COST-EFFECTIVENESS ANALYSIS OF MANAGED CARE FOR OSTEOPOROTIC HIP FRACTURES

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ผู้ป่วยที่กระดูกสะโพกหักจากภาวะโรคกระดูกพรุน ยังคงไม่ได้รับการตรวจวินิจฉัย รักษาและป้องกันการหักซ้ำในระยะยาวอย่างเหมาะสม จากปัญหาดังกล่าวนำมาซึ่งภาระค่าใช้จ่ายในการดูแลผู้ป่วยที่สูงขึ้น โดยผู้ป่วยที่เคยกระดูกสะโพกหักนั้นมีแนวโน้มที่จะเกิดการหักซ้ำมากกว่าคนปกติ นอกจากนี้ยังรวมถึงการมีภาวะแทรกซ้อนอื่นๆ ซึ่งทำให้คุณภาพชีวิตของผู้ป่วยลดลง โดยเฉพาะอย่างยิ่งในผู้ป่วยที่มีอายุมากกว่า 50 ปี เพื่อพัฒนาแนวทางการรักษาให้มีประสิทธิภาพมากขึ้น โรงพยาบาลจุฬาลงกรณ์ มีการรักษาแบบ “Managed care” ซึ่งมีแพทย์ออร์โธปิดิกส์ดูแลผู้ป่วยเป็นหลัก ทั้งการผ่าตัดและการป้องกันการหักซ้ำในระยะยาว การศึกษานี้มีวัตถุประสงค์เพื่อประเมินต้นทุน-ประสิทธิผลการรักษาในผู้ป่วยกระดูกสะโพกหักจากกระดูกพรุน เปรียบเทียบการรักษาแบบ Managed care จำนวน 110 คน กับการรักษาแบบ "Conventional care" หรือการรักษาแบบดั้งเดิม จำนวน 82 คน ซึ่งเน้นเฉพาะการจัดการระหว่างการผ่าตัดไม่ได้ให้ความสำคัญกับการป้องกันการหักซ้ำมากนักสำหรับการรักษาแบบดั้งเดิม โดยมุมมองของผู้ให้บริการ การศึกษานี้ได้เก็บข้อมูลย้อนหลัง ทำการวิเคราะห์โดยใช้แบบจำลองทางเศรษฐศาสตร์ มาร์คอฟ (Markov model) และได้กำหนดกรอบเวลาเป็นตลอดชีวิตหรือกระทั่งอายุ 100 ปี หรือเสียชีวิต

ผลการศึกษาหลังจากผู้ป่วยกระดูกสะโพกหัก 1 ปี พบว่ากลุ่ม Managed care มีอัตราการเสียชีวิตน้อยกว่ากลุ่ม Conventional care นอกจากนี้อัตราการเริ่มให้ยารักษาโรคกระดูกพรุน อัตราการตรวจ BMD และจำนวนการเข้ารับการตรวจแผนกผู้ป่วยนอกในกลุ่ม Managed care เพิ่มขึ้นอย่างมีนัยสำคัญทางสถิติเมื่อเปรียบเทียบกับกลุ่ม Conventional care ($P<0.001$) ต้นทุนต่อหน่วยของการรักษากลุ่ม Conventional care เท่ากับ 419,353 บาท และมีอายุที่ยืนยาวขึ้น 8.2 ปี ส่วนกลุ่ม Managed care ต้นทุนต่อหน่วยของการรักษาเท่ากับ 263,474 บาทและมีอายุที่ยืนยาวขึ้น 12.3 ปี เห็นได้ว่ากลุ่ม Managed care สามารถลดต้นทุนต่อหน่วยการรักษาได้ 38,019 บาท ต่อการมีอายุที่ยืนยาวขึ้นขึ้น 1 ปี ดังนั้นการรักษาแบบ Managed care ช่วยเพิ่มประสิทธิภาพในการรักษาผู้ป่วยกระดูกสะโพกหักจากกระดูกพรุนได้เป็นอย่างดีและมีความคุ้มค่าอย่างยิ่ง

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Osteoporotic fracture patients are still unidentified, untreated for osteoporosis. This group of patients is likely to have recurrent fractures and has more morbidity, these problems put a burden on the high cost of taking care of patients and poor clinical outcomes. The intervention for improving the quality of osteoporosis treatment, King Chulalongkorn Memorial Hospital (KCMH) calls “Managed care”. Managed care has an orthopedist who plays a crucial role in fragility fracture and long-term osteoporosis treatment. The purpose of this study is to access the cost-effectiveness of managed care for patients aged 50 years and over with osteoporotic hip fractures compared to “Conventional care” which focuses on only perioperative management does not provide secondary fracture prevention.

The economic evaluation is used a Markov decision-analytic model to estimate the incremental cost and effectiveness of each group and used provider perspective. Conventional care is recruited from 2012 to 2013 (N=110), managed care is recruited from 2017 to 2019 (N=82). At a one-year follow-up, the study found that the death rate is decreasing from 11.8% in conventional care to 3.7% in managed care (P=0.045). The rate of the initiated osteoporosis drug, rate of BMD test, adherence, and the number of OPD visits are significant increases in managed care when compared to conventional care (P<0.001). For base-case analysis, the average cost of conventional care is 419,353 baht and yielded the average life-year gained at 8.2 life-year gained. In addition, the average cost of managed care is 263,474 baht and yielded the average life-year gained at 12.3 life-year gained. From the result of the incremental cost, the managed care is cost-saving at 38,019 baht for one additional life-year gained. In conclusion, managed care is post-fracture recurrent prevention which can be closed the osteoporosis treatment gap and decrease fracture complications after sustained osteoporotic hip fracture and is suggested to be cost-saving.

