Hughes, 1998) Nevertheless, there are not strong evidences on effects of aging on gastrointestinal excretion of drugs.(Bumgartner, 2008)

Pharmacodynamic implies the pharmacologic effects of a drug, including drug action and side effects. Age-related changes in pharmacodynamic can result in greater therapeutic effect, as well as, an increased potential for toxicity.(Bumgartner, 2008) As every drug has its own special pharmacodynamic, its changes occurred in aging process are complicate and have not been well characterized in human. Certain drugs have been studied for altered pharmacodynamic in the elderly, such as, benzodiazepines. Increases in medication sensitivity have also been reported for calcium channel blockers, beta-mimetics and beta-blockers, warfarin or opioids.(Hughes, 1998)

2.2.2 Medication-related problems in the elderly

Hepler and Strand defined a medication-related problem (MRP) as “an event or circumstance involving drug treatment that actually or potentially interferes with the patient’s experiencing an optimum outcome of medical care.” Regarding to this, 8 categories of medication-related problems were indicated as follows. (Hepler. & Strand, 1990)

- **Untreated Indications:** The patient is not receiving a drug therapy that he or she is required for his or her medical problem.
- **Improper Drug Selection:** The patient is taking the wrong drug.
- **Sub-therapeutic Dosage:** The patient is being treated with too little of the correct drug with regard to his or her medical problem.
- **Failure to Receive Drugs:** The patient is not receiving drugs that cause his or her medical problem.
- **Over dosage:** The patient is being treated with too much of the correct drug with regard to his or her medical problem.
- **Adverse Drug Reactions:** The patient has a medical problem because of adverse drug reactions (ADR) or adverse events (AE).
- **Drug Interactions:** The patient has a medical problem because of a drug-drug, drug-food, or drug-laboratory interaction

- **Drug Use without Indication:** The patient is taking a drug for no medically valid indication.

Older people are at greatest risk of MRP because of age-related physiological changes, including, pharmacokinetic and pharmacodynamic changes, a higher incidence of multiple chronic diseases, and other conditions compared with other age groups. Another one, the elderly receive a number of prescribed and non-prescribed medications that contribute the high risk of MRP. It can cause a number of common and costly geriatric health problems, for instance, falls, cognitive loss, dehydration, incontinence, and depression, with subsequent loss of functional ability, inpatient admission, and decreased quality of life.(Simonson. & Feinberg, 2005)

Being cared by multiple physicians that order frequent changes in treatments without consulting each other also increases a risk of MRP in elderly patients. Others than that, physical disabilities and cognitive dysfunctions among elderly patients, who particularly use high-risk drugs, are factors associated with ADR.(Simonson. & Feinberg, 2005)

However, medication-related problems, e.g., inappropriate prescribing, adverse medication effects and drug interactions are commonly preventable in older people. In United States, over 1.9 million adverse drug events--of which over 25 per cent are preventable--occur annually among the 38 million Medicare enrollees. In the ambulatory study, the more serious adverse drug events were tendency to be preventable--72 per cent of serious, fatal adverse drug events were preventable compared to 34 per cent of significant adverse drug events. Additionally, errors resulting in those preventable adverse drug events are mostly at the prescribing and monitoring stages of medication use process. (Gurwitz et al., 2000 cited in Simonson & Feinberg, 2005)

2.3 Potentially Inappropriate Medication (PIM) use in the elderly

Drug Administration is to achieve definite outcomes, improving the patient's quality of life. Nevertheless, the potential outcomes, especially, patient's quality of life are always diminished. A cause of suboptimal outcomes among the elderly patients is inappropriate prescribing (IP), which includes inappropriate drug, dosage form, dose, route, dosage interval, or duration.(Hepler. & Strand, 1990) Having

emphasized that, inappropriate prescribing is likely a pattern of MRPs that commonly found in elderly drug use.

2.3.1 Definitions of potentially inappropriate medication

Terminologically, inappropriate prescribing is defined as the use of medicines that pose more risk than benefit, in particular where safer alternative exist. IP also includes inappropriate dose and duration of medicines, the prescription of medicines with clinically significant drug-drug and drug-disease interaction, and the under-use of potentially beneficial medications. (Spinewine et al., 2007 cited in Hamilton, Gallagher, and Mahony, 2009)

A systematic review paper used different terms, such as, “inappropriate medication”, “inappropriate medicines”, and “inappropriate prescription”, to search for articles studied about inappropriate prescribing. Accordingly, the discussion part is emphasized that many authors of IP article prefer to include the term “potentially inappropriate” in their description of estimates.(Guaraldo et al., 2011) Regarding to this, therefore, the terms “potentially inappropriate prescribing”, “potentially inappropriate prescription” and “potentially inappropriate medication” are used interchangeably. In Thailand, Winit-Watjana et.al, prefer the term “high-risk medication” to “potentially inappropriate medication” because it seemed more meaningful and has been primarily used by Thai health institutions.(Winit-Watjana et al., 2008) To be consistent with international nomenclature, this study uses potentially inappropriate medication or PIM as a medium.

2.3.2 Epidemiology of potentially inappropriate medication.

Prevalence and associated factors of PIM use in elderly were a part of epidemiological study of PIM. In addition, Screening tools for PIM were also reviewed throughout international and country articles. The literature search aimed to identify article that addressed the above topics. English language literature sources included from databases--Thomson Reuters web of knowledge (formerly ISI), ScienceDirect, Pub MED, World Health Organization: Library and Information Network for Knowledge Database (WHOLIS), Thai Library Integrated System (ThaiLis), Thai Health Systems Research Institute (HSRI), and Thai Ministry of Public Health (MOPH).

Relevant articles were reviewed for both English and Thai papers. Thai keyword search were left in parenthesis after English words in table 2.4. Any searched articles of PIM with specified diseases and specialized medicine are excluded. The numbers of articles identified through these search strategies are shown in the Table 2.4. However, only some of them were reference in this study.

Table 2.4: Literature search results for articles and review papers, excluding topics or journals aiming at specific disease or specialized medicine.

Keyword	Source	Results
1. Prevalence of potentially inappropriate medication		
“Prevalence (ความชุก)” AND “Potentially inappropriate medication use (การใช้ยาที่ไม่เหมาะสม)”	• Pub Med	25
	• ISI	21
	• Science Direct	115
	• WHOLIS	0
	• ThaiLis	0
	• HSRI	1
	• MOPH	0
2. Factors associated with Potentially inappropriate medication		
“Factors (ปัจจัย)” AND “Potentially inappropriate medication use (การใช้ยาที่ไม่เหมาะสม)”	• Pub Med	21
	• ISI	14
	• Science Direct	86
	• WHOLIS	0
	• ThaiLis	0
	• HSRI	0
	• MOPH	0
3. Potentially inappropriate medication and criteria or screening tools in elderly outpatient		
“Potentially inappropriate medication use (การใช้ยาที่ไม่เหมาะสม)”AND “criteria(เกณฑ์)” AND “Screening tool (เครื่องมือ)” AND “elderly outpatient (ผู้ป่วยนอกสูงอายุ)”	• Pub Med	2
	• ISI	0
	• Science Direct	23
	• WHOLIS	0
	• ThaiLis	0
	• HSRI	1
	• MOPH	0

Table 2.4: Literature search results for articles and review papers, excluding topics or journals aiming at specific disease or specialized medicine. (continued)

4. Potentially Inappropriate Medication use and outcomes in elderly outpatient		
Keyword	Source	Results
“Outcome (ผลลัพธ์)” AND “Potentially Inappropriate Medication(การใช้ยาที่ไม่เหมาะสม)”	• Pub Med	11
	• ISI	0
	• Science Direct	21
	• WHOLIS	0
	• ThaiLis	0
	• HSRI	0
	• MOPH	0

Note: Each interpreted Thai term or phase is put in parenthesis after English term or phase.

Evidently, a number of studies have reported that PIM prescribing in older people is common in the ambulatory setting, nursing homes, and the emergency department.(Page II et al., 2010)

2.3.2.1 Screening tools for potentially inappropriate medication.

To evaluate the appropriateness of prescribing, its process or outcome measures are assessed by explicit (criterion-based) or implicit (judgment-based). However, limitations of explicit measure are that this measure is drug or disease oriented and less or non-clinical judgment. Explicit criteria may not consider quality indicators of health care as defined by national guidelines for each patient and their preferences, nor do they address the burden of comorbidity. Whilst, implicit criteria are viewed as time-consuming measures. Importantly, there are many variations among prescribers regarding their knowledge and attitudes, which affect the reliability of tool. Ultimately, if there are not ideal tool to evaluate PIM prescribing in elderly, the strengths and weaknesses of both approaches should be taken into account.(Page II et al., 2010)

The selected literatures are only articles about explicit measure or criterion-based screening tool for PIM. Currently, there are 3 internationally

explicit tools to evaluate PIM prescribing among the elderly--Improved Prescribing in the elderly tool (IPET), Screening Tool of Older Persons (STOPP), and the Beers' criteria.

IPET is a Canadian Criteria with a list of the 14 most prevalent prescription errors identified from a long list of inappropriate prescription instances raised by an expert Canadian Consensus Panel in 1997. The IPET was initially validated in a prospective study of acutely hospitalized elderly patients that resulted 12.5 per cent of patients whose PIM were prescribed. However, there were a little use of this instrument exists outside of Canada, except an Irish study found that 22% of acutely hospitalized elderly were taking at least one inappropriate prescription medication at the point of admission. Moreover, the IPET only cited 14 instances of inappropriate prescribing, three of which relate solely to Tricyclic Antidepressants (TCA), which are infrequently used in current medical practice. (Page II et al., 2010)

STOPP was developed by a multidisciplinary team of Irish geriatricians, pharmacists, pharmacologists, and primary care physicians. The STOPP incorporated commonly encountered instances of PIM prescribing in the elderly that included drug–drug and drug–disease interactions, drugs that adversely affect older patients at risk of falls, and duplicate drug class prescriptions. Its criteria were set up according to relevant physiological systems for ease of use, and each criterion was accompanied by a concise explanation of the reason of potentially inappropriate prescriptions. The most common PIM identified by STOPP was the use of long-acting benzodiazepines, TCAs with clear-cut contraindications, first generation antihistamines, vasodilator drugs known to cause hypotension in patients with persistent postural hypotension, inappropriate use of NSAIDs and opiates, and duplicate drug class prescriptions such as two Angiotensin Converting Enzyme Inhibitors, two NSAIDs, two selective serotonin reuptake inhibitors or dual antiplatelet therapy without indication. The advantages of the STOPP consist of good inter-rater reliability, inclusion of both American and European medications, organization and structure based physiological systems, and short time to complete (3 minutes). However, this European tool is strongly based on the physiological conditions and needs to be evaluated in additional studies and in other settings. (Page II et al., 2010)

In Thailand, in 2007, Winit-Watjana et. al, also published a set of explicit criteria in order to evaluate any high-risk medication used among the elderly. Having said that the Winit-Watjana criteria are an only country-specific tool in detecting high-risk medications use in elderly.(Winit-Watjana et al., 2008)

In 1991, Beers and colleagues published the first set of explicit criteria for determining PIM use in nursing home residents. The list of drugs in Beers' criteria was reviewed by expert panel. Those Beers' drugs were high-risk medications that provide an unfavorable balance of risks and benefits by themselves and considering alternative treatments available. After the first publish, a list of Beers' drug was subsequently expanded and revised in 1997 and 2003 in order to suit all settings of geriatric care. In the latest revision, 53 medications or medication classes are included in the Beers' list and generally divided into three categories: avoid in older adults regardless of diseases or conditions (unconditional list), avoid in older adults with certain diseases and syndromes that the drug listed can exacerbate, and used with caution in older adults.(The American Geriatrics Society, 2012).

In this study, 2012 Beers criteria with unconditional list are applied purposively because of its easy applicability to administrative databases in outpatient compared to other explicit tools. The feasibility of Beers criteria in detecting PIM were clearly found by many international researches. (Page II et al., 2010) Overall, there are 139 PIM by unconditional list in 2012 Beers criteria. However, only 97 items are available in Thai health settings by Thai Food and Drug Administration (FDA). Of those items, 67 items are available in the National List of Essential Medicine (NLEM)--47 items for essential drug (ED) and 20 items for non-essential drug.(see appendix A)

2.3.2.2 Prevalence of potentially inappropriate medication.

In United States, Viswanathan et. al, conducted a study to determine the prevalence of PIM based on the 2002 Beers criteria among ambulatory patients aged 65 years or over. The number of prevalence shows that 13 per cent of all ambulatory visits made by over 65-year patient who received 1 medicine or more were prescribed at least 1 PIM or more(Viswanathan., Bharmal., & Joseph, 2005).

Having applied Beers criteria in a study from United Kingdom, Gallagher et. al, studied the prevalence of PIM among over 65-year elderly who were

admitted in accidental and emergency department following referral by general practitioner (GP) or by self referral in United Kingdom. It was found that 32 per cent of those elderly were prescribed at least one PIM or more prior to admission to hospital. (Gallagher, Barry, Ryan, Hartigan, & O'Mahony, 2008)

In Italy, a retrospective cohort study reported that approximately 26 per cent of outpatients had at least one PIM. Of these, 14 per cent received prescriptions for two medications of concern, and 2 per cent for three or more. (Maio, Del Canale, and Abouzaid, 2010)

In Japan, a cohort study of prevalence of PIM use with Beers was presented that 56 per cent of admitted patients aged 65 or over in acute care hospitals were prescribed at least one Beers list (BL) drug that approximately 45, 33 and 22 per cent of these older patients filled their prescriptions for a single BL, for 2 BL, and 3 or more BL drugs, respectively. (Sakuma et al., 2011)

In Thailand, the study of prevalence of PIM with 2012 Beers criteria in elderly had not been studied in accordance with the review of literature. However, a pilot survey of PIM with modified Beers criteria 2003 in research project of development of medicine list for screening and reducing medication-related problems in Thai elderly funded by HSRI shows that 28.9 per cent of elderly patients in a provincial hospital received medication with regard to use 2006 BL. (Ploylueamsang et al., 2012)

2.3.2.3 Associated factors of potentially inappropriate medication.

Factors that influence the PIM prescription regarding Beers criteria can be grouped into one of four categories as suggested by Tamblyn's conceptual framework: patient characteristics, physician-related variables, health care systems and medication-related variable. (Tamblyn, 1996) In addition, a study in rural china described the effects of health financing on providers' opinions and prescribing behavior that patient's health financing systems (insurance or out-of-pocket payment), financing methods for health facilities (general budget or fee for service), and payment methods for providers (salary or bonus) influenced provider prescribing. (Dong et al., 1999)

In a systematic review of PIM study, multivariable analyses of factors associated with PIM use are female sex and advanced age. The major factor is

the number of medications or prescription. (Guaraldo et al., 2011) Polypharmacy defined as medication used 5 items or more in a day is the covariate that most significantly associated with PIM. (Fulton & Allen, 2006)

In outpatient department, a cross-sectional study in 2 primary care settings in United States provided the relevant findings that patients who were female and/or receiving polypharmacy (more than 5 prescribed medications) have a tendency to expose PIM. Moreover, a number of primary care visits and increased age were also associated with a risk for being prescribed a PIM.(Buck et al., 2009) Besides that, a greater number of chronic conditions were factors associated with a number of BL drugs use.(Maio, Del Canale, & Abouzaid, 2010)

In addition, prescriber characteristics were significantly associated with the prescribing of PIM in some studies. Those characteristics are male sex, older age and family medicine/ general practice.(Lai et al., 2009)

Another study illustrated the association of the number of outpatient(OP)and inpatient(IP) visits to the use of PIM that the increase of out-and inpatient visits significantly associated with the elderly who use PIMs; two or more PIM group had the highest visits, followed by one PIM group and then the reference group after controlling for patient's sex, age and the Charlson Comorbidity index. Those prescribed one or more PIMs as compared to those prescribed no PIMs had increased inpatient visits (OR 1.99, 95% CI: 1.76–2.26); increased OP visits (OR 1.53, 95% CI: 1.43–1.63). (Fick et al., 2008)

The study of PIM prescribed in ambulatory care among elderly Taiwanese outpatients aged 65 years or more had similar result that patients who received PIM also had significantly more emergency department visits than those without PIM (0.27 vs 0.15 visits per patients, $p < 0.001$). Ultimately, those elderly patients who were prescribed with PIM had significantly higher mean number of inpatient admissions per patient than the nonuser (0.46 vs 0.27 respectively, $p < 0.001$). (Lai et al., 2009).

In the article written by Goulding summarized that the odds of potentially inappropriate prescribing were higher for outpatient visits with multiple drugs and double for female visits. It also presented that more prescribing of

potentially inappropriate pain relievers and central nervous system drugs were observed. (Goulding, 2004)

CHAPTER III

METHODS

This is the chapter of research methodology elaborating thoroughly in research design, study area, study population, sample size calculation, sampling method, measurement, data collection, data analysis, statistical technique, ethical consideration, limitation of the study, and expected benefit and application.

3.1 Research Design

This study is a cross-sectional study using the outpatient database in the Thai fiscal year 2012 (October 1, 2011-September 30, 2012).

3.2 Study Area

The research was studied at a district hospital in the Southern region of Thailand. It is a 60-bed hospital certified hospital standard by Hospital Accreditation (HA) Institution, Thailand. In dataset, there were 22 general practitioners (GP), and 6 internal medicine specialist who prescribed medications to outpatients in the fiscal years 2012.

3.3 Study Population

The total number of elderly outpatients in the study hospital was 5,948 in the fiscal year 2012. The inclusion criteria of study populations are outpatients who were 65 years old or older and had at least 1 prescribed medication from outpatient department in fiscal year 2012, which were 5,265 (N). The prescription was prescribed directly from prescriber in outpatient services. All outpatient prescriptions among all participants across the fiscal year 2012 was included. PIM users are defined as elderly outpatients who were prescribed at least 1 medication in unconditional Beer's list, while, nonusers were participants who were not. The exclusion criteria are any participants, whose outpatient prescriptions and/or personal information were incomplete.

3.4 Sample Size Calculation

Sample size was calculated on the basis of one of research hypotheses that higher age group in elderly outpatient (factor) are at higher risk of receiving PIM prescription (outcome) compared to lower age group in elderly outpatient, using a cross-sectional study. Power and Sample software version 3.0.43 with regard to

Schlesselman's method was applied in sample size calculation, analyzed by using uncorrected chi-square test.(Dupont and Plummer, 1998) The selected mode of dependent variable was dichotomous.

In a previous study, the percentage of elderly outpatients with PIM in Beers criteria age group over 85 years old was 12.6 and the percentage of those of ages 65-70 was 24.6. Regarding to this, it was assumed that the probability of outcome for compared group is equal to 0.25, and the probability of outcome for case is equal to 0.13. The proportion of compared group to case, which was adopted from the previous study, was 2 to 1.(Buck et al., 2009)

To conduct the study with power equal to 0.80 to compute for type II error and at significant level equal to 0.05 to predetermine the probability of 2-sided type I error, the number of calculated participants is 387 as detailed below.

$$n = \frac{\left(Z_{\alpha} \sqrt{2\bar{p}\bar{q}} + Z_{\beta} \sqrt{p_1 q_1 + p_0 q_0} \right)^2}{(p_1 - p_0)^2}$$

Where

n = Sample size of case = 129 and those of compared group =258

r = The ratio of the number of compared group to the number of case. (2:1)

p_0 = The probability of the outcome for patient who received non-PIM prescriptions (compared group=0.25).

p_1 = The probability of the outcome for patient who received PIM prescriptions (case=0.13)

$q_0 = 1 - p_0 = 0.75$

$q_1 = 1 - p_1 = 0.87$

$\bar{p} = (p_1 + r p_0) / (1+r) = 0.13$

$\bar{q} = 1 - \bar{p} = 0.87$

$Z_{\alpha} = 1.96$ and $Z_{\beta} = 1.28$

With estimate of 10 per cent of 387 participants who have the incomplete of data, therefore, overall 430 participants (n) are required for the study.

3.5 Sampling Method

A computerized systematic random sampling was applied to randomize any study units by Hospital Patient Number (HN) from sampling frame (the retrieved dataset of outpatient in the district hospital at the fiscal year 2012). Firstly, the identification number of each HN in sampling frame is coded. Secondly, the random interval (12) was calculated by the formula--overall HN in retrieved outpatient data set in fiscal year 2012 (5,265) divided by total number of participants (430). Thirdly, computerized generated random number (= 299) was to find random started number. Lastly, the data were selected from identification number, begin with random started number and then following random interval until completing the overall participants (430).

3.6 Measurement Tool

Outpatient database in HOSxp software and administrative hospital database were used for collecting individual characteristics of outpatient and prescriber information. The 2012 Beers criteria were applied as a screening tool for detecting any PIM in prescription. Unconditionally inappropriate list in 2012 Beers criteria for older adults were used in this study (see Appendix A). The meaning of “unconditionally inappropriate” is a medication generally considered inappropriate under all circumstances, with inappropriateness not dependent on the presence of particular diseases or receipt of specific dosage. (Rigler, Perera, Jachna, Shireman, & Eng, 2004). However, under- and over prescription were not measured in this study.

3.7 Data Collection

Regarding the study variables, the secondary dataset of patient and prescriber's characteristics was retrieved from HOSxp and administrative hospital database. HOSxp is a Thai hospital software used widely among public hospitals. It accumulated the data of prescription with patient's profile. In this study, the following outpatient's data were retrieved.

- Hospital No. (HN)
- Age
- Gender
- Prescriber's diagnosis with regard to ICD-10-TM codes

- Profiles of individual prescribed medication in each outpatient visits: generic name of medication, strength, frequency of administration, and date of prescription.
- Prescriber's identity code refers to any professions who prescribed each medication.
- Number of outpatient visits for individual outpatients during the Thai fiscal year 2012.
- Number of inpatient admissions of individual outpatients in the study hospital during the Thai fiscal year 2012.
- Thai Health insurance schemes for individual outpatients.

The administrative hospital database is the source for collecting the administrative data. In the study, human resource database is required in order to collect the prescribers' profile as follows:

- Prescriber's identity codes
- Types of prescribers: General practitioner (GP) Specialist (SP) Nurse, and others.
- Age
- Gender
- Length of years working in career.

PIM use is identified from profiles of prescribed medication with unconditionally inappropriate medication in 2012 Beers criteria.

3.8 Data Analysis

The retrieved data were entered into the worksheets in the licensed MS Excel 2007. All retrieved data was verified by 3 licensed pharmacists, including the researcher.

Data cleaning was achieved by running on the frequencies of all variables, as well as, outliers were checked in order to ensure the data had been entered accurately. Out of 430 cases with 2,130 prescriptions and then 2 prescriptions, which showed the missing data on the prescriber's diagnosis, were excluded.

In addition in some prescriptions, ICD-10 were not matched to some PIMs in the original dataset. For instance, there are more than 1 diagnosis codes or ICD-10 codes

in each PIM prescription but those diagnoses were not the indication to prescribe PIM. As a pharmacist, therefore, a matched-pair case between PIM and ICD-10 was done by the researcher with other 2 research assistants, who are also pharmacists, and 1 medical consultant, who is an internist.

Matching case was only done between ICD-10 and PIM, not for ICD10 and non PIM prescriptions. There are 3 categories among the matched-pair cases.

First of all, "PIM by the Beers' therapeutic indication" refers to any PIM used under the 2012 Beers' therapeutic indication.

Secondly, "PIM by potentially clinical used indication" is a PIM not assigned to the diagnosis under its therapeutic category in 2012 Beers, but the PIM could be matched to ICD-10 code that commonly used that drug. For example, Diazepam is a drug used in central nervous system to mainly treat sleeping disorders, anxiety, seizure, or periprocedural anesthesia. However, Diazepam could be assumed as potentially clinical used indication in Chronic obstructive pulmonary disease with acute exacerbation, unspecified that Diazepam is clinically used for sedated intubation in this case. This was judged by the research team on the basis of the existing database.

Thirdly, if any PIMs could not be matched to any given ICD-10 by the former two categories, those PIMs were assigned as "Unmatched-case(UM)" in the data.

However, the validity of matching ICD-10 and non-PIM medications had not been verified by the researcher or by any hospital staff in the study because of the incompleteness of some secondary data. Of all medications in 2012 Beers criteria, only those available in the hospital were used for this data analyses.

Each independent variables was coded individually and the dependent variables were coded as 1 for PIM and 0 for non PIM. The descriptive data were collected and managed by licensed software--MS Excel and MS Access--, and then analyzed by the licensed SPSS software version 17.

3.9 Statistical Technique

Patient and prescriber's characteristics were described. The number of elderly patients with PIM and the number of their PIM prescriptions were counted for subgroups stratified by ages, gender of patient, number of prescribed medications, health insurance schemes, number of prescriber's diagnosis, gender of prescriber, and

type of prescriber. The total number of inpatient admissions between patients who were prescribed PIM and those who were not also described.

Descriptive statistic was used for continuous data, such as, numbers, percentages and mean with standard deviations with the normally distributive data and median with the non-normally distributive data, for categorical data absolute numbers and percentage described characteristics of associated factors.

Analytical statistic is used for measuring statistically significant differences between PIM and non-PIM prescription. All data were considered as categorical data and Chi-square test was used.

Binary logistic regression was used for determining the statistical association of independent variables and the presence of PIM. Having studied for all independent variables by international researchers and given the small number of independent variables in this study, thus, all of them were put into logistic regression analysis in order to measure of the strength of association between independent variables and the dependent variable (the presence of PIM). The results were reported as individual odds ratio (OR) with 95% confidence interval (CI). A p-value < 0.05 was considered to be statistically significant. (See table 3.1)

Table 3.1: Statistic analysis for the study

Study Specific Objectives	Measures	Statistical Techniques
<p>1. To know the prevalence of PIM measured by the 2012 Beers criteria among elderly outpatients in a district hospital in the south of Thailand.</p>	<ul style="list-style-type: none"> • Characteristics of patient and prescriber • Prevalence of PIM (by 2 denominators: the number of outpatients and the number of their prescription) • Differences between PIM and nonusers 	<ul style="list-style-type: none"> • Descriptive Statistic: numbers, percentage, mean \pm standard deviation or median • Descriptive Statistic: absolute numbers, percentage • Inference Statistic: independent sample : Chi-square for categorical data
<p>2. To know the frequencies of prescribing 2012 Beers' PIM, disaggregated by pharmacological categories, diagnosis (matching each PIM to diagnoses), and classified indication, among elderly outpatients at a district hospital in the south of Thailand</p>	<ul style="list-style-type: none"> • Frequencies of prescribing PIM 	<ul style="list-style-type: none"> • Descriptive statistics: numbers, percentages

Table 3.1: Statistic analysis for the study (continued)

Study Specific Objectives	Measures	Statistical Techniques
3. To describe factors associated with prescribing PIM measured by the 2012 Beers criteria among elderly outpatients in a district hospital in the south of Thailand.	<ul style="list-style-type: none"> • Adjusted odds ratio (AOR) and 95% CI 	<ul style="list-style-type: none"> • Non-parametric statistic: Binary logistic regression.

Note: Statistical significance is expressed at the 5% level. ($p < 0.05$)

3.10 Ethical Considerations

Ethical approval (COA No.045/2013) was obtained from the Ethical Committee of Chulalongkorn University and the purpose and procedure of the research were clearly declared to the hospital director prior to retrieve the data. Before collecting the existing data, all purposes of the study and related information had been declared to the hospital director, which were eventually agreed by the hospital director to collect the data.

The researcher committed to follow steps that assure anonymity of the participating hospital, prescribers and patients. These steps are of particular importance to protect the reputation of the hospital and of the prescribers in case the research findings will reveal inappropriate prescriptions. The hospital name, the patients' name with hospital number and prescriber's name with identity code will not appear in any of the research and related documents.

The researcher entered the patients HN and prescriber ID in the first data set, secondly the researcher linked these two identifier numbers to a sequential research number, thirdly the researcher made a copy of the list with identifier numbers linked to the research sequential number and kept this copy in a safe and separate place, fourthly the researcher removed the identifier numbers from the initial data set and conducted all subsequent data analysis by using the research sequential number only. The separate, safely kept list linking identifier numbers to the sequential research

numbers were used only for data cross-checking, cleaning, and completion. At the end of the research, the linking list was eliminate.

CHAPTER IV

RESULTS

This chapter presents the results of study in 2 parts--descriptive results, which describe the characteristic of study sample, prevalence of PIM, following by results of logistic regression analysis, which presents the association between factors and the presence of PIM.

4.1 Descriptive Results

4.1.1 Patient

Out of 430 patients, 60.9 per cent (n=262) were female. The mean age of patients was 74.5 years (SD=6.2). The elderly outpatient aged 80 years or older comprised 20.7 per cent of all patients. Most patients were members of Universal Health Coverage Scheme (UHC), which accounted for 74 per cent of all schemes. The number of outpatient visits ranged between 1 and 7 (median [25,75%] = 3 [1,7]). The percentage of inpatient admissions were 14.7 per cent of all patients. (see details in table 4.1)

Table 4.1: Characteristics of the patient

Characteristics	Patient		
	Male (%) n=168(39.1)	Female(%) n=262(60.9)	Total (%) n=430(100)
Age range			
65-69 years	41(9.5)	79(18.4)	120(27.9)
70-74 years	51(11.9)	60(14.0)	111(25.8)
75-79 years	39(9.1)	71(16.5)	110(25.6)
>=80 years	37(8.6)	52(12.1)	89(20.7)
Mean \pm SD*	74.6 \pm 6.4	74 \pm 6.0	74.5 \pm 6.2
Thai Health Insurance Schemes,			
UHC	122(28.4)	196(45.6)	318(74.0)
SSS	1(0.2)	1(0.2)	2(0.5)
CSMBS	28(6.5)	39(9.1)	67(15.6)
Disability Fund	9(2.1)	15(3.5)	24(5.6)
Others (CAR, WF, Self-pay)	8(1.9)	11(2.6)	19(4.4)

Table 4.1: Characteristics of Patient (continued)

Characteristics	Number of Patients		
	Male (%) n=168(39.1)	Female(%) n=262(60.9)	Total (%) n=430(100)
Number of outpatient visits			
1-3	84(19.5)	142(33.0)	226(52.6)
4-6	30(7.0)	47(10.9)	77(17.9)
≥7	54(12.6)	73(17.0)	127(29.5)
Median(25%,75%)**	3.5(1,7)	3(1,7)	3 (1,7)
Number of inpatient admissions			
0	137(81.5)	230(87.8)	367(85.3)
≥ 1	31(18.5)	32(12.2)	63(14.7)
Median(25%,75%)**	0(0,0)	0(0,0)	0(0,0)
UHC=Universal Health Coverage, SSS=Social Security Scheme, CSMBS=Civil Servant Medical Benefit Scheme, CAR=Car Accident Insurance, WF=Employees 'workplace fund			

* The patient's age distribution is almost normal and mean median and mode are almost equivalent.

** The number of outpatient visits and inpatient admissions is not normal distribution.

4.1.2 Prescriber

For characteristics of prescriber, most of them were female (75.8 per cent). The median ages of all prescriber were 31 years. One-third of prescribers were general practitioner (GP) and 45 per cent of prescribers had worked less than 3 years during the study period while the median length of working in career were 6 years. (see details in table 4.2)

Table 4.2: Characteristics of the Prescriber

Characteristics	Number of Prescribers		
	Male (%) n=16(24.2)	Female(%) n=50(75.8)	Total (%) n=66(100)
Age range			
20-28	10(15.2)	21(31.8)	31(47.0)
29-37	3(4.5)	12(18.2)	15(22.7)
38-46	2(3.0)	9(13.6)	11(16.7)
47-55	1(1.5)	8(12.1)	9(13.6)
Median(25%,75%)**	26.5(26,35.75)	34.5(26.75,41.75)	31(26,40)
Types of prescriber			
General Practitioner (GP)	11(16.7)	11(16.7)	22(33.3)
Specialist(SP)	1(1.5)	5(7.6)	6(9.1)
Nurse	2(3.0)	24(36.4)	26(39.4)
Others (e.g. dentist, traditional medicine, rehabilitator)	2(3.0)	19(15.2)	12(18.2)
Length of working years in career			
≤3	10(15.2)	20(30.3)	30(45.5)
4-10	3(4.5)	10(15.2)	13(19.7)
11-20	1(1.5)	9(13.6)	10(15.2)
≥21	2(3.0)	11(16.7)	13(19.7)
Median(25%,75%)**	2(0.62,7.50)	8(2,20)	6(1.75,18.25)

** The prescriber's ages and length of working years in career is not normal distribution.

4.1.3 Prescription

Table 4.3 presents the characteristics of all 2,128 prescriptions that 56.8 per cent of them were prescribed to female patients. The median of medications per prescription taken was 5. The highest number of medications per prescription was 20 items. The most number of diagnoses ranged 1 to 2 ICD-10 codes per prescription (38.3 and 32.4 per cent for female and male, respectively).

Table 4.3: Characteristics of the Prescription

Characteristics	Number of Prescriptions		
	Male (%) n=920(43.2)	Female (%) n=1,208(56.8)	Total (%) n=2,128(100)
Age range			
65-69 years	153(7.2)	324(15.2)	477(22.4)
70-74 years	288(13.5)	308(14.5)	596(28.0)
75-79 years	293(13.8)	279(13.1)	572(26.9)
>=80 years	186(8.7)	297(14.0)	483(22.7)
Number of medications			
1-4	396(18.6)	521(24.5)	917(43.1)
5-7	288(13.5)	386(18.1)	674(31.7)
8-10	171(8)	213(10)	384(18.1)
11-14	64(3.0)	78(3.7)	142(6.7)
≥15	1(0.0)	10(0.5)	11(0.5)
Median(25%,75%)**	5(3,8)	5(3,7)	5(3,8)
Number of diagnoses (ICD-10) per prescription			
1-2	689(32.4)	814(38.3)	1,503(70.6)
3-4	211(9.9)	345(16.2)	556(26.1)
≥5	20(0.9)	49(2.3)	69(3.2)
Median(25%,75%)**	2(1,3)	2(1,3)	2(1,3)
Thai Health Insurance Schemes,			
UHC	663(31.2)	917(43.1)	1,580(74.2)
SSS	16(0.8)	5(0,2)	21(1.0)
CSMBS	162(7.6)	200(9.4)	362(17.0)
DF	66(3.1)	67(3.1)	133(6.2)
Others (CAR, WF, Self-pay)	13(0.6)	19(0.9)	32(1.5)
UHC=Universal Health Coverage, SSS=Social Security Scheme, CSMBS=Civil Servant Medical Benefit Scheme, CAR=Car Accident Insurance, WF=Employees 'workplace fund			

** The number of medications and diagnoses were not normal distribution.

4.1.4 Potentially Inappropriate Medication

The prevalence of PIM, involved by the number of patients who received one or more PIM and by the number of prescriptions which had one or more PIM, is presented in table 4.4. Overall, a half of the study patients (216 out of 430 patients) or 28 per cent of their prescriptions during the fiscal year 2012 received one or more PIM defined by the 2012 Beers criteria.

Table 4.4: Prevalence of PIM involving by number of patients and prescriptions

Fiscal Year	Total number of patients	Total number of patients' prescriptions	Total number of patients with at least 1 PIM (%)	Total number of patients' prescriptions with at least 1 PIM (%)
2012	430	2,128	214 (49.8)	598 (28.1)

In addition, table 4.5 presents the frequency of prescriptions by the overall number of PIMs in each prescription that the number of PIM ranged from 1 to 5 items. It showed that 23 per cent of all prescription had 1 PIM per prescription and the highest number of PIMs, was observed in only one prescription.

Table 4.5: Frequency of prescription categorized by total number of PIMs per prescription

Number of PIM	Frequency of prescriptions (n=2,128)	Percent
None	1,530	71.9
1	487	22.9
2	106	4.9
3	4	0.2
5	1	0.1

Besides that, the prevalence of PIM was presented monthly in table 4.6. Overall, the prevalence of PIM did not change seasonally during the study period. The highest prevalence of PIM prescription was observed in December, 2011 (35 per cent) and the lowest prevalence of PIM prescription was found in June, 2012.