Field of Study:	Health Economics and Health Care Management	Student's Signature .....
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CHAPTER I INTRODUCTION

1.1 Problem and Its Significance

Osteoporosis is a major medical problem that can cause fragility fracture in elderly people. In 2006, worldwide epidemic revealed that both men and women aged over 50 years will experience an osteoporotic fracture. The incidence has been increasing significantly, estimated to affect 200 million individuals worldwide, and leading to an osteoporotic fracture every 3 seconds [1]. The number of people living with osteoporosis across the world is dramatically increasing in the coming decades, because of ageing populations and lifestyle changing [2]. The burden in the USA showed that 8 million women and 2 million men will be experienced and leading to increase annual incidence of osteoporotic fractures from 1.7 million in 1990 to 6.3 million by the year 2050 [3, 4].

The effect of osteoporotic fracture will be increased morbidity, mortality, and the financial impact on society that causes cost burden. The most osteoporotic complication is a hip fracture which tends to decrease quality of life such as increasing chronic pain, mobility, disability [1, 5]. There are various studies revealed that secondary fracture shows highest risk within the first two years after a fracture about half of the prior patients [4, 6]. In 2005, The study from Chiang Mai shows that the hip fracture is increased both females and male. Most of patients who sustained a hip fracture has resulted in decreasing quality of life such as need gait aids, cannot do some activities in daily living. Moreover, mortality rate after hip fracture is the most serious, leading to a decrease in the expected survival at 12-20%. Another study in Thailand reports long-term mortality after sustained hip fracture at one-year mortality rates are 31% in males and 16% in females [7]. There are many evidence reports that patients who sustained osteoporotic fracture are inappropriately diagnosed and treated for osteoporosis [8-10].

According to the problems, it is very urgent situation in taking care osteoporosis patients after sustained fracture. To close the gap, case identification is

the first step to approach secondary fracture prevention. There are two major models of care that have been widely established to assure osteoporotic fracture patients receive osteoporosis management and recurrent fracture prevention. Firstly, the Orthogeriatric Services (OGS) focuses on hip fracture patients. This intervention includes early surgery, osteoporosis management which responsible by orthopedic and geriatrician or internal medicine clinicians. After acute care, patients will receive secondary fracture prevention program which providing bone health improvement and fall prevention. For Thailand context, orthopedist play important role in taking care osteoporotic fracture.

Another program called the Fracture Liaison Service (FLS) which established by the International Osteoporosis Foundation (IOF), is a coordinated model which focusing on patients who sustained a fragility fracture. This intervention includes fracture risk assessment and receive treatment in accordance with national clinical guidelines for osteoporosis. It is important to call for closing the gap of subsequent osteoporotic fracture, so models of secondary fracture prevention are maximized the possibility that the first fracture will also be the last.

Numerous studies at national, state and hospital levels across worldwide which implemented secondary prevention program such as Fracture Liaison Service or Orthogeriatric Service report that a significant of increasing patients' quality of life, can be closed post-fracture osteoporosis care gap and have a resulted in cost-effectiveness or cost saving. According to maximized effective secondary fracture prevention implementation, the study among worldwide shows how they adapted the best practice or clinical guideline of treatment to specific their local condition [4, 11-13].

The situation in Thailand is similarly to other countries, most osteoporotic fracture patients are still unidentified and untreated for osteoporosis. These problems put burden on high cost of taking care patients and poor clinical outcomes, especially in patients aged over 50 years and postmenopausal women. The report from Asia Pacific Audit Thailand in 2013 reports that there are still have poor initiated identification and no assessment in high-risk group and the audit recommends it is time to improve management of osteoporosis as early as possible.

In 2002, Thai Osteoporosis Foundation (TOPF) was established to response for enhancing osteoporosis and bone health management and collaborating with International Osteoporosis Foundation (IOF). In 2010, TOPF launched the clinical practice guideline for osteoporosis treatment which covered screening guidance and assessment tools (prior fracture status, age, Bone Mass Densitometry (BMD) and Fracture Risk Assessment Tool (FRAX). Specialists who responsible for osteoporosis treatment involve in endocrinologists, orthopedists, gynecologists, rehabilitation physicians and internal medicine physicians. According to healthcare service system in Thailand, osteoporosis treatment is recognized by an orthopedist who is specialty in bone management.

The intervention for improving the quality of osteoporosis treatment, King Chulalongkorn Memorial Hospital (KCMH) calls "managed care". The managed care has orthopedist plays a crucial role in fragility fracture and long-term osteoporosis treatment. Under responsibility, the intervention provides perioperative management which including an expedited surgery and managed post-operative complications, and secondary fracture prevention. For the case identification mainly occurs at inpatient ward, during admission patients refer to receive osteoporosis assessment and initiate drug treatment in case of having low bone mass density. To identify the impact of managed care on both cost and health outcome, the present study compares with "conventional care" which focusing on only perioperative management does not provide secondary fracture prevention. Additionally, the lack of economic evaluation studies in Thailand and the results from this study could be evidence to support the ongoing existing program, national policies, and financial incentive to reduce osteoporotic hip fracture.

1.2 Rational

The existing studies report that secondary fracture prevention is likely to improve clinical outcomes such as refracture rate, mortality rate, quality of life, and increased rate of assessment and appropriate treatment. Moreover, many studies show the cost-effectiveness of managed care, and some of the studies have resulted

in cost-saving. According to previous reasons, an existing of managed care at KCMH, the program calls managed care which including perioperative management and secondary fracture need to analyze cost and health outcome compares to conventional care by using the decisional analytic model approach. In addition, the different outcomes between these groups are no studies on cost-effectiveness in Thailand.

1.3 Research objective

1.3.1. Primary objective

To evaluate cost and health outcomes of managed care and conventional care in osteoporotic hip fracture at King Chulalongkorn Memorial Hospital.

1.3.2. Secondary objective

1.3.2.1 To measure the total cost of managed care and conventional care in osteoporotic hip fracture at King Chulalongkorn Memorial Hospital.

1.3.2.2 To determine the effectiveness of managed care and conventional care in osteoporotic hip fracture at King Chulalongkorn Memorial Hospital.