Table 4.6: Prevalence of PIM prescription by months in the fiscal year 2012

Fiscal Year 2012	PIM prescriptions (%) (n=598)	Non-PIM prescriptions (%) (n=1530)	Total number of prescriptions (%) (n=2,128)	Prevalence of PIM prescription by Month
October, 2011	52(8.7)	117(7.6)	169(7.9)	30.8
November, 2011	48(8.0)	114(7.5)	162(7.6)	29.6
December, 2011	56(8.0)	105(6.9)	161(7.6)	34.8
January, 2012	38(6.4)	119(7.8)	157(7.4)	24.2
February, 2012	54(9.0)	103(6.7)	157(7.4)	34.4
March, 2012	48(8.0)	127(8.3)	175(8.2)	27.4
April, 2012	50(8.4)	118(7.7)	168(7.9)	29.8
May, 2012	46(7.7)	132(8.6)	178(8.4)	25.8
June, 2012	43(7.2)	199(13.0)	242(11.4)	17.8
July, 2012	53(8.9)	135(8.8)	188(8.8)	28.2
August, 2012	60(10.0)	134(8.8)	194(9.1)	30.9
September, 2012	50(8.4)	127(8.3)	177(8.3)	28.2

The prevalence of PIM categorized by principal diagnosis groups (Pdx) was illustrated in table 4.7. Out of 2,128 prescriptions, all prescriptions with Pdx of Mental and behavioural disorders by ICD-10 codes (F00-F99) had at least 1 PIM (17/17). Following that, 65.4 per cent (17/26) of PIM prescription was observed with Pdx of diseases of nervous system (G00-G99), and 48.3 per cent of PIM with Pdx of diseases of genitourinary system.

However, the highest numbers of PIM prescriptions was diagnosed principally with diseases of the circulatory system (I00-I99), which comprised 164 PIM prescriptions, followed by Endocrine, nutritional and metabolic diseases (E00-E99; 87 PIM prescriptions) and Diseases of the respiratory system (J00-J99) and diseases of the musculoskeletal system and connective tissue (M00-M99), which each had 74 PIM prescriptions. (see details in table 4.7)

Table 4.7: Prevalence of PIM prescription categorized by principal diagnosis group (ICD-10)

ICD-10 code	Principal diagnosis group (ICD-10 category)	PIM Prescriptions (%) (n=598)	Non-PIM Prescriptions (%) (n=1,530)	Total number of prescriptions (%) (n=2,128)	Prevalence of PIM by Principal diagnosis group
F00-F99	Mental and behavioural disorders	17(2.8)	0(0)	17(0.8)	100.0
G00-G99	Diseases of the nervous system	17(2.8)	9(0.6)	26(1.2)	65.4
N00-N99	Diseases of the genitourinary system	14(2.3)	15(1.0)	29(1.4)	48.3
M00-M99	Diseases of the musculoskeletal system and connective tissue	74(12.4)	85(5.6)	159(7.4)	46.5
E00-E99	Endocrine, nutritional and metabolic diseases	87(14.5)	169(11.0)	256(12.0)	34.0
H00-H59	Diseases of the eye and adnexa	4(0.7)	9(0.6)	13(0.6)	30.8
L00-L99	Diseases of the skin and subcutaneous tissue	7(11.7)	16(1.0)	23(1.1)	30.4
R00-R99	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	53(8.9)	126(8.2)	179(8.4)	29.6
I00-I99	Diseases of the circulatory system	164(27.4)	421(27.5)	585(27.5)	28.0
A00-B99	Certain infectious and parasitic diseases	15(2.5)	47(3.1)	62(2.9)	24.2
J00-J99	Diseases of the respiratory system	74(12.4)	260(17.0)	334(15.7)	22.2
K00-K93	Diseases of the digestive system	44(7.4)	163(10.7)	207(9.7)	21.3
S00-T98	Injury, poisoning and certain other consequences of external causes	9(1.5)	36(2.4)	45(2.1)	20.0
H60-H65	Diseases of the ear and mastoid process	6(1.0)	28(1.8)	34(1.6)	17.6

Table 4.7: Prevalence of PIM prescription categorized by principal diagnosis group (ICD-10) (continued)

ICD-10 code	Principal diagnosis group (ICD-10 category)	PIM Prescriptions (%) (n=598)	Non-PIM Prescriptions (%) (n=1,530)	Total number of prescriptions (%) (n=2,128)	Prevalence of PIM prescription by Principal diagnosis group
D50-D89	Diseases of the blood and blood-forming organs and certain disorders involving the immune mechanism	1(0.17)	7(0.46)	8(0.4)	12.5
Z00-Z99	Factors influencing health status and contact with health services	12(2.01)	133(8.69)	145(6.8)	8.3
U00-U89	Codes for special purposes	0(0)	1(0.07)	1(0)	0
C00-D48	Neoplasms	0(0)	4(0.26)	4(0.2)	0
O00-O99	Pregnancy, childbirth and the puerperium (Retained intrauterine contraceptive device in pregnancy)	0(0)	1(0.07)	1(0)	0

According to table 4.8, among those elderly outpatient prescriptions, there were 19 medications as unconditionally PIM by 2012 Beers criteria. The top five most frequently prescribed those PIMs included Lorazepam, Diclofenac, Doxazocin, Ibuprofen, and Alprazolam. These five medications were accounted for 67 per cent of all PIM use.

The most common use of PIM classified by pharmacologic category was Benzodiazepine (BZDs), which were accounted for 37 per cent (259/716) of those PIM--26 per cent from short-and intermediate-acting and 11 per cent from long-acting agent. The second and third most common subtype of those pharmacologic category were Non-Cyclooxygenase (COX)-selective Nonsteroidal Anti-Inflammatory Drugs (NSAIDs) and Alpha-1-blocker, which comprised of 27 and 15 per cent of PIM, respectively.

In addition, 5 main therapeutic or system categories of PIM included Anticholinergic, excluded Tri-cyclic antidepressant (TCA), Cardiovascular system, Central nervous system, Gastrointestinal system and Pain medication were presented in table 4.8. Likewise the prescribing of PIM classified by pharmacologic category, PIM in central nervous system category was mostly found among PIM prescription (45 per cent [321/716]). Following that 27 per cent (193/716) of those PIMs were pain medication and 19 per cent (137/716) of those cardiovascular drugs.

Table 4.8: Frequency and percentage of prescribing PIM categorized by pharmacological category

PIM	Pharmacologic category**	Therapeutic /System Category*	Frequency of prescribing PIM (n=716)	Percent	Percent Cumulative
1. Lorazepam	Benzodiazepine (short-and intermediate-acting)	Central nervous system	125	17.5	17.5
2. Diclofenac	Non-Cox-selective NSAIDs	Pain medication	123	17.2	34.6
3.Doxazosin	Alpha-1-blockers	Cardiovascular	109	15.2	49.9
4.Ibuprofen	Non-Cox-selective NSAIDs	Pain medication	67	9.4	59.2
5.Alprazolam	Benzodiazepine (short-and intermediate-acting)	Central nervous system	57	8.0	67.2
6.Amitriptyline	Tertiary Tricyclic Antidepressants (TCAs)	Central nervous system	55	7.7	74.9
7.Dipotassium chlorazepate	Benzodiazepine (long-acting)	Central nervous system	48	6.7	81.6
8.Chlorpheniramine	First-generation antihistamine	Anticholinergics (excluded TCAs)	26	3.6	85.2
9.Digoxin	Antiarrhythmic drugs	Cardiovascular	26	3.6	88.8
10.Hydroxyzine	First-generation antihistamine	Anticholinergics (excluded TCAs)	22	2.9	91.9
11.Diazepam	Benzodiazepine (long-acting)	Central nervous system	18	2.5	94.4
12.Metoclopramide	Others	Gastrointestinal	17	2.4	96.8

Table 4.8: Frequency and percentage of prescribing PIM categorized by pharmacological category(continued)

PIM	Pharmacologic category**	Therapeutic /System Category*	Frequency of prescribing PIM (n=716)	Percent	Percent Cumulative
13.Clonazepam	Benzodiazepine (long-acting)	Central nervous system	10	14	98.2
14.Imipramine	Tertiary TCAs	Central nervous system	4	0.6	98.7
15.Mefenamic acid	Non-Cox-selective NSAIDs	Pain medication	3	0.4	99.2
16.Spiroinolactone	Antiarrhythmic drugs	Cardiovascular	2	0.3	99.4
17.Methyldopa	Alpha blockers central	Central nervous system	2	0.3	99.7
18.Trihexyphenidyl	Antiparkinson agents	Anticholinergics (excluded TCAs)	1	0.1	99.9
19.Thioridazine	Antipsychotic, first-generation agents	Central nervous system	1	0.1	100.0

*The prescription of all therapeutic categories of benzodiazepine sums up to 37 per cent of all PIM, and 27 and 15 per cent of all PIM were Non-COX-NSAIDs and Alpha-1-blocker, respectively.

** The prescription of all pharmacologic categories of central nervous system sums up to 45 per cent of all PIM, and 27 and 19 per cent of all PIM were pain medication and cardiovascular drugs, respectively.

The research team coupled any single PIM with a diagnosis by ICD-10 code that the results of matching each PIM to diagnosis were illustrated in table 4.9. Excepted UM, the three frequencies of diagnosis in association with PIM prescribing were diseases of the circulatory system (18 per cent), diseases of the musculoskeletal system and connective tissue (15 per cent), and mental and behavioural disorder(9 per cent).

Table 4.9: Frequency and percentage of prescribing PIM disaggregated by diagnosis

ICD_code	Diagnosis (ICD-10 category)	Frequency of PIM (N=716)	Percent
UM	Unmatched-code with any PIM list	171	23.9
I00-I99	Diseases of the circulatory system	129	18.0
M00-M99	Diseases of the musculoskeletal system and connective tissue	111	15.5
F00-F99	Mental and behavioural disorders	67	9.4
R00-R99	Symptoms, signs and abnormal clinical and laboratory findings, not elsewhere classified	58	8.1
N00-N99	Diseases of the genitourinary system	48	6.7
J00-J99	Diseases of the respiratory system	31	4.3
G00-G99	Diseases of the nervous system	28	3.9
K00-K93	Diseases of the digestive system	22	3.1
Z00-Z99	Factors influencing health status and contact with health services	13	1.8
A00-B99	Certain infectious and parasitic diseases	10	1.4
S00-T98	Injury, poisoning and certain other consequences of external causes	10	1.4
L00-L99	Diseases of the skin and subcutaneous tissue	9	1.3
H00-H59	Diseases of the eye and adnexa	4	0.6
E00-E90	Endocrine, nutritional and metabolic diseases	2	0.3
L00-L99	Diseases of the skin and subcutaneous tissue	9	1.3
H00-H59	Diseases of the eye and adnexa	4	0.6

Table 4.9: Frequency of prescribing PIM disaggregated by diagnosis (continued)

ICD-10 code	Diagnosis (ICD-10 category)	Frequency of PIM (N=716)	Percent
E00-E90	Endocrine, nutritional and metabolic diseases	2	0.3
H60-H95	Diseases of the ear and mastoid process	2	0.3
V01-Y98	External causes of morbidity and mortality	1	0.1

Table 4.10 illustrated the frequency of prescribing PIM disaggregated by existing ICD-10. With regard to this, most PIMs were used for various diagnoses. The three most frequency of PIM were Lorazepam, Diclofenac, and Doxazosin, which were about 17 per cent (125/716), 17 per cent(123/716), and 15 per cent (109/716), respectively. Noticeably, most PIM were matched to 2 or more diagnoses.

Having emphasized that Lorazepam, which is generally a drug used in central nervous system by its therapeutic category in Beers criteria, was mostly considered for diseases of the circulatory system coded "I00-I99" (53 out of 125 observations); this drug was clinically commonly used as a combined medication with antihypertensive drugs to decrease blood pressure. Whilst, 29 out of 125 observations in prescribing Lorazepam were used relevantly with mental and behavioral disorders (F00-F99) and 28 out of 125 its observations were not matched to any given diagnoses (UM).

Diclofenac is a pain-relief medication as indicated in Beers' therapeutic category or one of Non-COX-Selective NSAIDs, that clinically used in several diagnoses with regard to pain or anti-inflammatory. 74 out of 123 observations (60 per cent) in prescribing Diclofenac were used in diseases of the musculoskeletal system and connective tissue, which were the most frequent numbers.

Doxazosin is therapeutically categorized as cardiovascular drug that 49 out of 109 observations were used for diseases of circulatory system. Nevertheless, this drug was clinically used in hyperplasia of prostate, coded "N40", which comprised 42 out of 109 observations in prescribing Doxazosin.

However, 72 per cent of prescribing Alprazolam (41/57 observations) were not indicated by any given ICD-10 and then assigned to "UM". There were only 3 observations assigned to the code of diseases of nervous system (G00-G99), and another 3 observations assigned to mental and behavioural disorders (F00-F99) that both diagnoses seemingly related with Beers' therapeutic category of Alprazolam.

Digoxin is an antiarrhythmic drug used in treating cardiovascular disease. It was observed that 25 out of 26 observations (96 per cent) were mostly deemed to prescribe for relevant diagnosis--diseases of the circulatory system.

Table 4.10: Frequency and percentage of prescribing each of PIM items disaggregated by Diagnoses (ICD-10)

PIM	Diagnosis by ICD-10 codes																	
	A00-B99	E00-E90	F00-F99	G00-G99	H00-H59	H60-H95	I00-I99	J00-J99	K00-K93	L00-L99	M00-M99	N00-N99	R00-R99	S00-T98	UM	V01-Y98	Z00-Z99	Total
Chlorpheniramine	0	0	0	0	1	0	0	15	0	2	0	0	0	3	5	0	0	26
Amitriptyline	0	0	9	6	0	0	0	0	2	0	10	0	9	0	19	0	0	55
Chlorazepate	0	0	18	0	0	0	0	0	0	0	0	0	9	0	21	0	0	48
Diazepam	0	0	5	1	0	0	0	2	2	0	0	0	1	0	7	0	0	18
Diclofenac	4	0	0	4	1	0	0	4	1	1	74	3	8	5	13	1	4	123
Digoxin	0	0	0	0	0	0	25	0	0	0	0	0	0	0	1	0	0	26
Ibuprofen	0	0	0	2	0	2	0	7	9	2	27	3	6	2	3	0	4	67
Lorazepam	0	0	29	7	0	0	53	0	0	0	0	0	7	0	28	0	1	125
Mefanamic acid	0	0	0	0	0	0	0	0	0	0	0	0	2	0	1	0	0	3
Spironolactone	0	2	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	2
Doxazosin	0	0	0	0	0	0	49	0	0	0	0	42	1	0	14	0	3	109
Trihexyphenidyl	0	0	0	0	0	0	0	0	0	0	0	0	1	0	0	0	0	1
Hydroxyzine	2	0	1	0	2	0	0	0	0	4	0	0	0	0	13	0	0	22
Imipramine	0	0	0	0	0	0	0	0	0	0	0	0	0	0	4	0	0	4
Clonazepam	0	0	1	8	0	0	0	0	0	0	0	0	0	0	1	0	0	10
Methyldopa	0	0	0	0	0	0	2	0	0	0	0	0	0	0	0	0	0	2
Metoclopramide	4	0	0	0	0	0	0	0	8	0	0	0	5	0	0	0	0	17
Alprazolam	0	0	3	3	0	0	0	0	0	0	0	0	9	0	41	0	1	57
Thioridazine	0	0	1	0	0	0	0	0	0	0	0	0	0	0	0	0	0	1
Total	10	2	67	31	4	2	129	28	22	9	111	48	58	10	171	1	13	716

To match PIMs to the groups of classified indication, table 4.11 presented the results of matching PIM disaggregated by the classified indications--Beers' therapeutic indication, potentially clinical used indication, and unmatched indication provided as UM in the previous tables. Those PIMs were matched to the classified indications, which were the major category of ICD_10 codes. Unmatched indication was any ICD_10 codes, which could not be matched on the basis of Beers' therapeutic category or potentially clinical used indication. Table 4.11 illustrates the major ICD-10 codes disaggregated into the classified indications. In addition, the table of PIM disaggregated by classified indications with regard to the minor ICD-10 codes was described in appendix B.

Table 4.11: Results in matching each PIM with the classified indications by the major ICD_10 code.

PIM	Beers' therapeutic indication	Potentially clinical used indication
Chlorpheniramine	J00-J99, H00-H59, L00-L99	S00-T98
Amitriptyline	F00-F99, G00-G99	K00-K93, M00-M99, R00-R99,
Chlorazepate	F00-F99	R00-R99
Diazepam	F00-F99, G00-G99	J00-J99, K00-K93, R00-R99
Diclofenac	M00-M99, S00-T98	A00-B99, G00-G99, H00-H59, J00-J99, K00-K93, L00-L99, N00-N99, R00-R99, U00-U89, V01-Y98, Z00-Z99
Digoxin	I00-I99	-
Ibuprofen	M00-M99, S00-T98	G00-G99, H60-H95, J00-J99, K00-K93, L00-L99, N00-N99, R00-R99, U00-U89, Z00-Z99
Lorazepam	F00-F99, G00-G99	I00-I99, R00-R99, U00-U89, Z00-Z99

Table 4.11: Results in matching each PIM with the classified indications by the major ICD_10 code. (continued)

PIM	Beers' therapeutic indication	Potentially clinical used indication
Mefanamic acid	R00-R99	-
Spirolactone	-	E00-E90
Doxazosin	I00-I99	N00-N99, R00-R99, Z00-Z99
Trihexyphenidyl	R00-R99	-
Hydroxyzine	H00-H59, L00-L99	A00-B99, F00-F99, U00-U89
Imipramine	-	-
Clonazepam	F00-F99, G00-G99	-
Methyldopa	I00-I99	-
Metoclopramide	K00-K93	A00-B99, R00-R99
Alprazolam	F00-F99	R00-R99, S00-T98, Z00-Z99
Thioridazine	F00-F99	-

Table 4.12 provided the frequencies of prescribing PIM in relation to the above classified indications. To sum up, 298 out of 716 (41.6 per cent) observations were PIM, which was prescribed along with the Beers' therapeutic category.

PIM prescribed with potentially clinical used indication was provided that 34.5 per cent [247/716] of all observations were considered as clinically approved indications. Overall, the three most PIM were Lorazepam (27.1 per cent), Doxazosin (18.6 per cent), and Ibuprofen (15.0 per cent).

However, 23.9 per cent [171/716] of all PIM were UM that Alprazolam was the major UM. which accounted for 24 per cent, followed by Lorazepam, Chlorazepate, and Amitriptyline, which were 16.4, 12.3 and 11.1 per cent, respectively. Moreover, the result showed that 57.9 per cent of UM was PIM used in central nervous system categorized by Beers' therapeutic indication.

Table 4.12: Frequency of prescribing PIM disaggregated by classified indications.

(n=716)

PIM	By Beers' therapeutic indication	Percent	By Potentially clinical used indication	Percent	Unmatched case	Percent
Chlorpheniramine	18	6.0	3	1.2	5	2.9
Amitriptyline	15	5.0	21	8.5	19	11.1
Chlorazepate	18	6.0	9	3.6	21	12.3
Diazepam	6	2.0	5	2.0	7	4.1
Diclofenac	78	26.2	32	13.0	13	7.6
Digoxin	25	8.4	0	0	1	0.6
Ibuprofen	27	9.1	37	15.0	3	1.8
Lorazepam	30	10.1	67	27.1	28	16.4
Mefanamic acid	2	0.7	0	0	1	0.6
Spirolactone	0	0	2	0.8	0	0
Doxazosin	49	16.4	46	18.6	14	8.2
Trihexyphenidyl	1	0.3	0	0	0	0
Hydroxyzine	6	2.0	3	1.2	13	7.6
Imipramine	0	0	0	0	4	2.3
Clonazepam	9	3.0	0	0	1	0.6
Methyldopa	2	0.7	0	0	0	0
Metoclopramide	8	2.7	9	3.6	0	0
Alprazolam	3	1.0	13	5.3	41	24.0
Thioridazine	1	0.3	0	0	0	0
Total	298	100.0	247	100.0	171	100.0

4.2 Results of Analysis of Inferential Statistic

Within the 2012 Beers criteria for older adults, there is a subset of medications considered potentially inappropriate medications and classes to avoid, that is, these medications are considered as "unconditional list of PIM" in this study regardless of dose, duration, or individual's medical condition. Thai health insurance schemes were collapsed by only 2 groups--UHC and non-UHC in order to have enough sample size in data analysing with Chi-square test.

Table 4.13 provided the difference of patient characteristics between PIM and non-PIM prescription. Prescriptions with at least one PIM were observed frequently in advanced age groups. (e.g. 70-74 versus 75-79 years old: 27.9 and 34.4 per cent in PIM versus 72.1 and 65.6 per cent in non-PIM, respectively, $p < 0.001$). No significant differences were observed in genders and Thai health insurance schemes between patients who were given PIM and Non PIM prescriptions.

Table 4.13: Differences between patient's characteristics and outpatient PIM prescription versus non-PIM prescription.

Characteristics	PIM prescription (%)(n=598)	Non-PIM (%)(n=1,530)	Total number of prescriptions (%)(n=2,128)	p-value*
Gender				0.305
Female	350(29.0)	858(71.0)	1,208(100.0)	
Male	248(27.0)	672(73.0)	920(100.0)	
Patient's Age				<0.001
65-69 years	100(21.0)	377(79.0)	477(100.0)	
70-74 years	166(27.9)	430(72.1)	596(100.0)	
75-79 years	197(34.4)	375(65.6)	572(100.0)	
>=80 years	135(28.0)	348(72.0)	483(100.0)	
Health Insurance Schemes				0.186
UHC	456(28.9)	1,124(71.1)	1,580(100.0)	
Non-UHC	142(25.9)	406(74.1)	548(100.0)	

For some prescriber characteristics, PIM and non-PIM prescriptions had significant differences in types of prescribers, for instance, by general practitioners (29.3 per cent versus 70.7 per cent, $p < 0.001$) or by specialists (33.5 per cent versus 66.5 per cent, $p < 0.001$) and prescriber who worked many years in their careers ($p = 0.006$). (see details in table 4.14)

Table 4.14: Differences between prescriber's characteristics and outpatient PIM prescription versus non-PIM prescription.

Characteristics	PIM prescription(%) (n=598)	Non-PIM prescription (%)(n=1,530)	Total number of prescriptions (%) (n=2,128)	p-value
Prescriber's Gender				0.552
Female	361(27.6)	945(72.4)	1,306(100.0)	
Male	237(28.8)	585(71.2)	822(100.0)	
Prescriber's Age				0.333
20 - 28	314(26.7)	864(73.3)	1,178(100.0)	
29 - 37	79(28.7)	196(71.3)	275(100.0)	
38 - 46	127(31.3)	279(68.7)	406(100.0)	
47 - 55	78(29.0)	191(71.0)	269(100.0)	
Types of prescriber				<0.001
GP	418(29.3)	1,011(70.7)	1,429(100.0)	
SP	75(33.5)	149(66.5)	224(100.0)	
Nurses	100(24.0)	316(76.0)	416(100.0)	
Others(dentist, traditional medicine, rehabilitator)	5(8.5)	54(91.5)	59(100.0)	
Lengths of years working				0.006
≤3	311(26.5)	864(73.5)	1,175(100.0)	
4-10	83(31.6)	180(68.4)	263(100.0)	
11-20	119(34.6)	225(65.4)	344(100.0)	
≥21	85(24.6)	261(75.4)	346(100.0)	

Table 4.15 presents the differences between prescription's characteristics and PIM versus non-PIM prescriptions among the elderly outpatient. Prescriptions with at least one PIM and without PIM showed significant differences in number of medications (e.g. 5-7 medications: 30.4 per cent in PIM versus 69.6 per cent in non-PIM,

$p < 0.001$), multiple diagnoses (e.g. 3-4 diagnoses: 37.4 per cent in PIM versus 62.6 per cent in non-PIM, $p < 0.001$). Moreover, it seems that the more number of medications and the more number of diagnoses were a likelihood of more number of PIM prescriptions, such as, prescriptions with 8-10 medications had 46 per cent of all prescriptions as PIM (177/384) and increase to 51 per cent (73/142) in prescription with 11-14 medications.

Table 4.15: Differences between prescription's characteristics by outpatient PIM prescription versus non-PIM prescription.

Characteristics	PIM prescription (%) (n=598)	Non-PIM prescription (%) (n=1,530)	Total number of prescriptions (%) (n=2,128)	p-value*
Number of medications				<0.001
1-4	134(14.6)	783(85.4)	917(100.0)	
5-7	205(30.4)	469(69.6)	674(100.0)	
8-10	177(46.1)	207(53.9)	384(100.0)	
11-14	73(51.4)	69(48.6)	142(100.0)	
≥ 15	9(81.8)	2(18.2)	11(100.0)	
Number of diagnoses (ICD-10)				<0.001
1-2	362(24.1)	1,141(75.9)	1,503(100.0)	
3-4	208(37.4)	348(62.6)	556(100.0)	
≥ 5	28(40.6)	41(59.4)	69(100.0)	

* Chi-square test, $p < 0.05$

In table 4.16, the number of outpatient visits and inpatient admissions were presented and the unit of analysis was patient. PIM and non-PIM user had significant differences by the frequency of outpatient visits, such as, patients who had 7 outpatient visits or more (75.6 per cent for PIM versus 24.4 per cent for non-PIM,

$p < 0.001$). None of significant difference was observed in inpatient admissions between the groups.

Table 4.16: Differences between Outpatient visits and Inpatient admissions and PIM versus non-PIM prescriptions during the fiscal Years 2012

Characteristics	Patients with at least 1 PIM (%) (n=214)	Patient without PIM (%) (n=216)	Total number of patients (%) (n=430)	p-value
Outpatient visits				<0.001
1-3	82(36.3)	144(63.7)	226(100.0)	
4-6	36(46.8)	41(53.2)	77(100.0)	
≥ 7	96(75.6)	31(24.4)	127(100.0)	
Inpatient admissions				0.07
0	176(48.1)	191(52.0)	367 (100.0)	
≥ 1	38(60.3)	25(39.7)	63(100.0)	

In table 4.17, the binary logistic regression analysis was employed on all independent variables. Prior to analysis, prescriber's age and length of years working and number of diagnoses were treated as continuous variables in order to reverse the multicollinearity. Moreover, Thai health insurance schemes were re-categorized by only 2 groups--UHC and non-UHC-- because there were less number of data in some schemes to analyze by logistic regression.

The odds ratio for each factor is an estimation of multiplicative effect of a single unit increase in that factor on the odds of presence of PIM, holding all the other covariates constant. Coefficient, odds ratio, 95% Confidence Interval (95% CI) for odds ratio, and p-value were presented.

In table 4.17, only independent variables showed significant differences in 4.13-4.16 were taken into the logistic regression model. Patient's age and number of medications presented a positively significant association to the presence of PIM. In contrast, there were negatively significant associations between number of outpatient

visits and the presence of PIM, as well as, between types of prescriber (nurses and other health professionals) and the presence of PIM. To consider the goodness of fit for logistic regression model, however, Hosmer & Lemeshow test showed the value of Chi-square (16.172) with the significant level less than 0.05 ($p=0.040$) that indicated the poor fit of model by these factors.

Table 4.17: Results of binary logistic regression for PIM with patient, prescriber, and prescription's characteristics among the study outpatient prescriptions. (analysis of partial factors)

Factors	Regression Coefficient(B)	Standard Error(S.E.)	Odds Ratio (OR)	95%CI	P-value
Patients					
Age	0.018	0.009	1.018	1.001-1.035	0.038
Number of Outpatient visits					
1-3	-	-	1	-	-
4-6	-0.559	0.180	0.572	0.402-0.813	0.002
≥ 7	-0.395	0.147	0.674	0.505-0.898	0.007
Prescriber					
Types of prescriber					
GP	-	-	1	-	-
SP	-0.006	0.163	0.994	0.722-1.368	0.968
Nurses	-0.510	0.226	0.601	0.386-0.935	0.024
Others(dentist, traditional medicine, rehabilitator)	-0.860	0.483	0.423	0.164-1.090	0.075
Lengths of years working	0.14	0.009	1.015	0.996-1.033	0.120

Hosmer & Lemeshow test: Chi-square=16.172 , $p=0.040$, $R^2_{\text{cox\&snell}} = 0.100$

Table 4.17: Results of binary logistic regression for PIM with patient, prescriber, and prescription's characteristics among the study outpatient prescriptions. . (analysis of partial factors) (continued)

Factors	Regression Coefficient(B)	Standard Error(S.E.)	Odds Ratio (OR)	95%CI	P-value
Prescription					
Number of medications					
1-4	-	-	1	-	-
5-7	0.888	0.132	2.430	1.876-3.147	<0.001
8-10	1.606	0.157	4.980	3.665-6.769	<0.001
11-14	1.845	0.213	6.326	4.170-9.596	<0.001
≥15	3.213	0.804	24.853	5.136-120.257	<0.001
Number of disease groups (ICD-10)	0.016	0.051	1.016	0.920-1.121	0.759

Hosmer & Lemeshow test: Chi-square=16.172 , p=0.040 , $R^2_{\text{cox\&snell}} = 0.103$

Table 4.18 presents the model of logistic regressions with the full independent variables. Compared to the above model, Hosmer & Lemeshow test indicated the good fit of this model with regard to the less chi-squared value (13.227) and significant level = 0.103.

The results show the significantly positive association between the presence of PIM and the number of medications. There was the more likelihood of a patient receiving PIM at outpatient department increased significantly when the patient was prescribed more medications ($p<0.01$). Compared to the reference group, an elderly patient who was prescribed more than 15 medications had 25-fold in receiving at least 1 PIM prescription ($p<0.01$).

Table 4.18 also presents the positive association between ages of patient and the presence of PIM prescription (OR=1.018, $p=0.040$, CI=1.001-1.035), as well as, the statistically significantly negative association between the number of outpatient visits and the presence of PIM prescription.

Compared to the reference group, an elderly patient who had 4-6 outpatient visits is 0.6-fold in receiving PIM, as well as, an elderly outpatient who had 7 or more outpatient visits is 0.7-fold in receiving PIM. (Outpatient visits: 4-6 vs. ≥ 7 : OR = 0.581 [95% CI=0.408-0.828], $p=0.003$ vs. OR=0.704 [95% CI=0.526-0.943], $p=0.019$). Therefore, it had a likelihood of an elderly outpatient who had more frequent outpatient visits were prescribed less PIM prescription.

However, no statistically significant association between the presence of PIM and patient's gender, number of diagnoses, health insurance schemes, inpatient admissions, prescriber's gender, age, types of prescriber and length of prescriber's years work was observed in this study.

Table 4.18: Results of binary logistic regression for PIM with patient prescriber and prescription's characteristics among the study outpatient prescriptions. (analysis of all factors)

Factors	Regression Coefficient(B)	Standard Error (S.E.)	Odds Ratio (OR)	95%CI	p-value
Patients					
Gender					
Male	-	-	1	-	-
Female	0.084	0.105	1.088	0.885-1.337	0.423
Age	0.018	0.009	1.018	1.001-1.035	0.040
Thai Health insurance schemes					
Non-UHC	-	-	1	-	-
UHC	0.088	0.120	1.092	0.864-1.380	0.462
Number of Outpatient visits					
1-3	-	-	1	-	-
4-6	-0.543	0.181	0.581	0.408-0.828	0.003
≥7	-0.351	0.149	0.704	0.526-0.943	0.019
Number of inpatient admissions					
0	-	-	1	-	-
≥1	-0.156	0.127	0.856	0.668-1.098	0.220
Prescribers					
Gender					
Male	-	-	1	-	-
Female	0.020	0.120	1.020	0.806-1.290	0.869
Ages	0.100	0.050	1.105	1.002-1.218	0.046

Hosmer & Lemeshow test: Chi-square= 5.325, p= 0.722, $R^2_{\text{cox\&snell}} = 0.103$

Table 4.18: : Results of binary logistic regression for PIM with patient prescriber and prescription's characteristics among the study outpatient prescriptions. (analysis of all factors) (continued)

Factors	Regression Coefficient(B)	Standard Error (S.E.)	Odds Ratio (OR)	95%CI	P-value
Prescriber					
Types of prescriber					
GP	-	-	1	-	-
SP	0.001	0.165	1.001	0.725-1.383	0.993
Nurses	-0.133	0.285	0.874	0.500-1.526	0.636
Others(dentist, traditional medicine, rehabilitator)	-0.595	0.498	0.552	0.208-1.463	0.232
Lengths of years working	-0.088	0.051	0.916	0.829-1.012	0.084
Prescription					
Number of medications					
1-4	-	-	1	-	-
5-7	0.913	0.133	2.491	1.919-3.234	<0.001
8-10	1.636	0.158	5.133	3.763-7.001	<0.001
11-14	1.877	0.215	6.535	4.290-9.956	<0.001
≥15	3.227	0.808	25.198	5.168-122.867	<0.001
Number of disease groups (ICD-10)	0.018	0.051	1.018	0.920-1.125	0.732

Hosmer & Lemeshow test: Chi-square= 5.325, p= 0.722, $R^2_{\text{cox\&snell}} = 0.103$

CHAPTER V

DISCUSSION CONCLUSION AND RECOMMENDATION

5.1 Discussion

The main 5 parts of discussion were emphasized--prevalence of PIM, the association of study factors and the presence of PIM , comparative studies of PIM screening tools, quality of ICD-10 codes and strengths and limitations of this study.

5.1.1) Prevalence of PIM

In this study, the prevalence of PIM was 28.1 per cent involving outpatient prescriptions or 49.81 per cent involving all patients who had at least 1 PIM prescription. It differed from a study among Taiwanese elderly patients in ambulatory care, who were members of Taiwanese National Health Insurance program was conducted that the prevalence of PIM prescribing was 19.1 per cent of 176,661,994 ambulatory care visits involving a prescription or approximately 63.8 per cent of all elderly people who received at least 1 PIM once a year during 2001-2004. (Lai et al., 2009) The different prevalence between these two studies maybe due to these implications.

First of all, by Taiwanese study's implication, a little copayment from Taiwanese patients caused the more increase of outpatient visits and then lead to receive more drugs at outpatient department. (Lai et al., 2009) Likewise the Taiwanese study, the Thai elderly age over 65 years are members of Universal Health Coverages (UHC) or Civil Servant Medical Benefit (CSMBS) Schemes. The increasing number of outpatient services and prescriptions among the Thai elderly is observed because there is not copayment in public health services and pharmacy expenses for the elderly outpatients in both schemes. Having found that, the more number of prescribing medications are explicitly factors associated with receiving PIM by inferential statistical analyses.

The other implications of the high prevalence of PIM are inadequate pharmacist counseling when a number of medications are given to elderly patients in hospitals, failure to provide comprehensive drug evaluation for older people, and the lack of awareness of the risks of prescribing PIM among primary care physicians and hospital outpatient departments . (Lai et al., 2009) Noticeably, the

prevalence of PIM involving patient in this study was less than that in Taiwanese study because the number of patients in Taiwanese study were larger than this study.

The prevalence of PIM in this study, however, remains in the international range. Compared to a systematic review study by Guaraldo et al, the prevalence of PIM used in elderly outpatients in this study hospital was in the range from 11.5 to 62.5 per cent. (Guaraldo, Cano, Damasceno, & Rozenfeld, 2011)

In accordance with the items of PIM, the data also presented that 45 per cent of all PIM in central nervous system was mostly frequently used among the elderly outpatient in the study hospital. Lorazepam and Diclofenac, which comprised of 34 per cent out of all PIM observations, and Doxazosin (15%) were more frequently prescribed than other PIMs.

Compared to the study by Maio V., et al, they conducted a cohort study of PIM prescribing among 23,662 elderly Italian outpatients that NSAIDs were the most frequently prescribed (35.7 per cent), followed by Ticlopidine (17.6 per cent), and Doxazosin (15.5 per cent). (Maio, Del Canale, and Abouzaid, 2010) The difference of ranked items between the Italian cohort and this study is the result of difference of available drug lists among the study health settings in both studies. In this study, for instance, the district hospital did not have Ticlopidine as a drug in hospital formulary list of drugs.

Having emphasized in Taiwan studied by Lai et al antihistamines with anticholinergic effects was the most frequently occurring PIM (27.6 per cent of PIM prescriptions). The most second and third rank of drug class in PIM list were muscle relaxants and antispasmodics (22.6 per cent of PIM prescriptions) and long-acting Benzodiazepines (13.7 per cent of PIM prescriptions). (Lai et al., 2009)

Compared to Taiwan study, the similar result was observed that Non-Cox-selective NSAIDs and Benzodiazepine (short-and intermediate-acting) and cardiovascular drugs were the most first, second and third frequently prescribed, which were 27, 26, and 19 per cent of all PIM observations, respectively.

The implication of similar findings of PIM used in outpatient department in both studies is that patients who use outpatient services generally present with an acute condition (e.g. injury, pain, fever, or sleeping disorders) or

chronic diseases, mainly on cardiovascular diseases. (Lai et al., 2009) In the Thai study, the highest prevalence of PIM involving outpatient prescriptions across principle diagnosis codes (ICD-10) was 100 per cent found in Mental and behavioural disorders and then 65.4 per cent found in prescriptions with diseases of nervous system. Lorazepam, one of Benzodiazepine groups was frequently prescribed among Thai elderly outpatients in the district hospital.