1.3.2.3 To evaluate the additional cost per additional life-year gained of managed care compared to conventional care in osteoporotic hip fracture at King Chulalongkorn Memorial Hospital.

1.3.2.4 To evaluate the context of orthopedists is play a crucial role in osteoporotic hip fracture treatment.

1.4 Scope of the study

The target of this study is osteoporotic hip fracture patients aged 50 and over. The intervention was divided into two groups such as managed care and conventional care. Managed care included patients from 2017 to 2019, the data received from an orthopedist who responses to fragility hip fracture and medical record. For conventional care the data collected from 2012 to 2013, data receives from the hip fracture registry which is the data collected by the orthopedist. This

study is a retrospective study, needs to clarify the model of hip osteoporotic care at KCMH between two interventions, managed care provides perioperative management and secondary fracture prevention, conventional care provides only perioperative management, also cost in terms of cost-effectiveness analysis.

1.5 Hypothesis

The managed care which provides perioperative management and secondary fracture prevention by an orthopedist is more cost-effective than conventional care in osteoporotic hip fracture.

1.6 The benefit of the study

This study focused on analyzing the clinical effectiveness and cost-effectiveness of managed care which provides perioperative management and secondary fracture prevention compared to conventional care which provides only perioperative management. In an evaluation of cost-effectiveness analysis by using a Markov model to measure incremental cost and incremental life-year gained. Regarding the result can be evidence to support the ongoing exiting intervention, national policies, and financial incentives to reduce the burden of osteoporotic hip fracture in acute care and post-fracture care.

CHAPTER II BACKGROUND

2.1 Prevalence of osteoporosis

Many countries across the world have been moving to an aging society, the prevalence of osteoporosis is an increasingly significant problem. Osteoporosis is divided into primary and secondary causes, primary osteoporosis is the most found in postmenopausal women, which is related to estrogen deficiency called 'type I' and in another by an age that involves both men and women aged over 70 years called 'type II'. Secondary osteoporosis is caused by endocrine disorder, chronic renal disease, inflammatory arthropathy, and connective tissue disorders. Most of the osteoporotic patients are primary osteoporosis are likely to have high fragility bone and risk of fracture [14, 15].

In a survey in Thailand from 2000 to 2001, the result shows that the age-adjusted prevalence in women is 19.8% of lumbar spine and 13.6% femoral neck [16]. In addition, there is another report revealed that the prevalence of osteoporosis was 19.3% and 24.7% at the femoral neck and lumbar spine [17].

2.2 Incidence of hip fractures

A silent disease that can cause the most recurrent fracture in elderly people, many countries across the world have been moving to aging society, the study from the US projected the annual incidence of osteoporotic fractures is likely to increase from 1.7 million in 1990 to 6.3 million within 2050 [8].

In Thailand, the population aged over 60 years is increasing rapidly. The total population will increase from 68 million in 2010 to 73 million in 2050. The percent of people aged over 60 years is 12 million by 2010 and 19 million by 2050, respectively. The study from Chiangmai University found that patients aged over 70 years old, age-specific incidence increased exponentially. The highest incidence of hip fractures is seen in patients aged more than 85 years [15]. The report from the osteoporotic of Canada revealed that annual osteoporotic hip fracture incidence shows the highest

incidence among other chronic diseases including heart attack, breast cancer, and stroke, respectively (Figure 1) [18].

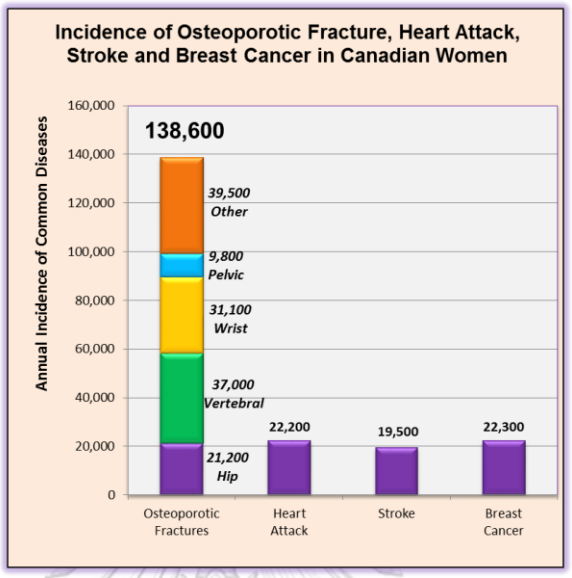


Figure 1 Annual incidence of osteoporotic fracture compared to other chronic diseases

2.3 Osteoporosis related morbidity and mortality

In terms of the highest osteoporotic fracture burden, hip fracture is the most severe when compared to other fracture sites. There are a variety of impacts of hip fractures after one year such as mortality rate at 20%, need more assistance at 85%, require home care at 20% [4]. Hip fractures tend to increase the level of chronic pain, decrease mobility and disability [5]. In addition, this kind of fracture is represented the highest subsequent fracture after two years of hip fracture [4].

There is an existing incidence of hip fracture studies in Chiangmai, Thailand in 2005. The results showed that the incidence of hip fracture is increasing in both men and women. In addition, around 22.1% of osteoporotic hip fracture patients are not ambulatory, 10% using gait aids, and the remaining (67.9%) are decreasing quality of life [7]. The overall average length of hospitalization is 17-22.7 days. In terms of measurement, the modified SF-12 health survey is used to access the quality of life, the results showed that patients who sustained hip fractures are likely to decrease in

health perception, mental health, physical, social function, and pain when compared to general people. Moreover, comparing with other fracture sites, previous hip fracture patients tend to exceed the highest morbidity (figure 2) [19].

In terms of mortality rate, osteoporosis is the sixth leading cause of death among Thai women, the result of mortality rate increased from 1 to 3 when compared to other causes. Hip fracture is the most serious fracture in terms of reduced the survival rate by 12-20% and affected the hazard of death which is an increase over 10-fold in the first 6 weeks after fracture [20].