5.1.2) Frequency of PIM prescriptions

According to the list of drugs in hospital formulary, there were 25 items of PIM . Of all items, 19 PIMs were observed throughout the study prescriptions. Moreover, 17 out of 19 items are essential drugs (ED) that commonly prescribed to the elderly outpatients, in particular. (see appendix A) It is evident that elderly outpatients in this Thai study hospital had a likelihood of receiving PIM prescriptions with regard to the high proportion of PIM items as ED in the list of hospital formulary.

Regarding the frequency of prescribing PIM divided into 3 main classified indications, there were 171 (24%) out of 716 observations assigned as Unmatched case (UM); the indication of those PIMs was unclear with regard to the existed database. The highest percentage of UM drug were in the psychotropic group ; Alprazolam (24.0 per cent), followed by Lorazepam (16.4 per cent), and Amitriptyline (11.1 per cent). However, it was assumed that the proper diagnosis codes of UM were missing in the records because the data were not audited by the prescriber or by the staff in charge of data entry. The researcher had not means to verify this assumption. 24% missing diagnoses may have affected the analyses of the association between PIM and diagnosis. Eventually, it is explicitly seen that 24 per cent of PIM occurrences in the study prescriptions were unmatched cases, which their proper indications were decided neither by the given ICD-10 codes, nor by potentially clinical indication.

5.1.3) The association of the study factors and the presence of PIM

According to the results of inferential statistic, statistically significant differences in patient prescriber and prescription characteristics between PIM and non-PIM prescriptions tested by Chi-square were observed in patient's age,

types of prescriber, and length of prescriber's years work, number of medications, number of diagnoses and numbers of outpatient visits.

Eventually, the association between all independent variables and the presence of PIM were analyzed by logistic regression. Number of outpatient visits and medications were likely to have a statistically significant association with the presence of PIM, as well as, patient's age had a likelihood of significant association with the presence of PIM.

Regarding the examined PIM use-related factors, female sex, advanced age, and large number of medications were generally the most important factors. (Guaraldo et al., 2011). In contrast, the study at this district hospital shows non significant association between patient's gender and the presence of PIM as well as a cohort research, studied by Azakawa and team, found that among 6,628 Japanese elderly patients due to the selection of study population compared with the other studies. (Akazawa et al., 2010)

A cross-sectional study of 61,251 elderly outpatients in 2 primary care settings in United States showed that patients who were female and/or receiving polypharmacy (over 5 medications used in a day) have a likelihood of receiving PIM. Moreover, a number of primary care visits and increased age were also associated with a risk for being prescribed a PIM.(Buck et al., 2009) Another study resulted that a greater number of chronic conditions were factors associated with a number of Beers' drugs use.(Maio, Del Canale, & Abouzaid, 2010)

In this study, however, a number of outpatient visits showed the significantly negative association with the presence of PIM. It was assumed that patients who frequently visited the outpatient department received less PIM prescription than patients in reference group (1-3 visits). It was explained that most elderly outpatients with the chronic diseases usually visited their doctors by appointed schedule, and receive a high number of medications within fewer scheduled OPD visits. The high number of medications in spite of fewer visits increases the likelihood of prescribing PIMs.

Moreover, none of prescriber's characteristics associated significantly with PIM prescription by logistic regression analysis. This is in contrast with an international study where prescriber characteristics--male sex, older age and

family medicine/ general practice were significantly associated with the presence of PIM.(Lai et al., 2009) The various types of prescriber implied the non-significant association between prescriber's characteristics and PIM in this study.

In this study, 39.4 per cent of prescribers were nurse who prescribed some medications in case of refilled prescriptions among those patients who have a normal clinical signs and symptoms with their chronic diseases along with the hospital criteria of clinical practice. Likewise the seven countries, the UK, the USA, Canada, Sweden, New Zealand, Australia, and Ireland enacted legislation in 2007 to allow nurses and midwives prescribing of medicines under criteria related to employment and the normal use of the medical product. Naughton et al. reported an equal risk of inappropriate prescribing with the potential for drug errors between nurse's and physician's prescriptions. (Naughton et al., 2012)

5.1.4) Comparative studies of 2012 Beers criteria and other tools

To assess 2012 Beers criteria, Marcum and Hanlon compared Beers to STOPP criteria because it is another common explicit tool in order to assess potentially inappropriate medication for older patients. Comparing between Beers and STOPP in the list of "drug to avoid", it was found that there is a concordance in these 2 measures. One thing is that the use of NSAIDs in older adult is high risk, in particular those who were diagnosed with heart failure, chronic renal failure, and peptic ulcer disease. In addition, both the Beers and STOPP criteria included Tricyclic antidepressants as a class of drugs that can exacerbate a number of conditions including falls or fractures and dementia or cognitive impairment.(Marcum & Hanlon, 2012)

Nevertheless, there are the discordances between these 2 measures due to the different patterns of prescribing quality in the United States compared with those in Europe where certain medication classes were possibly more problematic than others. Another differences between these 2 measures were the uses of Benzodiazepines. Beers included both short-and long-acting in the list of "drug to avoid", whilst, STOPP included only the long-acting Benzodiazepines. Having said that, there are many comprehensive evidences showed that all Benzodiazepines lead to adverse effects in the elderly.(Marcum & Hanlon, 2012)

Another study from Ireland showed that the rate of identification of PIM was greater in Beers than in IPET; one of explicit measurements of PIM established in Canada. It is explicit that 2012 Beers criteria contain a much more comprehensive list of medications to be avoided in the elderly (34 medications in total) compared with 2000 IPET's (14 medications). However, it is asserted that the list of medication in Beers criteria are redundant because those medications are either not available in Ireland, have been discontinued, or are not readily prescribed. (Ryan et al., 2009) Whilst Beers criteria are useful to compare prevalence of PIM internationally, they are nevertheless not particularly proper to routine clinical screening because Beers criteria are rather cumbersome to use and not well organized in any users friendly way. (Ryan et al., 2009)

Having studied at this district hospital, overall PIMs in the list of medication in the study hospital formulary were 25 items of the whole medications in 2012 Beers list. In the study dataset, however, there were only 19 items prescribed to elderly outpatients during the study period. According to this, it is rather useful to use Beers in order to identify particular problem areas than to use the whole of Beers' list in primary care.

5.1.5) Unmatched case and quality of ICD-10 codes

In the study, the most frequently prescribed drugs were all types of Benzodiazepines, which were 37 per cent of all drug classes, followed by non-COX-selective NSAIDs (27 per cent). Regarding the classified indications, 57 per cent of UM cases were Benzodiazepines. Moreover, those Benzodiazepines were prescribed to some elderly outpatients who had dizziness and giddiness (R42). This casts doubt on those PIM prescriptions whether they had been outweighed benefits to risks prior to give Benzodiazepines to the elderly outpatients.

A physician, who is an internist and the research consultant, emphasized that the procedure of prescribing medication via electronic medical prescription did not block any prescriber who order any sleeping pills without the accurate code of ICD-10; prescriber usually assigns only principle diagnosis code then order all medications for the diagnosis including other diagnoses, which were not recorded in their medical orders. By this doctor's experiences, most elderly patients complained about their sleeping problems and Benzodiazepines were

frequently given to those elderly patient ,though, the related-ICD-10 code was not assigned in their prescriptions.

Another implication of the issue of quality of assigning ICD-10 is that there are complications in ICD-10 codes that easily confute prescribers, in selecting a correct ICD-10 code. A study resulted that codes assigned by less experienced coders were significantly better than those assigned by more experienced ones (OR = 3.54; CI95 = 2.08–6.01). Higher educated coders had better codes than lower educated coders. On the other hand, memory-based coding significantly decreased coding accuracy compared with coding through ICD-10 book (OR = 2.44; CI95 = 1.46–4.05). Coding accuracy was similar when codes were based on the face sheet compared to coding based on the review of the entire medical record. (Farzandipour, Sheikhtaheri, and Sadoughi, 2010) Hence, the quality of ICD-10 coded in outpatient database is the major concern in order to match a single diagnosis with PIM.

5.1.6) Strengths and limitations of study

One of strengths of the study is that PIM assessment with the latest version of Beers criteria in elderly outpatient prescriptions at primary healthcare setting like a Thai district hospital is the first ever in Thailand. By literature review, the previous studies were conducted in larger hospital and at patient's home and used different criteria in assessing PIM. Comparing to those previous studies, the prevalence of PIM was measured in the large number of outpatient prescriptions. The retrieved data was collected from electronic medical records and administrative database, which provided more complete and consistent data.

However, there were several limitations in this study. One of those limitations is the application of Beers criteria applied to, any medications prescribed in this hospital. Therefore, prevalence of PIM was calculated only from the hospital outpatient prescriptions; self-medication and other sites of prescription (e.g. health centre) used outside the hospital were not measured in this study.

Moreover, the unconditionally inappropriate list of medication in Beers criteria was applied and any medications was considered as PIM regardless of specific diseases or other health conditions and under-or over use of medications among those participants.

This study could not judge whether 2012 Beers criteria is an effective tool in assessing PIM in the hospital. The reasons for prescribing any specific medications to elderly patients were not known.; The study was not designed to investigate whether the prescribers assessed that benefits outweighed risks when they prescribed those PIM. The researcher could not contact directly those prescribers due to their anonymity . Therefore, the reasons and completeness of diagnosis codes were not assessed.

Bias was also possible due to unobserved factors, such as knowledge or perceptions among prescribers to the use of PIM, which were not studied or logistic regression could not adjust for all potential confounding effects. The unit of analysis in inferential statistic is outpatient prescriptions that there might be the issue of multiplicity, which is a multiple count of PIM in participants' prescriptions. This could affect the significance and 95% confidential interval in the study result.

Ultimately, this study could not examine the cause-effect relationship between associated factors use and PIM use because it is a cross-sectional study that cannot prove whether all participants adhere to use their prescribed medication. In addition, this study was conducted in a district hospital that the result cannot be generalized to other district hospitals or different type of hospital.

5.2 Conclusion

This study is the first study of prevalence of and factors associated with PIM prescriptions measured by Beers criteria 2012 among the elderly outpatients at a district hospital in the south of Thailand. The retrospective data of outpatient prescriptions and administrative database of all prescribers in outpatient department across the fiscal years 2012 (October 1, 2011-September 30, 2012) were retrieved and analysed. 430 out of 5,265 elderly outpatients were systematically randomized sampled with their 2,128 outpatient prescriptions across the study year. To sum up, The overall prevalence of PIM was 28.1 per cent of all outpatient prescriptions or 49.81 per cent of all patients who had at least 1 PIM prescription. Number of medications and outpatient visits were likely to have a significant association with the presence of PIM, as well as, patient's age had a likelihood of significant association with the presence of PIM.

5.3 Recommendation

5.3.1 Research recommendation

For further studies, adverse effects associated with PIM should be measured by tools.

Alternative drugs used in any therapeutic categories or specific pharmacological class of medications, such as, Benzodiazepines, Non-COX-NSAIDs, and Cardiovascular drugs should be studied. The list of alternative safer drugs should be then made ready available to the prescribers in order to reduce the frequency of PIM. The developed PIM screening tool must be valid, specific and clinically applicable and it must state explicitly the alternative medication that provides cost-benefit to prescribe it instead of giving PIM.

Both explicit and implicit criteria in assessing PIM should be used in further studies. Comparative studies of effectiveness among the tools used in Thai hospitals should be evaluated, including appropriateness, validity and specificity. The other PIM screening tools--STOPP, IPET, MAI and a country-specific criteria developed by Ploylueamsang et al.--should be compared each other.

Additionally, qualitative studies are strongly recommended in order to gain more understandings about knowledge, perception, or attitudes of prescribers in prescribing PIM to the old patients.

5.3.2 Programmatic recommendation

In the light of the results of the above studies, then, country-specific criteria in assessing PIM should be developed in order to properly measure PIM prescription. Among these criteria, priority should be given to Specific-disease criteria, in particular central nervous system drugs and Benzodiazepines.

To assess PIM prescribing effectively, besides that, the accuracy, relevancy and completeness of ICD-10 in dataset is a major concern. To achieve completeness and correctness, a blockage of the of data entry should be introduced so that the prescribers cannot enter the medications if they have not previously entered the ICD codes or if they have entered the inappropriate ICD code for a given medication.

Because many prescribers are involved in outpatient prescriptions , the validity and completeness of information in outpatients 'prescriptions should be regularly audited by experts, as it already happened in inpatients prescriptions.

Eventually, rationale drug use in elderly outpatients must be become a concern for all prescribers and evaluate the benefit to risk before prescribing PIM in order to not rather bring those elderly patients into the risks than benefits.

REFERENCES

- Buck, M. et al. (2009). Potentially Inappropriate Medication Prescribing in Outpatient Practices: Prevalence and Patient Characteristics Based on Electronic Health Record. *The American Journal of Geriatric Pharmacotherapy*7(2): 84-92.
- Bumgartner, D. (2008). *Polypharmacy and Drug Interactions in Elderly In-and Outpatients*. Doktor der gesamten Heilkunde, Medizinischen Universität Graz, Austria.
- Chen, Y. C. et al. (2009). Potentially inappropriate medication for emergency department visits by elderly patients in Taiwan. *Pharmacoepidemiol Drug Saf* 18(1): 53-61.
- Chunharas, S. et al. (2011). *Situation of the Thai Elderly 2010*. Foundation of Gerontology Research and Development Institute.
- Dong, H. J., Bogg, L., Rehnberg, C., & Diwan, C. V. (1999). Health financing policies - Providers' opinions and prescribing behavior in rural China. *International Journal of Technology Assessment in Health Care*. 15(4): 686-698.
- Farzandipour, M., Sheikhtaheri, A., & Sadoughi, F. (2010). Effective factors on accuracy of principal diagnosis coding based on International Classification of Diseases, the 10th revision (ICD-10). *International Journal of Information Management*. 30(1): 78-84.
- Fick, D. M., Mion, L. C., Beers, M. H., and Jennifer, L. W. (2008). Health outcomes associated with potentially inappropriate medication use in older adults. *Res Nurs Health* 31(1): 42-51.
- Fulton, M. M., and Allen, E. R. (2006). Polypharmacy in the Elderly: A Literature Review. *Journal of the American of Nurse Practitioners* 17(4): 123-131.
- Gallagher, P. F., Barry, P. J., Ryan, C., Hartigan, I., and O'Mahony, D. (2008). Inappropriate prescribing in an acutely ill population of elderly patients as determined by Beers' Criteria. *Age Ageing* 37(1): 96-101.
- Goulding, M. (2004). Inappropriate medication prescribing for elderly ambulatory care patients. *Archives of Internal Medicine*164(3): 305-312.

- Guaraldo, L., Cano, F. G., Damasceno, G. S., and Rozenfeld, S. (2011). Inappropriate medication use among the elderly: a systematic review of administrative databases. [Review]. *BMC Geriatr* 11: 79.
- Hepler., C. D., and Strand, L. M. (1990). Opportunities and responsibilities in Pharmaceutical care. *American Journal Hospital Pharmacy* 47: 533-543.
- Hughes, S. G. (1998). Prescribing for the elderly patient: why do we need to exercise caution?. *British Journal Clinical Pharmacology* 46: 531-533.
- Lai, H. Y. et al. (2009). Prevalence of the prescribing of potentially inappropriate medications at ambulatory care visits by elderly patients covered by the Taiwanese National Health Insurance program. *Clin Ther* 31(8): 1859-1870.
- Maiorino, V., Del Canale, S., and Abouzaid, S. (2010). Using explicit criteria to evaluate the quality of prescribing in elderly Italian outpatients: a cohort study. *J Clin Pharm Ther* 35(2): 219-229.
- Marcum, Z. A., and Hanlon, J. T. (2012). Commentary on the new American Geriatric Society Beers criteria for potentially inappropriate medication use in older adults. [Research Support, N.I.H., Extramural]. *Am J Geriatr Pharmacother* 10(2): 151-159.
- Ministry of Social Development and Human Security. (2003). *The Act on Older Persons B.E. 2546 (2003A.D.)*. Retrieved from http://www.oppo.opp.go.th/info/pororborENG_2003.pdf.
- National Institute of Aging and Health. (2011). *Global Health and Aging*. World Health Organization.
- Naughton, C., Drennan, J., Hyde, A., Allen, D., O'Boyle, K., Felle, P., & Butler, M. (2013). *An evaluation of the appropriateness and safety of nurse and midwife prescribing in Ireland*. [Research Support, Non-U.S. Gov't]. *J Adv Nurs*, 69(7): 1478-1488.
- Orimo, H. et al. (2006). Reviewing the definition of "elderly". *Geriatrics and Gerontology International* 6(3): 149-158.
- Page II, R. L., Linnebur, S. A., Bryant, L. L., and Ruscini, J. M. (2010). Inappropriate prescribing in the hospitalized elderly patient: Defining the problem, evaluation, tools, and possible solutions. *Clinical Interventions in Aging* 5: 75-87.

- Ploylueamsang, C. et al. (2012). *QUM2.2: Development of medicine list for screening and reducing medication-related problems in Thai elderly. (Minute)*. Quality Use of Medicine Project, Health System Research Institution. (Unpublished Manuscript)
- Rigler, S., Perera, S., Jachna, C., Shireman, T., and Eng, M. (2004). Comparison of Association Between Disease Burden and Inappropriate Medication Use Across Three Cohorts of Older Adults. *The American Journal of Geriatric Pharmacotherapy* 2: 239-247.
- Ryan, C., O'Mahony, D., Kennedy, J., Weedle, P., Barry, P., Gallagher, P., & Byrne, S. (2009). Appropriate prescribing in the elderly: an investigation of two screening tools, Beers criteria considering diagnosis and independent of diagnosis and improved prescribing in the elderly tool to identify inappropriate use of medicines in the elderly in primary care in Ireland. [Comparative Study]. *J Clin Pharm Ther* 34(4): 369-376.
- Sakuma, M. et al. (2011). Epidemiology of potentially inappropriate medication use in elderly patients in Japanese acute care hospitals. *Pharmacoepidemiol Drug Saf* 20(4): 386-392.
- Sakunpanich, T. (2011). Performance of Health Care for elderly and impact on Public Health Care Financing during 2011-2022. Health System Research Institutions.
- Simonson, W., and Feinberg, J. L. (2005). Medication-Related Problems in the Elderly. *Drugs Aging* 22(7): 559-569.
- Tharvornwattanayong, W., Anothayanon, J., Reungsakul, N., Sriphiromrak, P., and Chomjan, R. (2011). High-risk Medications use in Thai Elderly Patients: Case study in Wangtaku, Nakhon Pathom. *Journal of Health Systems Research* 5(2): 187-194.
- The American Geriatrics Society, (2012). American Geriatrics Society updated Beers Criteria for potentially inappropriate medication use in older adults. *J Am Geriatr Soc* 60(4): 616-631.
- Tamblyn, R. (1996). Medication use in seniors: Challenges and solutions [Review]. *Therapie* 51(3): 269-282.

- Viswanathan., H., Bharmal., M., and Joseph, T. (2005). Prevalence and Correlates of Potentially Inappropriate Prescribing Among Ambulatory Older Patients in the Year 2001: Comparison of Three Explicit Criteria. *Clinical Therapeutics* 27(1): 88-99.
- Winit-Watjana, W., Sakulrat, P., and Kespichayawattana, J. (2008). Criteria for high-risk medication use in Thai older patients. *Arch Gerontol Geriatr* 47(1): 35-51.
- World Health Organization. Definition of an older or elderly person [Online]. 1997. Available from : <http://www.who.int/healthinfo/survey/ageingdefnolder/en/index.html> [2012, June 24]

APPENDICES

Appendix A

Unconditionally list of potentially inappropriate medication for older adults in 2012 Beers criteria) and its categories by National List of Essential Medicine. *

No.	Unconditional list of PIM	FDA approval in Thailand	Classifications in National List of Essential Medicine (NLEM)	Available item in the study hospital formulary	Available prescribed item in the study dataset
1	Alprazolam	Yes	Essential Drug(ED)	Yes	Yes
2	Amiodarone	Yes	Essential Drug(ED)	Yes	No
3	Amitriptyline	Yes	Essential Drug(ED)	Yes	Yes
4	Amobarbital	No	Not available	No	No
5	Aripiprazole	Yes	Not available	No	No
6	Asenapine	No	Not available	No	No
7	Aspirin >325 mg/day	Yes	Essential Drug(ED)	No	No
8	Belladonna alkaloids	Yes	Non Essential Drug (NED)	No	No
9	Benzatropine (oral)	Yes	Not available	No	No
10	Brompheniramine	Yes	Essential Drug(ED)	No	No
11	Butabarbital	No	Not available	No	No
12	Butalbital	No	Not available	No	No
13	Carbinoxamine	Yes	Non Essential Drug (NED)	No	No
14	Carisoprodol	Yes	Not available	No	No
15	Chloral hydrate	Yes	Essential Drug(ED)	Yes	No
16	Chlordiazepoxide	Yes	Not available	No	No
17	Chlordiazepoxide-amitriptyline	Yes	Essential Drug(ED)	No	No
18	Chlordiazepoxide-amitriptyline	Yes	Essential Drug(ED)	No	No
19	Chlorpheniramine	Yes	Essential Drug(ED)	Yes	Yes

Unconditionally list of potentially inappropriate medication for older adults in 2012 Beers criteria) and its categories by National List of Essential Medicine.

(continued)

No.	Unconditional list of PIM	FDA approval in Thailand	Classifications in National List of Essential Medicine (NLEM)	Available item in the study hospital formulary	Available prescribed item in the study dataset
20	Chlorpromazine	Yes	Not available	No	No
21	Chlorpropamide	Yes	Essential Drug(ED)	No	No
22	Chlorzoxazone	Yes	Not available	No	No
23	Clemastine	Yes	Not available	No	No
24	Clidinium-chlordiazepoxide	Yes	Non Essential Drug (NED)	No	No
25	Clomipramine	Yes	Essential Drug(ED)	No	No
26	Clonazepam	Yes	Essential Drug(ED)	Yes	Yes
27	Clonidine	Yes	Essential Drug(ED)	No	No
28	Clorazepate dipotassium	Yes	Non Essential Drug (NED)	Yes	Yes
29	Clozapine	Yes	Not available	No	No
30	Cyclobenzaprine	No	Not available	No	No
31	Cyproheptadine	Yes	Essential Drug(ED)	No	No
32	Desiccated thyroid	No	Not available	No	No
33	Dexbrompheniramine	No	Not available	No	No
34	Dexchlorpheniramine	Yes	Not available	No	No
35	Diazepam	Yes	Essential Drug(ED)	Yes	Yes
36	Diclofenac	Yes	Essential Drug(ED)	Yes	Yes
37	Dicyclomine	Yes	Essential Drug(ED)	No	No
38	Diflunisal	Yes	Non Essential Drug (NED)	No	No
39	Digoxin >0.125 mg/day	Yes	Essential Drug(ED)	Yes	Yes
40	Diphenhydramine (oral)	Yes	Essential Drug(ED)	No	No

Unconditionally list of potentially inappropriate medication for older adults in 2012 Beers criteria) and its categories by National List of Essential Medicine.

(continued)

No.	Unconditional list of PIM	FDA approval in Thailand	Classifications in National List of Essential Medicine (NLEM)	Available item in the study hospital formulary	Available prescribed item in the study dataset
41	Dipyridamole, oral short-acting (does not apply to the extended-release combination with aspirin)	Yes	Non Essential Drug (NED)	No	No
42	Disopyramide	No	Not available	No	No
43	Dofetilide	No	Not available	No	No
44	Doxazosin	Yes	Essential Drug(ED)	Yes	Yes
45	Doxepin >6 mg/day	Yes	Non Essential Drug (NED)	No	No
46	Doxylamine	Yes	Not available	No	No
47	Dronedarone	No	Not available	No	No
48	Ergot mesylates	No	Not available	No	No
49	Estazolam	No	Not available	No	No
50	Estrogens with or without progestins	Yes	Essential Drug(ED)	No	No
51	Eszopiclone	No	Not available	No	No
52	Etodolac	Yes	Not available	No	No
53	Fenoprofen	No	Not available	No	No
54	Flecainide	Yes	Essential Drug(ED)	No	No
55	Fluphenazine	Yes	Essential Drug(ED)	Yes	No
56	Flurazepam	Yes	Not available	No	No
57	Glyburide	No	Not available	No	No
58	Growth hormone	Yes	Non Essential Drug (NED)	No	No
59	Guanabenz	No	Not available	No	No
60	Guanfacine	No	Not available	No	No

Unconditionally list of potentially inappropriate medication for older adults in 2012 Beers criteria) and its categories by National List of Essential Medicine.

(continued)

No.	Unconditional list of PIM	FDA approval in Thailand	Classifications in National List of Essential Medicine (NLEM)	Available item in the study hospital formulary	Available prescribed item in the study dataset
61	Haloperidol	Yes	Essential Drug(ED)	Yes	No
62	Hydroxyzine	Yes	Essential Drug(ED)	Yes	Yes
63	Hyoscyamine	Yes	Essential Drug(ED)	No	No
64	Ibuprofen	Yes	Essential Drug(ED)	Yes	Yes
65	Ibutilide	No	Not available	No	No
66	Iloperidone	No	Not available	No	No
67	Imipramine	Yes	Essential Drug(ED)	Yes	Yes
68	Indomethacin	Yes	Essential Drug(ED)	No	No
69	Insulin, sliding scale	No	Not available	No	No
70	Isoxsuprine	No	Not available	No	No
71	Ketoprofen	Yes	Non Essential Drug (NED)	No	No
72	Ketorolac, includes parenteral	Yes	Not available	No	No
73	Lorazepam	Yes	Essential Drug(ED)	Yes	Yes
74	Loxapine	No	Not available	No	No
75	Lurasidone	No	Not available	No	No
76	Meclofenamate	No	Not available	No	No
77	Mefenamic acid	Yes	Non Essential Drug (NED)	Yes	Yes
78	Megestrol	Yes	Essential Drug(ED)	No	No
79	Meloxicam	Yes	Non Essential Drug (NED)	No	No
80	Meperidine	Yes	Essential Drug(ED)	No	No

Unconditionally list of potentially inappropriate medication for older adults in 2012 Beers criteria) and its categories by National List of Essential Medicine.

(continued)

No.	Unconditional list of PIM	FDA approval in Thailand	Classifications in National List of Essential Medicine (NLEM)	Available item in the study hospital formulary	Available prescribed item in the study dataset
81	Mephobarbital	No	Not available	No	No
82	Meprobamate	No	Not available	No	No
83	Mesoridazine	No	Not available	No	No
84	Metaxalone	No	Not available	No	No
85	Methocarbamol	No	Not available	No	No
86	Methyldopa	Yes	Essential Drug(ED)	Yes	Yes
87	Methyltestosterone	Yes	Non Essential Drug (NED)	No	No
88	Metoclopramide	Yes	Essential Drug(ED)	Yes	Yes
89	Mineral oil, oral	Yes	Essential Drug(ED)	No	No
90	Molindone	No	Not available	No	No
91	Nabumetone	Yes	Not available	No	No
92	Naproxen	Yes	Essential Drug(ED)	No	No
93	Nifedipine, immediate release	Yes	Non Essential Drug (NED)	No	No
94	Nitrofurantoin	Yes	Essential Drug(ED)	No	No
95	Olanzapine	Yes	Not available	No	No
96	Orphenadrine	Yes	Non Essential Drug (NED)	No	No
97	Oxaprozin	Yes	Not available	No	No
98	Oxazepam	No	Not available	No	No
99	Paliperidone	No	Not available	No	No
100	Pentazocine	Yes	Not available	No	No

Unconditionally list of potentially inappropriate medication for older adults in 2012 Beers criteria) and its categories by National List of Essential Medicine.

(continued)

No.	Unconditional list of PIM	FDA approval in Thailand	Classifications in National List of Essential Medicine (NLEM)	Available item in the study hospital formulary	Available prescribed item in the study dataset
101	Pentobarbital	Yes	Not available	No	No
102	Perphenazine	Yes	Essential Drug(ED)	Yes	No
103	Perphenazine-amitriptyline	Yes	Essential Drug(ED)	No	No
104	Phenobarbital	Yes	Essential Drug(ED)	Yes	No
105	Pimozide	Yes	Not available	No	No
106	Piroxicam	Yes	Essential Drug(ED)	No	No
107	Prazosin	Yes	Essential Drug(ED)	No	No
108	Procainamide	Yes	Not available	No	No
109	Promazine	No	Not available	No	No
110	Promethazine	Yes	Not available	No	No
111	Propafenone	Yes	Essential Drug(ED)	No	No
112	Propantheline	No	Not available	No	No
113	Quazepam	No	Not available	No	No
114	Quetiapine	Yes	Not available	No	No
115	Quinidine	Yes	Not available	No	No
116	Reserpine (>0.1 mg/day)	Yes	Not available	No	No
117	Risperidone	Yes	Not available	No	No
118	Scopolamine	No	Not available	No	No
119	Secobarbital	No	Not available	No	No
120	Sotalol	Yes	Not available	No	No

Unconditionally list of potentially inappropriate medication for older adults in 2012 Beers criteria) and its categories by National List of Essential Medicine.

(continued)

No.	Unconditional list of PIM	FDA approval in Thailand	Classifications in National List of Essential Medicine (NLEM)	Available item in the study hospital formulary	Available prescribed item in the study dataset
121	Spironolactone >25 mg/day	Yes	Essential Drug(ED)	Yes	Yes
122	Sulindac	Yes	Non Essential Drug (NED)	No	No
123	Temazepam	Yes	Non Essential Drug (NED)	No	No
124	Terazosin	Yes	Non Essential Drug (NED)	No	No
125	Testosterone	Yes	Non Essential Drug (NED)	No	No
126	Thioridazine	Yes	Essential Drug(ED)	Yes	Yes
127	Thiothixene	Yes	Not available	No	No
128	Ticlopidine	Yes	Essential Drug(ED)	No	No
129	Tolmetin	No	Not available	No	No
130	Triazolam	Yes	Not available	No	No
131	Trifluoperazine	Yes	Not available	No	No
132	Triflupromazine	No	Not available	No	No
133	Trihexyphenidyl	Yes	Essential Drug(ED)	Yes	Yes
134	Trimethobenzamide	No	Not available	No	No
135	Trimipramine	No	Not available	No	No
136	Tripolidine	Yes	Non Essential Drug (NED)	No	No
137	Zaleplon	No	Not available	No	No
138	Ziprasidone	Yes	Not available	No	No
139	Zolpidem	Yes	Non Essential Drug (NED)	No	No

**Out of 139 PIMs with unconditional, 97 items are available by Thai FDA approval, Of those 97 items, 47 items are ED and 20 items are NED, while, the rest of 30 items are not available in NLEM. 25 out of 67 items in NLEM were used in the study hospital but 19 out of 25 items were observed in the study prescriptions.*

Appendix B

Rationale of available potentially inappropriate medications in 2012 Beers criteria for older adults in the study hospital.

Organ System/ Therapeutic category/ Drug(s)	Rationale
<i>Anticholinergics (excludes TCAs)</i>	
<p>First-generation antihistamines (as single agent or as part of combination products)</p> <ul style="list-style-type: none"> • Chlorpheniramine • Hydroxyzine 	<p>Highly anticholinergic; clearance reduced with advanced age, and tolerance develops when used as hypnotic; increased risk of confusion, dry mouth, constipation, and other anticholinergic effects/toxicity.</p>
<p>Antiparkinson agents</p> <ul style="list-style-type: none"> • Trihexyphenidyl 	<p>Not recommended for prevention of extrapyramidal symptoms with antipsychotics; more effective agents available for treatment of Parkinson disease.</p>
<i>Cardiovascular</i>	
<p>Alpha1 blockers</p> <ul style="list-style-type: none"> • Doxazosin 	<p>High risk of orthostatic hypotension; not recommended as routine treatment for hypertension; alternative agents have superior risk/benefit profile.</p>
<p>Alpha blockers, central</p> <ul style="list-style-type: none"> • Methyldopa 	<p>High risk of adverse CNS effects; may cause bradycardia and orthostatic</p>

	hypotension; not recommended as routine treatment for hypertension
<p>Antiarrhythmic drugs (Class Ia, Ic, III)</p> <ul style="list-style-type: none"> • Amiodarone 	<p>Data suggest that rate control yields better balance of benefits and harms than rhythm control for most older adults.</p> <p>Amiodarone is associated with multiple toxicities, including thyroid disease, pulmonary disorders, and QT interval prolongation.</p>
<ul style="list-style-type: none"> • Digoxin >0.125 mg/day 	<p>In heart failure, higher dosages associated with no additional benefit and may increase risk of toxicity; decreased renal clearance may lead to increased risk of toxic effects.</p>
<ul style="list-style-type: none"> • Spironolactone >25 mg/day 	<p>In heart failure, the risk of hyperkalemia is higher in older adults if taking >25 mg/day or taking concomitant NSAID, ACEI, ARB, or potassium supplement.</p>
<i>Central Nervous System</i>	
<p>Tertiary TCAs, alone or in combination:</p> <ul style="list-style-type: none"> • Amitriptyline • Imipramine 	<p>Highly anticholinergic, sedating, and cause orthostatic hypotension.</p>

<p>Antipsychotics, first- (conventional) and second- (atypical) generation</p> <p>First-Generation (Conventional) Agents</p> <ul style="list-style-type: none"> • Fluphenazine • Haloperidol • Perphenazine 	<p>Increased risk of cerebrovascular accident (stroke) and mortality in persons with dementia.</p>
<ul style="list-style-type: none"> • Thioridazine 	<p>Highly anticholinergic and greater risk of QT-interval prolongation.</p>
<p>Barbiturates</p> <ul style="list-style-type: none"> • Phenobarbital 	<p>High rate of physical dependence; tolerance to sleep benefits; greater risk of overdose at low dosages.</p>
<p>Benzodiazepines</p> <p><i>Short- and intermediate-acting:</i></p> <ul style="list-style-type: none"> • Alprazolam • Lorazepam <p><i>Long-acting:</i></p> <ul style="list-style-type: none"> • Clorazepate • Clonazepam • Diazepam 	<p>Older adults have increased sensitivity to benzodiazepines and decreased metabolism of long-acting agents. In general, all benzodiazepines increase risk of cognitive impairment, delirium, falls, fractures, and motor vehicle accidents in older adults.</p> <p>May be appropriate for seizure disorders, rapid eye movement sleep disorders, benzodiazepine withdrawal, ethanol withdrawal, severe generalized anxiety disorder, periprocedural anesthesia, end-of-life care.</p>
<p>Chloral hydrate</p>	<p>Tolerance occurs within 10 days and risk outweighs the benefits in light of overdose with doses only 3 times the recommended dose.</p>

<i>Gastrointestinal</i>	
Metoclopramide	Can cause extrapyramidal effects including tardive dyskinesia; risk may be further increased in frail older adults.
<i>Pain Medications</i>	
<p>Non-COX-selective NSAIDs, oral</p> <ul style="list-style-type: none"> • Diclofenac • Ibuprofen • Mefenamic acid 	<p>Increases risk of GI bleeding/peptic ulcer disease in high-risk groups, including those >75 years old or taking oral or parenteral corticosteroids, anticoagulants, or antiplatelet agents.</p> <p>Use of proton pump inhibitor or misoprostol reduces but does not eliminate risk. Upper GI ulcers, gross bleeding, or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3–6 months, and in about 2%–4% of patients treated for 1 year. These trends continue with longer duration of use.</p>
<p><i>Abbreviations:</i> ACEI, angiotensin converting-enzyme inhibitors; ARB, angiotensin receptor blockers; CNS, central nervous system; COX, cyclooxygenase; CrCl, creatinine clearance; GI, gastrointestinal; NSAIDs, nonsteroidal anti-inflammatory drugs; SIADH, syndrome of inappropriate antidiuretic hormone secretion; TCAs, tricyclic antidepressants</p>	

Appendix C

Potentially Inappropriate medication with the classified indications--Beers' therapeutic indication and potentially clinical used indication