In other studies, after the first year of sustained a hip fracture, the mortality rate is increased by about 17%. Moreover, the results showed that the proportion of death from hip fracture in women is as high as 1 in 6 women and higher than breast cancer patients after one year [21].

As previously described, osteoporosis has been showing significant mortality and morbidity which impact on public health burden. Although the number of deaths in osteoporosis is similar to lung cancer but the government has less awareness of this particular disease. Thus, raising awareness and educated more information on osteoporosis especially concerning prevention, are the best strategies to close the secondary prevention gap.

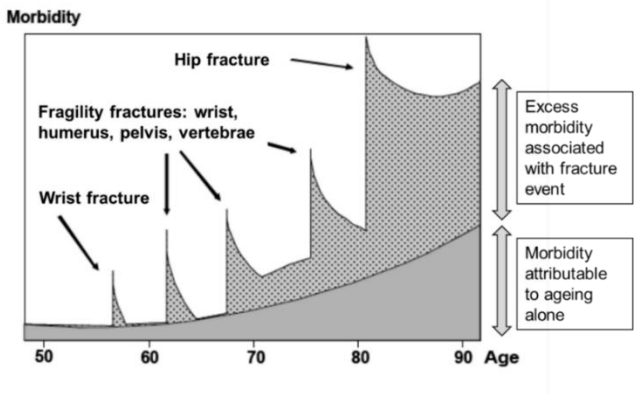


Figure 2 Morbidity rate of prior hip fracture

2.4 Osteoporosis related cost

Osteoporosis is affected not only public health burden but also cost burden. The morbidity has been caused burden of medical, social, and financial implications that are many supporting evidence. In the United Kingdom, osteoporosis costs were approximately 60,140,340 US$ (£1.8 billion) each year which was born by the National Health Service (NHS) and the government [22]. In 2003, the International Osteoporosis Foundation (IOF) audit reports that annual osteoporotic fractures cost in Europe is approximately to be 25 billion and similar to the US, in each year provides cost or treatment around US$17 billion [23].

There is a report from a societal perspective in Thailand, costs of related-hip fracture are reported to be 8,393-17,400 USD in the first year after fracture [24] and the rate of morbidity and mortality of osteoporotic fractures are significantly related to health care resources that provide of hospitalization, outpatient care, and long-term care. The result shows the number of hospitalization is 22.7 days with a median of 17 days [25].

2.5 The problem of osteoporosis management in Thailand

Hip fracture patients are likely to be under-diagnosed and under-treated, using DXA is not considered normal for screening patients who might have high risk. However, for the treatment of high-risk fracture patients, anti-osteoporotic agents being well established. The results of the survey found that only 7% of the patients were diagnosed with osteoporosis and less than 1% received BMD measurement by DXA less [26].

The treatments are associated with osteoporosis patients including calcium or calcium plus vitamin D, the percentage of this group shows at lower than 50% and calcium, vitamin D, and antiresorptive agents at only 4.2% [27]. As previously mentioned, patients with osteoporotic fracture that represented high risk group are not identification and treatment even though there have been already developed guidelines for osteoporosis treatment [20]. For osteoporotic medications are included

bisphosphonates such as alendronate, risedronate, ibandronate, SERMs like raloxifene, calcitonin, strontium ranelate, PTH, vitamin D analogs, and vitamin K which approved by the Thai Food and Drug Administration (Thai FDA) [17, 28, 29].

The government has been less concerned about this particular disease, for example, reimbursement is not provided Social Security Scheme (SSS), can be reimbursed only in public hospitals which usually provided Civil Servant Medical Benefit Scheme (CSMBS) and Universal Health Coverage (UHC) and determined claim by the government. There are indicators for reimbursement that whether patients meet the criteria by the physician. Insurance is available only in public hospitals.

On behalf of healthcare professionals, there is a moderate level of awareness among orthopedic surgeons, rheumatologists, gynecologists, and endocrinologists. In the contrast, physicians who work with other specialists tend to have less awareness when compared to the previously mentioned group and in other health services.

2.6 Osteoporosis treatment at King Chulalongkorn Memorial Hospital

According to lacking evidence-based and central database from Thai Osteoporosis Foundation that should be showed overall of structural interventions both conventional care and managed care. Thus, the information is derived from an orthopedist interview at the Department of Orthopedics.

Before 2017, the department of orthopedics is less aware of the secondary fracture prevention program. Most orthopedists at that time are focusing on how to manage perioperative effectively. Perioperative provides fracture treatment (surgery or non-surgery) and taking care of complications from the operation. In the case of osteoporosis treatment, most of them have been followed up by another specialty such as an endocrinologist.

Since 2017, many hospitals in Thailand are wide raise awareness of secondary fracture prevention programs, they try to appropriately adapt the best practice of the FLS and OGS model and osteoporosis treatment guidelines from TOPF to their local conditions. The department of orthopedics at KCMH also adapts for establishing secondary fracture prevention names managed care. Managed care also includes

perioperative management and concern more about surgery time e.g. patients need to operative within 48 hours after a sustained fracture. To improve the quality of taking care of patients post-fracture, managed care adds on secondary fracture prevention program which provides case identification, osteoporosis assessment, and initiation of treatment.

The component and details of interventions between managed care and conventional care show in the table below.

Table 1 The component of managed care and conventional care

Component of intervention	Managed care	Conventional care
Patient identification	Yes, by an orthopedist	No
Osteoporosis assessment	Inpatient by orthopedist	No
Initiation of treatment	Mainly inpatient or some case initiate at outpatient	No
Type of fracture	Hip fracture	Hip fracture
Age	50 years and over	50 years and over
Responsibility	-Perioperative management -Secondary fracture prevention	-Perioperative management

CHAPTER III LITERATURE REVIEW

3.1 Osteoporosis disease

Osteoporosis disease information is derived from osteoporosis treatment guidelines launched by the Thai Osteoporosis Foundation (IOF) [20].