PIM	ICD-10 codes by Beers' therapeutic indication	ICD-10 codes by Potentially clinical used indication
CHLORPHENIRAMINE	Acute conjunctivitis\, unspecified	Allergy\, unspecified
	Acute pharyngitis\, unspecified	Injury of conjunctiva and corneal abrasion without mention of foreign body
	Acute upper respiratory infection\, unspecified	
	Acute nasopharyngitis [common cold]	
	Allergic urticaria	
AMITRIPTYLINE	Anxiety disorder\, unspecified	Retained dental root
	Nonorganic sleep disorders	Gonarthrosis\, unspecified
	Nonorganic sleep disorder\, unspecified	Spondylolisthesis Thoracolumbar region
	Migraine\, unspecified	Spondylosis unspecified Lumbosacral region
	Tension-type headache	Low back pain Thoracolumbar region
	Carpal tunnel syndrome	Muscle strain Pelvic region and thigh
		Impingement syndrme of shoulder
		Dizziness and giddiness
DIPOTASSIUMCLORAZEPATE	Anxiety disorder, unspecified	Headache\, unspecified
	Nonorganic sleep disorders	Palpitations
	Nonorganic insomnia	Dyspnoea
	Nonorganic sleep disorder, unspecified	Dizziness and giddiness
		Headache, unspecified (TM)
DIAZEPAM	Alcohol acute intoxication	Malaise and fatigue
	Nonorganic sleep disorder, unspecified	Chronic obstructive pulmonary disease with acute exacerbation, unspecified
	Status epilepticus, unspecified	Retained dental root
DICLOFENAC	Gout	Malaise and fatigue
		Other and unspecified gastroenteritis and colitis of infectious origin

Arthritis\, unspecified Shoulder region	Tinea cruris
Arthritis\, unspecified Ankle and foot	Tension-type headache,Tension headache
Primary gonarthrosis\, bilateral	Transient cerebral ischaemic attack, unspecified
Gonarthrosis\, unspecified	Carpal tunnel syndrome,CTS
Infantile idiopathic scoliosis Lumbar region	Cataract, unspecified
Spondylosis unspecified Lumbar region	Acute pharyngitis, unspecified
Spinal stenosis Lumbosacral region	Chronic rhinitis
Low back pain	Loss of teeth due to accident, extraction or local periodontal disease
Low back pain Multiple sites in spine	Cellulitis, unspecified
Low back pain Thoracolumbar region	Urinary calculus, unspecified
Low back pain Lumbar region	Acute cystitis
Low back pain Site unspecified	Cough
Dorsalgia\, unspecified Lumbosacral region	Pelvic and perineal pain
Muscle strain	Abdominal pain, unspecified
Muscle strain Multiple sites	Dizziness and giddiness
Muscle strain Shoulder region	Headache, unspecified (TM)
Muscle strain Pelvic region and thigh	Fall
Muscle strain Other	Dental examination
Muscle strain Site unspecified	Follow-up examination after unspecified treatment for other conditions
Medial epicondylitis	Attention to surgical dressings and sutures
Myalgia	Medical care, unspecified
Myalgia Shoulder region	
Myalgia Site unspecified	
Pain in limb	
Osteomyelitis	
Osteochondritis dissecans	
Chondrocostal junction syndrome [Tietze]	
Chondrocostal junction syndrome [Tietze] Site unspecified	
Acquired deformity of neck	

DICLOFENAC	Contusion of breast	
	Sprain and strain of other and unspecified parts of thorax	
	Superficial injury of unspecified body region	
	Open wound of unspecified body region	
DIGOXIN	Essential (primary) hypertension	
	Atrial fibrillation and flutter	
	Heart failure, unspecified	
IBUPROFEN	Idiopathic gout	Migraine\, unspecified
	Idiopathic gout Ankle and foot	Tension-type headache
	Arthritis\, unspecified Ankle and foot	Acute serous otitis media
	Gonarthrosis\, unspecified	Nonsuppurative otitis media\, unspecified
	Haemarthrosis Lower leg	Acute pharyngitis due to other specified organisms
	Stiffness of joint\, not elsewhere classified Multiple sites	Acute pharyngitis\, unspecified
	Infantile idiopathic scoliosis Lumbar region	Acute tonsillitis\, unspecified
	Spondylosis unspecified Lumbosacral region	Acute bronchitis\, unspecified
	Low back pain Lumbar region	Pulpitis
	Low back pain Lumbosacral region	Chronic apical periodontitis
	Muscle strain Multiple sites	Periapical abscess without sinus
	Muscle strain Shoulder region	Chronic periodontitis
	Muscle strain Site unspecified	Other specified diseases of jaws
	Gluteal tendinitis Ankle and foot	Cellulitis\, unspecified
	Medial epicondylitis Shoulder region	Acute lymphadenitis\, unspecified
	Myalgia Site unspecified	Hyperplasia of prostate
	Pain in limb	Orchitis\, epididymitis and epididymo-orchitis without abscess
	Pain in limb Shoulder region	Dizziness and giddiness
	Chondrocostal junction syndrome [Tietze] Multiple sites	Headache\, unspecified
	Open wound of other parts of foot	Follow-up examination after unspecified treatment for other conditions
	Superficial injury of unspecified body region	Prophylactic surgery\, unspecified
		Attention to surgical dressings and sutures
		Medical care\, unspecified

LORAZEPAM	Mental and behavioural disorders due to use of alcohol at dependence syndrome	Essential (primary) hypertension
	Schizophrenia\,unspecified\,continuous (including treatment resistant)	Unstable angina
	Anxiety disorder\, unspecified	Chronic ischaemic heart disease\, unspecified
	Nonorganic sleep disorders	Endocarditis\,valve disorders in diseases classified elsewhere
	Nonorganic insomnia	Palpitations
	Nonorganic sleep disorder\, unspecified	Dizziness and giddiness
	Sleep disorder\, unspecified	Headache, unspecified (TM)
	Idiopathic peripheral autonomic neuropathy	Malaise and fatigue
	Follow-up examination after combined treatment for other conditions	
MEFENAMICACID	Pelvic and perineal pain	
SPIRONOLACTONE		Non-insulin-dependent diabetes mellitus type 2 at without complications
DOXAZOSIN	Essential (primary) hypertension	Hyperplasia of prostate
		Headache, unspecified (TM)
		Medical care\, unspecified
		Issue of repeat prescription
TRIHEXYPHENIDYL	Malaise and fatigue	
HYDROXYZINE	Entropion and trichiasis of eyelid	Tinea cruris
	Acute conjunctivitis, unspecified	Candidiasis of vulva and vagina (N77.1*)
	Allergic contact dermatitis, unspecified cause	Nonorganic sleep disorders
	Lichen simplex chronicus	
	Dermatitis, unspecified	
IMIPRAMINE		
CLONAZEPAM	Nonorganic sleep disorder, unspecified	
	Anoxic brain damage, not elsewhere classified	
METHYLDOPA	Essential (primary) hypertension	
METOCLOPRAMIDE	Gastritis, unspecified	Diarrhoea and gastroenteritis of presumed infectious origin
	Dyspepsia	Other and unspecified gastroenteritis and colitis of infectious origin
		Gastroenteritis and colitis of unspecified origin

METOCLOPRAMIDE		Hiccough
		Abdominal pain, unspecified
		Nausea and vomiting, unspecified
		Dizziness and giddiness
ALPRAZOLAM	Nonorganic sleep disorders	Palpitations
	Nonorganic sleep disorder, unspecified	Dizziness and giddiness
	Sleep disorder, unspecified	Issue of repeat prescription
THIORIDAZINE	Schizophrenia, unspecified	

Appendix D

Template of datasheet collection with variables

	Pt_sex	Pt_age	Insure	OPrx_dat	OPrx_no	OP_pdx	OP_sdx_1_5	Med code1_20	Prescribe	Presc_type	Presc_sex	Presc_age	Presc_wkyer	AN	IP_date	OPvis_count	Hosp_freq	Med_count	PIM	PIM1_5	Dx1_5
HN																					
<p>Abbreviations: HN = Hospital Number Pt_sex= Sex of patient (male or female) Pt_age= Age of patient Insure = Insurance code OPrx_date = Outpatient_Principal diagnosis OPrx_no = Prescription no. OP_pdx = Outpatient_Primary diagnosis OP_sdx1_5 = Outpatient_Secondary diagnosis (maximum 5 fields) Medcode1_20 = Outpatient medication (maximum 20 fields) Prescriber = Code of prescriber who prescribed outpatient medication Presc_type = Code of prescriber's type who prescribed outpatient medication Presc_sex = Prescriber sex (male or female) Presc_age = Prescriber's age Presc_wkyr = Prescriber's years of work AN = Admission Number IP_date = Inpatient Admission date OPvis_count = Number of outpatient visits Hosp_freq = Number of inpatient admissions Med_count = Number of medications per prescription PIM = Presence of PIM PIM1_5= PIM code (maximum 5 items) DX1_5= Matched-diagnosis codes to PIM (maximum 5 items)</p>																					

Appendix E

Information Sheet for Hospital Director

Title of Project: Prevalence of Potentially Inappropriate Medication (PIM) and Factors Associated with PIM Elderly Outpatient Prescriptions at a District Hospital in the Southern Region of Thailand.

Student Investigators: Mr. Tanavij Pannoi

Contact Information: 26/72 Porkhunthale 17/1, Makamtia District, Mueang, Surat-Thani, 84000, Thailand, Tel: +6681-979-610-9, +6677-405-026, E-mail: joob103@gmail.com

1. You are invited to participate in this study. It is essential that you should be kindly informed the brief of study information, including the rationale of study. Please look into this document deliberately and feel free to ask student investigator any unclear statements or further information.
2. *This research is a master thesis study, which is a partial fulfillment of graduation in Master of Public Health program at College of Public Health Science, Chulalongkorn University. The study aims to find the prevalence of PIM and factors associated with PIM assessed by the American Geriatric Society of Beers criteria 2012 in elderly outpatient prescription at a district hospital in the Southern Region of Thailand.*
3. *The general objective of the study is to contribute to the improvement of service quality by a more rational use of medication in elderly with no intention whatsoever to have involved physicians prosecuted and to promote “social justice” for the elderly when seeking health service in the hospital. The specific objectives of the study are (1) To know the prevalence of PIM measured by the 2012 Beers criteria among elderly outpatients at a district hospital in the south of Thailand and (2) To describe factors associated with prescribing PIM measured by the 2012 Beers criteria among elderly outpatients at a district hospital in the south of Thailand.*
4. *Information of study populations:*

- 4.1 *Study populations are elderly outpatients aged 65 years or more*
 - 4.2 *The total number of sample size is 430 elderly outpatients with a systematic randomized sampling.*
 - 4.3 *The patients' data will be retrieved from the retrospective outpatient data in electronic medical record (HOSxp), comprising of Hospital No. (HN), Age , Gender (Male/Female), Prescriber's diagnosis with regard to ICD-10 codes, Profiles of individual prescribed medication in each outpatient visits: generic name of medication, strength, frequency of administration, and date of prescription, physician's identity code who ordered each prescription, identity code of users who transcribed physician prescription (in only case of transcribed prescription), number of outpatient visits for individual outpatients in the Thai fiscal year 2012, number of admissions in inpatient department for individual outpatients in the Thai fiscal year 2012, health insurance schemes*
 - 4.4 *The physicians' information will be retrieved from the administrative databases, which are physician's identity codes, types of prescribers: General practitioner (GP) or Specialist (SP), age, gender, length of years working in career.*
5. *The lengths of study period are 7 months from the literatures review to thesis completion. It will spend 5 weeks on data collection and analyses.*
 6. *We want you to be aware of the possible risks associated with participation in this research. The researcher will take the following steps to assure anonymity of the participating hospital, prescribers and patients. These steps are of particular importance to protect the reputation of the hospital and of the prescribers in case the research findings will reveal inappropriate prescriptions. The hospital name, the patients' name with hospital number and prescribers' name with identity code will never appear in any of the research related documents. The researcher will enter the patients HN and prescriber ID in the first data set, secondly the researcher will link these two identifier numbers to a sequential research number, thirdly will make a copy of the list with identifier numbers linked to the research*

sequential number and keep this copy in a safe and separate place, fourthly the researcher will remove the identifier numbers from the initial data set and conduct all subsequent data analysis by using the research sequential number only. The separate, safely kept list linking identifier numbers to the sequential research numbers will only be used if required for data cross-checking, cleaning, and completion. At the end of the research the linking list will be eliminated.

7. *With regard to the permission of the director of the hospital, there is no need to have physicians' consent prior to collect data at the study site.*
8. The benefits of the study are to provide the preliminary data compared to other international studies and to use in developing specified country-tool for assessing PIM among Thai elderly outpatient. Your hospital could apply the result in order to develop hospital practice guideline or program for caring the elderly outpatient.
9. Your participation to the study is voluntary. There are not any impacts to your career and to any desired benefits regarding your career's promotions.
10. If you have any questions regarding the study, you can ask the student investigator any time. You will be informed immediately by the student investigator if there are further potential benefits or risks with regard to this study.
11. Assistant researcher or data collector is deemed appropriately to receive the optimal per diem, as well as, your hospital will be paid for provided data.
12. In the event that you develop any negative reactions, or are concerned that you may, please contact the student investigator at the above contact information or at **the Ethical Review Committee for Research involving Human Research Subjects, Health Science Group, Chulalongkorn University, 4th floor of Institution Building 2, Chulalongkorn 62, Payathai Road, Pathumwan, Bangkok, 10330, Tel. 0-2218-8147, 0-2218-8141, Fax. 0-2218-8147 E-mail: eccu@chula.ac.th**

เอกสารชี้แจงข้อมูลโครงการวิจัยสำหรับผู้อำนวยการโรงพยาบาล

ชื่อโครงการวิจัย ความชุกของการใช้ยาที่มีแนวโน้มไม่เหมาะสม และปัจจัยที่สัมพันธ์ต่อการใช้ยาที่มีแนวโน้มไม่เหมาะสมจากการประเมินใบสั่งยาของผู้ป่วยนอกสูงอายุ ณ โรงพยาบาลชุมชนแห่งหนึ่งทางภาคใต้ของประเทศไทย

ชื่อผู้วิจัย นายธนะวิชัย ปานน้อย **ตำแหน่ง** นิสิตปริญญาโท

สถานที่ติดต่อ(ที่ทำงาน) -

(ที่บ้าน) 26/72 ซ.พ่อบุญทะเล 17/1 ต.มะขามเตี้ย อ.เมือง จ.สุราษฎร์ธานี

โทรศัพท์ (ที่ทำงาน) -

โทรศัพท์ที่บ้าน 077-405-026

โทรศัพท์มือถือ 081-979-6109

E-mail: joob103@gmail.com

1. ขอเรียนเชิญท่านเข้าร่วมในการวิจัยก่อนที่ท่านจะตัดสินใจเข้าร่วมในการวิจัย มีความจำเป็นที่ท่านควรทำความเข้าใจว่างานวิจัยนี้ทำเพราะเหตุใด และเกี่ยวข้องกับอะไร กรุณาใช้เวลาในการอ่านข้อมูลต่อไปนี้อย่างละเอียดรอบคอบ และสอบถามข้อมูลเพิ่มเติมหรือข้อมูลที่ไม่ชัดเจนได้ตลอดเวลา
2. โครงการนี้เป็นการศึกษาวิจัยซึ่งเป็นวิทยานิพนธ์ก่อนจบการศึกษาระดับปริญญาโท สาขาวิชาสาธารณสุขศาสตร์ (หลักสูตรนานาชาติ) ของวิทยาลัยวิทยาศาสตร์สาธารณสุข จุฬาลงกรณ์มหาวิทยาลัย เกี่ยวกับความชุกของการใช้ยาที่มีแนวโน้มไม่เหมาะสม และปัจจัยที่สัมพันธ์ต่อการใช้ยาที่มีแนวโน้มไม่เหมาะสมดังกล่าวในผู้ป่วยสูงอายุ โดยประเมินจากใบสั่งยาผู้ป่วยนอกสูงอายุ ณ โรงพยาบาลแห่งหนึ่งทางภาคใต้ของประเทศไทย โดยใช้ Beers criteria 2012 เป็นแนวทางในการประเมิน
3. วัตถุประสงค์ของการวิจัย
 - 3.1 วัตถุประสงค์หลัก: เพื่อใช้ในการปรับปรุงบริการสาธารณสุขให้มีคุณภาพ โดยสนับสนุนให้เกิดการใช้ยาอย่างสมเหตุผลในผู้ป่วยสูงอายุ โดยมีได้มุ่งหมายเพื่อให้คุณให้โทษแต่ประการใดต่อผู้สั่งจ่าย ทั้งนี้เพื่อเป็นการสนับสนุนให้เกิดความเป็นธรรมทางสังคมสำหรับผู้ป่วยเมื่อใช้บริการสาธารณสุขในโรงพยาบาล
 - 3.2 วัตถุประสงค์รอง 1: เพื่อหาความชุกของการใช้ยาที่มีแนวโน้มไม่เหมาะสมผู้ป่วยสูงอายุ โดยประเมินจากใบสั่งยาผู้ป่วยนอกสูงอายุ และใช้ Beers criteria 2012 เป็นแนวทางในการประเมิน
 - 3.3 วัตถุประสงค์รอง 2: เพื่อหาความสัมพันธ์ระหว่างปัจจัยที่มีผล ต่อการใช้ยาที่มีแนวโน้มไม่เหมาะสมดังกล่าวในผู้ป่วยสูงอายุ โดยประเมินจากใบสั่งยาผู้ป่วยนอกสูงอายุ และใช้ Beers criteria 2012 เป็นแนวทางในการประเมิน
4. รายละเอียดของกลุ่มประชากรหรือผู้มีส่วนร่วมในการวิจัย
 - 4.1 ประชากรเป้าหมายในการวิจัย คือ ผู้ป่วยนอกสูงอายุตั้งแต่ 65 ปีขึ้นไป