Causes of osteoporosis

Osteoporosis is a common metabolic bone disease, there are two types of osteoporosis that have different causes such as primary osteoporosis and secondary osteoporosis. Primary osteoporosis was called 'type I', it is related to the normal process of advancing age and menopause, the most fragility fracture was caused by this condition that leading to increasing fragility fracture. Secondary osteoporosis was called 'type II' which is caused by specific clinical disorders e.g. endocrine disorder, chronic renal disease, inflammatory arthropathy, and connective tissue disorders.

Characteristics of osteoporotic bone

Normally women will have to reach peak bone mass during the age of 25 to 30 years. In terms of losing bone mass density, men are likely to have a lower rate of bone loss than women. In women, a high loss bone mass is happened during the perimenopausal period and slowed down after menopause. At age 60 years, women and men are equal rates of bone loss. As mentioned before, the strength of the bone is based on bone mass density and osteoporotic bone is represented by low bone mass and microarchitectural deterioration of bone tissue, these groups are likely to have a high risk of fragility fracture. The definition of a low BMD that the World Health Organization is mentioned based on BMD results. According to BMD measurement, DEXA has represented the gold standard due to it is the most accurate and more precision which provides scanning of the lumbar spine, the hip, and the distal radius. There are 4 criteria such as normal, osteopenia, osteoporosis, and severe/established osteoporosis. Osteoporosis Diagnosis is based on T-score which is represented in (Table 2).

Table 2 Diagnosis of osteoporosis based on the World Health Organization criteria

Diagnosis	Findings
Normal	Bone density within normal limit, value more than or equal to -1 SD when compared to the average bone mass of puberty woman (T-score ≥ -1)
Osteopenia	Bone density within normal limit, a value between -1 and -2.5 SD when compared to the average bone mass of puberty woman (_2.5 < T-score < -1)
Osteoporosis	Bone density within normal limit, a value equal to or less than -2.5 SD when compared to the average bone mass of puberty woman (-2.5 < T-score < -1) (T-score ≤ -2.5)
Severe/established osteoporosis	Bone density within normal limit, a value equal to or less than _2.5 SD when compared to the average bone mass of puberty woman (T-score ≤ -2.5) and with fragility fracture

Prevention of Osteoporosis

In terms of osteoporosis prevention, there are various related factors such as follows

- Nutrient, Calcium, and vitamin D, the recommendation would be to obtain calcium at 800-1000 mg/day. In addition, vitamin D is recommended at 5-15 mcg/day.

-Lifestyle modification, avoids coffee and caffeinated beverages, salty food control chronic diseases that present a risk for osteoporosis, and avoid steroid drugs not more than 3 ml/day.

*-**Fall prevention***

Falling is one of the serious causes that can be caused by a fragility fracture. There are 2 main factors of falling as intrinsic factors; based on underlying diseases, a

history of falls, impaired sensory function, muscle weakness, extrinsic factors; involves in an environment such as the wet floor, inappropriate waling aid, and inappropriate shoes. Fall risk assessment provides Falls Risk Assessment Tool (FRAT), Falls Risk Assessment Scores (FRAS). Moreover, assessing balance is important as well, tools that are widely used for assessing such as timed up and go test, chair stand test, functional reach, single-leg stance, and tandem stance.

Osteoporosis Treatment

Bisphosphonates are the most potential osteoporotic drug that can be a reduced rate of the spine and hip fractures. This class of drugs provides the two main oral drugs used which are Alendronate and Risedronate; a once-monthly drug used.

3.2 Model of secondary fracture prevention

Regarding the International Osteoporosis Foundation (IOF) reports the major secondary fracture prevention that established worldwide such as Fracture Liaison Services (FLS) and Orthogeriatric Services (OGS) [30].

According to the systematic approach that shows top-down adopted by the Department of Health for England in 2009 showed the pyramid of secondary fracture prevention which provided major fracture care (hip and spine fractures), recognize the risk of recurrent fracture and early giving intervention to link stepwise showed that the FLS or the OGS represents the program of secondary prevention (figure 3) [31].

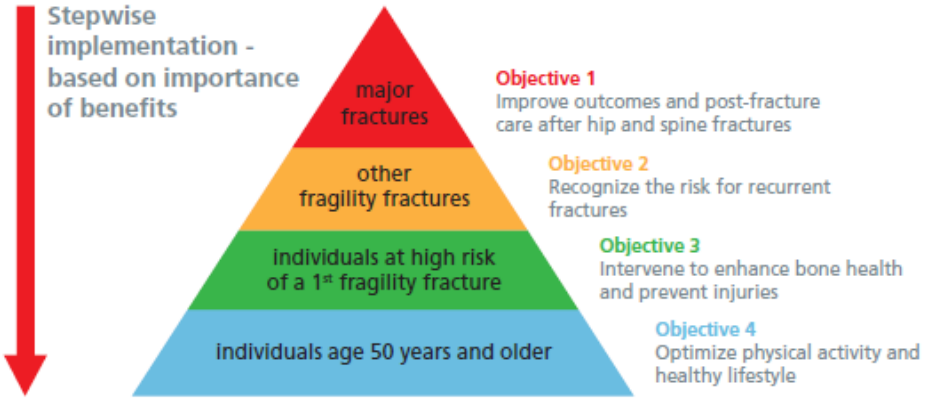


Figure 3 Achieve consensus on a systematic approach

3.2.1 Fracture Liaison Services (FLS)

In 2013, according to a systematic review on post-fracture, the study summarized provides a classification of the model as below [32].

1. Type A model of care

The main characteristics including identification, assessment, and treatment of patients as part of service. During the process, a dedicated coordinator working on as a coordinator in the Fracture Liaison Service. Normally, the coordinator is responsible for managing electronic patient lists and communicate with the orthopedic department to maximize appropriate management.

In terms of a multidisciplinary approach, there are previous studies in Thailand that conducted osteoporotic hip fracture patients at one-year follow-up. The results showed that clinical outcomes improved when patients received underwent surgery less than 48 hours in which decreasing complications perioperative and postoperative, the studies obtained less mortality rate and refracture rate rather than a comparator group.

For assessment provides an evaluation of clinical risk factors, a BMD scan, radiographic. In addition, some cases need to exclude secondary causes of osteoporosis pathology tests. Treatment based on the results of the assessment by initiated osteoporosis drugs.

2. Type B model of care

The difference from type A models of care is initiated osteoporosis drug process by the primary care. The concepts for other processes that are related to identify and assess are similar to type A models of care.

3. Type C model of care

In general, patients who have fragility fractures are provided information about osteoporosis and lifestyle such as nutrition or falls prevention. Moreover, assessment and treatment conditions are also advised but no plan to assess or initiated treatment immediately, and most of these processes are based on patients' needs. The type C model is tended to be a

less intensive intervention when compared with types A and B. For another component, the PCP involves communication with patients by face-to-face, letter, telemedicine.

4. Type D model of care

Patients receive education about osteoporosis only and no diagnosis and treatment initiation. The communication between patients and health workers provides by non-physicians like a nurse or other health professionals.

The results showed that type A and type B are cost-effective, although these have various definitions of effectiveness. In terms of conventional care is represented by type D that means patients receive only education. The clinical outcomes in many existing studies are not effective, the reason why conventional care is unable to yield a better outcome.

Structure of Fracture Liaison Service (FLS) in many countries.

Many studies represent successfully of the secondary prevention program. The model consists of a coordinator who coordinates in a multidisciplinary team to maximize patient management. To explain more on how each country adopts the best practice from FLS to local conditions, this study provides the example of the UK, Canada, and the US.

UK National Osteoporosis Society Clinical Standard for FLS

The National Osteoporosis Society (NOS) has established in 1986, NOS provided diagnosis, prevention, and treatment of osteoporosis. In 2012, try to lead the FLS campaign to set up a fall prevention team called a multidisciplinary Falls and Fracture Alliance. UK National Osteoporosis Society Clinical Standard for FLS provides key objectives of an FLS as below [33].

Identification: New fragility fracture identify, can be developed to extend to include a prior fragility fracture.

Investigation: Including risk assessment with DXA, screening of secondary osteoporosis, and assessment of fall risk.

Information: Providing additional information about screening as BMD testing, the important osteoporosis drug treatment, and risk fracture prevention.

Intervention: For low bone mass patients including osteoporosis drug treatment.

Integration: Taking care of patients as a multidisciplinary team.

Quality: Improving data collection and audit.

Osteoporosis initiation at Canada

Osteoporosis Canada (OC) launched the campaign "Make the first break the last with Fracture Liaison Service" in 2013. Canada had developed OC FLS Registry, an online database that provides across the hospital in Canada. the key objectives are provided 8 practices of an FLS [34].

1. Coordinator plays role in delivering service.
2. Finding new fragility fracture and/or vertebral fracture.
3. The FLS needs to provide at least one of the fracture types (hip, spine, wrist, shoulder) by following major osteoporotic fractures from the World Health Organization.
4. FLS models are classified into 4 levels (Type A, B, C, D).
5. Patients need to receive fracture risk assessment.
6. Patients in a high-risk group should be provided by the Type A or Type B model.
7. Integration with primary care such as risk assessment, osteoporosis treatment.
8. Collecting baseline data in a high-risk group and for initiating drugs.

US National Bone Health Alliance's FLS initiative

The US National Bone Health Alliance (NBHA) has been launched in 2010, NBHA works as a public-private partnership to include resources or expertise to promote bone health, diagnosis, treatment, and prevention of osteoporosis. For adapting FLS to exiting service, NBHA expanded to set Medicare, managed care, and focusing more on the private sector [35]. Examples of a model in the US are Kaiser Permanente's Healthy Bones program focusing on reduction in hip fracture rate since 1998 [36, 37]. Another is the Geisinger Health System osteoporosis disease management program, the result in this program shows cost savings over 5 years of implementation [38, 39].

3.2.2 Orthogeriatric Services (OGS)

The OGS, there are various service names as Orthopaedic-Geriatric Co-Care Services or Geriatric Fracture Centres, the aim of this model provides the best practice for hip fracture patients who are admitted to hospital and referred to receive secondary fracture prevention which includes case identification, assessment, and initiated treatment. Normally, the service model comprises orthopedists who taking care of fragility fractures in acute care and collaborating with a geriatrician. During hospital admission, they manage patient complications and refer patients to get osteoporosis treatment [40].

The Fragility Fracture Network (FFN) launched a guideline that focuses on expedited surgery and effective management in the acute phase. For example, OGS in the UK has endorsed best practices in hip fracture as detailed below.

1. Patients who sustained hip fractures should be admitted to the orthopedic ward within 4 hours.

2. In case that needs surgery, patients should have surgery within 48 hours.

3. Patients should be assessed and took care of to minimize pressure ulcers.

4. Patients who have fragility fractures should be received routine assessment at an orthopedic ward.

5. Patients who have fragile hip fractures should be assessed for osteoporosis to prevent recurrent fractures.

6. Patients who have fragility fractures should be followed fall prevention by multidisciplinary interventions.

In addition to described above, there are various names of secondary fracture programs and various concepts of program implementation, it depends on their existing conditions. In terms of summarizing two major models of care, FLS mostly focuses on secondary prevention program which provides 4 models (Type A, B, C, and D) and has a dedicated coordinator to communicate and manage cases among health professionals. For OGS model focuses on perioperative management in a hip fracture which includes an expedited surgery, minimize patient complications, and concerns on osteoporosis disease, orthopedist plays role in this program. According to the major role of FLS and OGS, the study of model of secondary fracture

prevention summarizes that to maximize post osteoporotic hip fracture management in elderly patients, the OGS is supported the FLS to deliver optimal management for the patient. These services are not only decreasing hospitalization but also decreasing mortality and disability rate in the long term [40].