- 4.2 จำนวนผู้เข้าร่วมการวิจัย คือ นอกสูงอายุจำนวน 430 คน ซึ่งได้จากการสุ่มอย่างเป็นระบบ
- 4.3 ข้อมูลผู้ป่วยที่ใช้ในการวิจัย คือ ข้อมูลผู้ป่วยนอกสูงอายุดังกล่าวย้อนหลังใน Electronic medical record ของผู้ป่วยนอกสูงอายุภายในปีงบประมาณพ.ศ. 2555 ประกอบด้วยข้อมูลทั่วไปของผู้ป่วย (เพศ อายุ) ข้อมูลการวินิจฉัยโรค ข้อมูลใบสั่งยาของผู้ป่วย (เฉพาะผู้ป่วยนอก) ทุกใบสั่งยาพร้อมกับข้อมูลทั่วไปของแพทย์ผู้สั่งใช้ในใบสั่งยาแต่ละใบ (เพศ อายุ ระยะเวลาทำงาน แพทย์เวชปฏิบัติทั่วไปหรือเฉพาะทาง) ข้อมูลจำนวนครั้งในการใช้บริการผู้ป่วยนอก และจำนวนครั้งการเข้ารับการรักษาประเภทผู้ป่วยในของโรงพยาบาล ข้อมูลสิทธิสวัสดิการของผู้ป่วยที่รับผิดชอบค่าใช้จ่ายเมื่อเป็นผู้ป่วยนอก โดยผู้ป่วยที่มีข้อมูลดังกล่าวไม่ครบถ้วนจะไม่ถูกใช้ในการวิจัยนี้
- 4.4 ข้อมูลแพทย์ที่ใช้ในการวิจัย คือ รหัสประจำตัวแพทย์ในโรงพยาบาล ประเภทของแพทย์ (แพทย์เวชปฏิบัติทั่วไป หรือแพทย์เฉพาะทาง) อายุ เพศ และระยะเวลาการประกอบอาชีพแพทย์หลังจบการศึกษาจนถึงปีงบประมาณ 2555
5. กระบวนการในการวิจัยจะใช้เวลาประมาณ 7 เดือน นับตั้งแต่การทบทวนวรรณกรรมจนถึงการเขียนรายงานเป็นรูปเล่มวิทยานิพนธ์ โดยใช้เวลาประมาณ 5 สัปดาห์ในการเก็บและวิเคราะห์ข้อมูล
6. ผู้วิจัยต้องการให้ท่านตระหนักว่างานวิจัยชิ้นนี้อาจมีความเสี่ยงต่อการเข้าร่วมในการวิจัยของ โรงพยาบาลและแพทย์ ดังนั้นเพื่อป้องกันความเสี่ยงที่อาจเกิดขึ้น ผู้วิจัยให้คำมั่นแก่ผู้อำนวยการ โรงพยาบาลที่จะปฏิบัติตามขั้นตอนต่อไปนี้ เพื่อรับประกันว่าข้อมูลที่เกี่ยวข้องกับชื่อผู้ป่วย ชื่อหน่วยงานของท่าน และแพทย์ในหน่วยงานท่านจะถูกเก็บรักษาเป็นความลับ ไม่มีการเผยแพร่ในรายงานหรือเอกสารอื่นใดที่เกี่ยวข้อง และเป็นขั้นตอนสำคัญในการปกป้องเกียรติยศและชื่อเสียงของโรงพยาบาลและแพทย์ในกรณีที่เกิดการวิจัยพบว่ามีแนวโน้มของใบสั่งยาที่ไม่เหมาะสมเกิดขึ้นในโรงพยาบาลของท่าน โดยในขั้นแรกผู้วิจัยจะใส่ข้อมูลเลขประจำตัวผู้ป่วย และเลขประจำตัวของแพทย์ลงในชุดข้อมูลเท่านั้น จากนั้นผู้วิจัยจะเชื่อมข้อมูลเลขประจำตัวทั้ง 2 ชุดข้อมูล และเรียงลำดับข้อมูลตามลำดับที่ชุดข้อมูลโดยลงรหัสข้อมูลสำหรับการวิจัยชิ้นนี้เท่านั้น ในขั้นตอนต่อมาผู้วิจัยจะสำเนาข้อมูลที่เรียงลำดับแล้ว และนำข้อมูลดังกล่าวแยกเก็บรักษาในสถานที่ที่ปลอดภัย จากนั้นในขั้นตอนการวิเคราะห์ข้อมูลเลขประจำตัวผู้ป่วยและแพทย์จะถูกลบจากแผ่นงาน เหลือเพียงรหัสข้อมูลสำหรับการวิจัยเท่านั้น การใช้แผ่นงานชุดแรกที่เก็บไว้ในที่ปลอดภัยนั้นจะกระทำเมื่อมีการสอบถามความถูกต้องของข้อมูล การแก้ไขข้อมูล และการตรวจสอบความสมบูรณ์ของข้อมูลเท่านั้น เมื่อเสร็จสิ้นการวิจัยนี้แล้วข้อมูลในชุดแรกจะถูกทำลายทิ้งทันที
7. ในการเก็บและทบทวนข้อมูลของ โรงพยาบาล ผู้วิจัยจะสามารถกระทำได้เมื่อได้รับการอนุมัติจากผู้อำนวยการ โรงพยาบาลเป็นลายลักษณ์อักษรเท่านั้นและถือเป็นอันสิ้นสุด โดยไม่ต้องผ่านการอนุมัติจากแพทย์อื่น ๆ ในโรงพยาบาลของท่าน
8. ผลของการศึกษาวิจัย จะเป็นข้อมูลพื้นฐานเปรียบเทียบกับข้อมูลจากประเทศอื่น ๆ ที่มีการศึกษาก่อนหน้า และใช้เป็นข้อมูลเบื้องต้นในการสร้างหรือพัฒนาเครื่องมือในการประเมินการใช้ยาที่มีแนวโน้มไม่เหมาะสม

ในผู้สูงอายุสำหรับประเทศไทยต่อไป สำหรับโรงพยาบาลของท่านอาจใช้ข้อมูลดังกล่าวในการพัฒนางานเชิงรุกที่เกี่ยวข้องการดูแลการใช้ยาในกลุ่มนี้ในผู้สูงอายุต่อไป

9. การให้ข้อมูลสำหรับการวิจัยเป็นไปโดยสมัครใจ และไม่มีผลได้ผลเสียต่อการปฏิบัติหน้าที่และประโยชน์ใดๆ ที่ท่านพึงได้รับ
10. หากท่านมีข้อสงสัยให้สอบถามเพิ่มเติมได้โดยสามารถติดต่อผู้วิจัยได้ตลอดเวลา และหากผู้วิจัยมีข้อมูลเพิ่มเติมที่เป็นประโยชน์หรือโทษเกี่ยวกับการวิจัย ผู้วิจัยจะแจ้งให้ท่านทราบอย่างรวดเร็ว
11. เจ้าหน้าที่ในโรงพยาบาลของท่านที่ช่วยในการสืบค้นข้อมูล และหน่วยงานของท่านในฐานะเจ้าของข้อมูลจะได้รับค่าตอบแทนที่เหมาะสมในการให้ข้อมูลสำหรับการศึกษานี้
12. หากท่านไม่ได้รับการปฏิบัติตามข้อมูลดังกล่าวสามารถร้องเรียนได้ที่ คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน กลุ่มสหสถาบัน ชุดที่ 1 จุฬาลงกรณ์มหาวิทยาลัย ชั้น 4 อาคารสถาบัน 2 ซอยจุฬาลงกรณ์ 62 ถนนพญาไท เขตปทุมวัน กรุงเทพฯ 10330 โทรศัพท์ 0-2218-8147 หรือ 0-2218-8141 โทรสาร 0-2218-8147E-mail: eccu@chula.ac.th

Appendix F
Hospital Director's Permission Form

Address: *(inserted hospital address)*

Date: *(inserted date)*

To the Ethical Review Committee for Research involving Human Research Subjects, Health Science Group, Chulalongkorn University.

As being the hospital director of *(inserted name of hospital)*, I have read the information presented in the information sheet for hospital director about a study being conducted by **Mr.Tanavij Pannoi**, a master student under the supervision of **College of Public Health Science at Chulalongkorn University**.

I agree to provide him with the secondary information and data, illustrated in the information sheet for hospital director, in accordance with the study of **Prevalence of Potentially Inappropriate Medication (PIM) and Factors Associated with PIM in Elderly Outpatient Prescriptions at a district hospital in the Southern Region of Thailand**.

I have been clearly informed about the study rationale, study objectives, study methodology, possible risks, and benefits regarding the study from the student investigator.

I have had the opportunity to ask any questions related to this study, to receive satisfactory answers to my questions, and any additional details I wanted.

I have received the investigator's full commitment to total confidentiality and anonymity for the information provided by the hospital in particular that the name of hospital, hospital director, physicians, and patients will not be included or in any other

way associated with the data collection and in any written reports, documents, and publications of this study.

I am aware that I may withdraw from the study without loss of any credentials or impacts with regard to my career.

I have been informed that if I have any comments or concerns resulting from my participation in this study, I may contact **the Ethical Review Committee for Research involving Human Research Subjects, Health Science Group, Chulalongkorn University, 4th floor of Institution Building 2, Chulalongkorn 62, Payathai Road, Pathumwan, Bangkok, 10330, Tel. 0-2218-8147, 0-2218-8141, Fax. 0-2218-8147 E-mail: eccu@chula.ac.th**

With full knowledge of all foregoing, I agree, of my own free will, to sign this document and I have been given a copy of information sheet for hospital director and a copy of this document.

(signed by Hospital Director)

Signature of Hospital Director

Tanavij Pannoi

Signature of Student Investigator

(signed by Witness)

Signature of Witness

หนังสือแสดงความยินยอมให้ผู้วิจัยเก็บข้อมูลเพื่อการวิจัย

ที่.....(ที่อยู่โรงพยาบาล).....

วันที่ เดือน.....พ.ศ.

เรียน คณะกรรมการจริยธรรมการวิจัยในคน กลุ่มสถาบัน ชุดที่1 จุฬาลงกรณ์มหาวิทยาลัย

ข้าพเจ้าในฐานะผู้อำนวยการ โรงพยาบาลซึ่งได้ลงนามท้ายหนังสือนี้ ขอแสดงความยินยอมให้ผู้วิจัย คือ นายธนวิษั ปานน้อย ซึ่งมีที่อยู่ปัจจุบัน คือ 26/72 ซ.พ่อขุนทะเล 17/1 ต.มะขามเตี้ย อ.เมือง จ.สุราษฎร์ธานี โทรศัพท์ 081-979-6109 เก็บข้อมูลการวิจัย เรื่อง ความชุกของการใช้ยาที่มีแนวโน้มไม่เหมาะสม และปัจจัยที่สัมพันธ์ต่อการใช้ยาที่มีแนวโน้มไม่เหมาะสมจากการประเมินใบสั่งยาของผู้ป่วยนอก สูงอายุ ณ โรงพยาบาลชุมชนแห่งหนึ่งทางภาคใต้ของประเทศไทย ในโรงพยาบาลแห่งนี้

ข้าพเจ้าได้รับทราบรายละเอียดเกี่ยวกับที่มาและวัตถุประสงค์ในการทำวิจัย รายละเอียดขั้นตอนต่างๆ ที่จะต้องปฏิบัติหรือได้รับการปฏิบัติ ความเสี่ยง/อันตราย และประโยชน์ซึ่งจะเกิดขึ้นจากการวิจัยเรื่องนี้ โดยได้อ่านรายละเอียดในเอกสารชี้แจงข้อมูลโครงการวิจัยสำหรับผู้อำนวยการโรงพยาบาลโดยตลอด และได้รับคำอธิบายจากผู้วิจัย จนเข้าใจเป็นอย่างดีแล้ว

ข้าพเจ้าจึงสมัครใจเข้าร่วมในโครงการวิจัยนี้ ตามที่ระบุไว้ในเอกสารชี้แจงข้อมูลโครงการวิจัยสำหรับผู้อำนวยการโรงพยาบาลโดยข้าพเจ้ายินยอมให้ผู้วิจัยสามารถเก็บ ทบทวน และนำข้อมูล คือ ข้อมูลผู้ป่วยนอกสูงอายุดังกล่าวย้อนหลังในฐานข้อมูลเวชระเบียนของผู้ป่วยนอกสูงอายุและฐานข้อมูลทรัพยากรบุคคลของโรงพยาบาล ภายในปีงบประมาณพ.ศ. 2555 ซึ่งประกอบด้วยข้อมูลทั่วไปของผู้ป่วย (เพศ อายุ) ข้อมูลการวินิจฉัยโรค ข้อมูลใบสั่งยาของผู้ป่วย (เฉพาะผู้ป่วยนอก) ทุกใบสั่งยา พร้อมกับข้อมูลทั่วไปของแพทย์ผู้สั่งยาในใบสั่งยาแต่ละใบ (เพศ อายุ ระยะเวลาทำงาน แพทย์เวชปฏิบัติทั่วไปหรือเฉพาะทาง) ข้อมูลจำนวนครั้งในการใช้บริการผู้ป่วยนอก และจำนวนครั้งการเข้ารับการรักษาประเภทผู้ป่วยในของโรงพยาบาล ข้อมูลสิทธิสวัสดิการของผู้ป่วยที่รับผิดชอบค่าใช้จ่ายเมื่อเป็นผู้ป่วยนอก มาใช้สำหรับการทำวิจัยในครั้งนี้

ข้าพเจ้ามีสิทธิถอนตัวออกจากการวิจัยเมื่อใดก็ได้ตามความประสงค์ โดยไม่ต้องแจ้งเหตุผล ซึ่งการถอนตัวออกจากการวิจัยนั้น จะไม่มีผลกระทบใด ๆ ต่อข้าพเจ้าทั้งสิ้น

ข้าพเจ้าได้รับคำรับรองว่า ผู้วิจัยจะปฏิบัติต่อข้าพเจ้าตามข้อมูลที่ระบุไว้ในเอกสารชี้แจงข้อมูลโครงการวิจัยสำหรับผู้อำนวยการโรงพยาบาลและข้อมูลใดๆ ที่เกี่ยวข้องกับโรงพยาบาล แพทย์ และผู้ป่วย ผู้วิจัยจะเก็บรักษาเป็นความลับ โดยจะนำเสนอข้อมูลการวิจัยเป็นภาพรวมเท่านั้น ไม่มีข้อมูลใดในการรายงานที่จะสามารถระบุถึงข้อมูลต่าง ๆ ที่กล่าวมาแล้วข้างต้น

หากข้าพเจ้าไม่ได้รับการปฏิบัติตรงตามที่ได้ระบุไว้ในเอกสารชี้แจงผู้เข้าร่วมการวิจัย ข้าพเจ้าสามารถร้องเรียนได้ที่ คณะกรรมการพิจารณาจริยธรรมการวิจัยในคน กลุ่มสถาบัน ชุดที่ 1 จุฬาลงกรณ์มหาวิทยาลัย ชั้น 4 อาคารสถาบัน 2 ซอย

จุฬาลงกรณ์ 62 ถนนพญาไท เขตปทุมวัน กรุงเทพฯ 10330 โทรศัพท์ 0-2218-8147, 0-2218-8141 โทรสาร
0-2218-8147 **E-mail: eccu@chula.ac.th**

ข้าพเจ้าได้ลงลายมือชื่อไว้เป็นสำคัญต่อหน้าพยาน ทั้งนี้ข้าพเจ้าได้รับสำเนาเอกสารชี้แจงข้อมูลโครงการวิจัยสำหรับ
ผู้อำนวยการโรงพยาบาล และสำเนาหนังสือแสดงความยินยอมเข้าร่วมการวิจัยไว้แล้ว

ลงชื่อ

.....
(.....)

ผู้วิจัยหลัก

ลงชื่อ

.....
(.....)

ผู้อำนวยการโรงพยาบาล

ลงชื่อ

.....
(.....)

พยาน

Appendix G

Ethical Certificate of Approval

AF 02-12



The Ethics Review Committee for Research Involving Human Research Subjects,
Health Science Group, Chulalongkorn University
Institute Building 2, 4 Floor, Soi Chulalongkorn 62, Phayathai Rd., Bangkok 10330, Thailand,
Tel: 0-2218-8147 Fax: 0-2218-8147 E-mail: eccu@chula.ac.th

COA No. 045/2013

Certificate of Approval

Study Title No.189.1/55 : PREVALENCE OF POTENTIALLY INAPPROPRIATE MEDICATION (PIM) AND FACTORS ASSOCIATED WITH PIM IN ELDERLY OUTPATIENT PRESCRIPTIONS AT A DISTRICT HOSPITAL IN THE SOUTHERN REGION OF THAILAND

Principal Investigator : MR.TANAVIJ PANNOI

Place of Proposed Study/Institution : College of Public Health Sciences,
Chulalongkorn University

The Ethics Review Committee for Research Involving Human Research Subjects, Health Science Group, Chulalongkorn University, Thailand, has approved constituted in accordance with the International Conference on Harmonization – Good Clinical Practice (ICH-GCP) and/or Code of Conduct in Animal Use of NRCT version 2000.

Signature:  Signature: 
(Associate Professor Prida Tusanapradit, M.D.) (Assistant Professor Dr. Nuntaree Chaichanawongsaraj)
Chairman Secretary

Date of Approval : 20 February 2013 **Approval Expire date** : 19 February 2014

The approval documents including

- 1) Research proposal
- 2) Patient/Participant Information Sheet
- 3) Researcher



Protocol No. 189.1/55
Date of Approval..... 20 FEB 2013
Approval Expire Date..... 19 FEB 2014

The approved investigator must comply with the following conditions:

1. The research/project activities must end on the approval expired date of the Ethics Review Committee for Research Involving Human Research Subjects, Health Science Group, Chulalongkorn University (ECCU). In case the research/project is unable to complete within that date, the project extension can be applied one month prior to the ECCU approval expired date.
2. Strictly conduct the research/project activities as written in the proposal.
3. Using only the documents that bearing the ECCU's seal of approval with the subjects/volunteers (including subject information sheet, consent form, invitation letter for project/research participation (if available)).
4. Report to the ECCU for any serious adverse events within 5 working days
5. Report to the ECCU for any change of the research/project activities prior to conduct the activities.
6. Final report (AF 03-12) and abstract is required for a one year (or less) research/project and report within 30 days after the completion of the research/project. For thesis, abstract is required and report within 30 days after the completion of the research/project.
7. Annual progress report is needed for a two-year (or more) research/project and submit the progress report before the expire date of certificate. After the completion of the research/project processes as No. 6.

BIOGRAPHY

First and last name: Tanavij Pannoi

Date of birth: April 11, 1981

Place of birth: Surat-Thani, Thailand

Education:

Sukhothai Thammathirat University, Thailand **2008**

B.B.A. (Marketing)

Prince of Songkla University, Thailand **2004**

B.Pharm (elective in Pharmaceutical Administration)

Work Experience:

International Health Policy Program, Nonthaburi, Thailand **2012**

Research Assistant

Taksin Hospital, Suratthani, Thailand **2011**

Hospital pharmacist

Bangkok Hospital Samui, Suratthani, Thailand **2008**

Hospital pharmacist

Sirindhorn College of Public Health, Trang, Thailand **2004**

Lecturer

Current position:

Lecturer in Department of Social and Administrative Pharmacy, School of Pharmacy at Walailuk University, Nakhonsri-Thammarat, Thailand.

Publication:

National Health Accounts 2009-2010, International Health Policy Program, Ministry of Public Health, Thailand.