3.3 Cost-effectiveness study

Cost-effectiveness of secondary prevention fracture: Other countries

Australia

Patients with non-vertebral osteoporotic fractures are divided into two groups such as a clinic-based intervention that provide standardized evaluations and treatment. The methodology is used in a 10-year simulation model, the results showed that a clinic-based intervention can be increased costs by $1486 per patient and improved QALYs by 0.089 years when compared to standard care [4].

USA

The study focuses on Fracture Liaison Service which provides hospital-based care for perioperative hip fracture patients. Interventions in this study provides co-managed by a multidisciplinary team and another model is targeted only at high-risk through using lifetime horizon. The outcomes from this study show that co-management is cost-effective and tend to cost saving of $66,879 when compared to targeted high-risk group [41].

Japan

The results of the Osteoporosis Liaison Service (OLS) reported that patients with osteoporosis hip fracture aged 65 and older are cost-effective when compare with no drug therapy. The OLS has obtained an additional lifetime cost of $3396 per patient and resulting in an ICER of $28,880 per QALY gained [13].

Singapore

a secondary fracture prevention program provides Patient Targeted and Integrated Management for Active Living (OPTIMAL) program in public hospitals that is managed by coordinators. The two-year completed follow-up patients are evaluated

(N=287). The report showed clinical and cost outcomes effectiveness. In addition, the rate of assessment and treatment are clearly defined [42].

Clinical effectiveness analysis of managed care in osteoporosis

In terms of clinical outcomes, many consequences can be represented better outcomes when compared amongst other types of service. The study from the Glasgow Osteoporosis and Fall Strategy showed that the rate of hip fracture reduced by 7.3% from 1998 to 2008 when compared to 17% of the whole England population. The data is assumed all patients on treatment for 5 years even though some case has already lost follow-up [43].

Another study that confirms the results of clinical effectiveness is from the Concord study which provides of non-vertebral fracture patients found that rate of refracture reducing by 80% when compared to standard care. For the control group represents before the implementation of FLS, the results show no significant decreased refracture risk in all fractures reduced by 30% in this age group, reduced solely in hip fractures aged 80 or less than [44]. The effect of treatment using cohort study from PGH's FLS study reported rate of secondary fracture decreasing within 1 year from 30% to 0% [25]. The type A model showed that re-fracture rates are the lowest rate of refracture when compared amongst other types, a significant improvement in refracture rates after 4 years, from 19.7 % to 4.1 % in the control group and the intervention group, respectively. Additionally, the overall over 3 years of patients with hip fractures showed relative risk reduction at 37.2 %.

Cost-effectiveness of secondary prevention fracture: The existing studies in Thailand

Cost-Utility Analysis of Osteoporotic Hip Fractures in Thais

In 2008, there is a prospective study in osteoporotic hip fracture. Focusing on both consequence and cost by using a societal perspective. Health utility is used EQ-5D to assess and then adjusted to a time trade-off. The average age is 75.6 years old, most patients underwent operative procedures like hemiarthroplasty or internal fixation. The cost-utility of a hip fracture is lower than in other developed countries

due to various factors as insufficient rehabilitation. The result in this study shows the median total cost per year at $4,210.60, median QALY at 0.636 and the cost per QALY is $6,620.52. It has a high impact on 78.8% of the Thai Gross National Product. When compared underdeveloped countries with developed countries, prevention of hip fracture is called for better action [24].

Cost Analysis of Osteoporotic Hip Fractures

A cohort study from Ramathibodhi hospital studied all new osteoporotic hip fracture patients. The purpose is the estimated total cost and determines factors related to costs. The result of the study revealed that in terms of cost, the median total cost and median direct cost of hip fracture treatment in 1 year is 116,458.6 Baht. And 59,881.6 Baht, respectively. The consequence shows the indirect cost per live-year saved is 118,168.3 Baht. There is the effect of preoperative status that is related to direct cost. In the further, Thai elderly are called for the appropriate solution to prevent hip fracture that can be reduced cost and had good health [45].

Cost-Effectiveness Analysis of Various Screening Methods for Osteoporosis in Perimenopausal Thai Women.

There are 5 screening programs including Dual-energy X-ray absorptiometry (DXA), Quantitative ultrasound sonography (QUS), risk index (clinical risk factors), two-step screening with QUS followed by DXA, and screening with risk index followed by DXA, compared to without intervention and universal treatment without screening. Target group provided osteoporosis in perimenopausal Thai women. The current situation showed that the most cost-effective strategy is no intervention and postmenopausal group with high-risk index screening. Cost-effective screening guidelines are still unclear and need to clarify more in a further study [46].

Evidence to Inform Decision Makers in Thailand: A Cost-Effectiveness Analysis of Screening and Treatment Strategies for Postmenopausal Osteoporosis

The study focuses on providing a budget for systematic screening in postmenopausal women. The study aims to convince for revision of the National List of Essential Medicines as evidence-based for supporting decision maker. The results in the screening of young age showed that The Osteoporosis Self-Assessment Tool and sequential dual-energy X-ray absorptiometry tended to be better value for

money. Even though the cost per QALY in older age groups is insignificant and providing osteoporosis drugs in secondary prevention can be obtained a considerably higher cost per QALY gained more than including primary prevention [47].

Economic Evaluation of Drug Treatment for Fracture Prevention in Thai Postmenopausal Women with Osteoporosis without Fracture History

This study focused on evaluated four osteoporosis drugs as oral bisphosphonates, raloxifene, strontium ranelate, and denosumab compared to no treatment. The results represent in cost-utility of drug treatment in Thai postmenopausal, using adverse events from drugs, and measure the budget impact over 5 years through a Markov model. The result shows that cost-effective provides oral bisphosphonates at 65 years with a BMD T-score less than or equal to –2.5 but have a huge budget impact. In terms of cost, the incremental cost-effectiveness ratio (ICER) is 130,049 THB per QALY, and the annual budget impact is 15,964 million THB. According to the results, need to negotiate drug prices and convince the Subcommittee, Development of the National List of Essential Medicines (NLEM) to consider more on clinical risk factors [48].

Overall data obtain from a few Asian countries reported that the situation needs to close the osteoporosis care and post-fracture care gap [13]. As described above, the results in setting up secondary fracture prevention such as FLS models which mainly on closing the care gap of fracture and enhancing communication among health care professionals. Some setting combines the protocol of hip fracture treatment at the acute phase and provide the FLS program for follow up patients in long-term. As described previously, various settings throughout the world showed cost and clinical effectiveness in the FLS or OGS model In the Thailand setting, there is a few studies of cost-effectiveness in secondary fracture prevention. A clinical study from General Police Hospital's Fracture Liaison Service shows clinical effectiveness in terms of decreasing refracture rate, morbidity, and mortality rate and increasing rate of treatment initiation. Other existing studies, from Ramathibodhi, reported that outcomes of hip fracture patients are more clinically effective [45].

3.4 Concept of economic evaluation

There are 4 types of economic evaluation [49].

1. **Cost-Minimization Analysis (CMA)**

The evaluation of the cost of intervention without considering the outcome. CMA concerns only cost, and the outcome is, similarly, CMA will be identified the lowest cost of different interventions. However, it is not appropriate to use CMA as a full economic evaluation.

2. **Cost-Effectiveness Analysis (CEA)**

The evaluation provides both cost and outcome. In terms of the results, it is represented in the cost per unit of outcome or outcome per unit of cost.

3. **Cost-Benefit Analysis (CBA)**

The evaluation to compare the cost and benefit of interventions. The result shows in monetary terms. This kind of economic evaluation, the challenge is to convert the outcome or consequence into the monetary term.

4. **Cost-Utility Analysis (CUA)**

The evaluation to compare both cost and outcome of interventions. For outcome in CUA, Quality-Adjusted Life Years (QALYs) is widely used.

3.5 Markov model

Markov cycle, the period that represents are called “cycles”, time period depends on the disease and under evaluation period. There are monthly or annual cycles. According to economic evaluation, using the transition probability to measure how patients move from one state to the next state. Thus, the Markov cycle is not only showed the use of resources and health outcomes but also reports related factors.

Markov state represents the model that can show patients move from one health state to another state based on the transitional probabilities. Cost is included in the model and multiplied by the number of patients in each state. The outcome of the Markov model shows in terms of accumulative cost and life years.

For accounting, the first stage in the model, clinical, cost, and risk factors are calculated in different states of the disease. It is important to consider these stages of the disease are mutually exclusive because at the same time patient cannot be in more than one state of disease [49].

3.6 Decision trees

The assumption that taken by characteristic analysis of the nature of the disease and the effect of intervention in a specific decision model. The decision tree represents the individual possibility of prognosis. For model stimulation, we can account for event stimulation in terms of state-transition models or discrete event simulation models. A decision tree has started with a single node that shows the number of branches of possible outcomes. In terms of nodes, there are three different kind of nodes such as chance nodes, decision nodes, and end nodes. A chance node is certainly the probabilities of results. A decision node is a decision to be made, and an end node is showed the final outcomes of a decision path. Firstly, all decision analyses require specifying the clinical problem, the time frame of the analysis, and the relevant patient population. Secondly, they are accounted for the transition probability of transferring to another health state or a health event. Finally, in terms of decision analysis, require information about the payoff related to state or event [49].

3.7 Transition probability

It is important to consider using proper transition probability in the decision analytic model because it can be affected the results directly. There are three important issues that should be considered. First, the transition probability should be derived from the systematic review. Second, in case there are many sources of information, meta-analysis is used to define the rationale of selection by pooled the results. Finally, if the information is derived from primary data, the study needs to

clarify the step of probability estimation. Moreover, using the probability that represents the population should be considered generalized.

In addition, for some chronic diseases such as cancer, the transition probabilities may be increased when time is in advance. If individual data are available, we can use survival analysis to calculate the time-dependent probabilities.

According to underlying disease in patients, survival analysis is mostly used in the medical field to handle the censor's data. Normally, the survival model is used in the Cox proportion hazards model which is the semiparametric survival model. The baseline hazard is fixed so it cannot be used to implement time-dependency in the Markov model [49].

3.8 Outcome measurement

Life-year gained is the consequence that is measured in this study. The first step is to account for the number of patients who died within a one-year follow-up. The probability of death is derived from age-specific mortality rates which are divided into 5 groups as 50-59, 60-69, 70-79, 80-89, and ≥90 years old. In each cycle, person-year represents the year gained that comes from all states excluding the death state. The final step is the summation of all of person-year every cycle length and divided by 1000 (a large number of repeating in Monte Carlo simulation).

3.9 Cost

Cost is commonly used to study depending on perspective and patient perspective. In terms of cost calculation, it is taking substantial time and effort, so in the study, the researcher must know the precision of costing.

There are many levels of hospital costing, the most precise costing to least precise, are as follows, micro-costing, case-mix group, disease-specific per diem, average per diem, and cost to charge ratio. In terms of accounting for cost to charge ratio which used for converting hospital charges to cost multiplied by charges to cost

to charge ratio. Cost to charge ratio is showed an appropriate costing method for trade-off between accuracy and resources used [49].

3.10 Uncertainty and sensitivity analyses

Uncertainty provides two types such as structure uncertainty and parameter uncertainty. Structural uncertainty is derived from the internal structure of the model. Parameter uncertainty is the uncertainty of the true value of parameters using in the model. Sensitivity analysis represents a tool that examines the effect of input data and model uncertainty. There are provided two types as follows [49].

3.10.1 Deterministic sensitivity analysis (DSA)

One-way sensitivity analysis is normally used in DSA by accounting standard deviation, 95% confidence interval during fixed other variables, after that the results are measured. For presentation, a tornado diagram is used to show the result of one-way sensitivity. The tornado diagram is showed the magnitude of influence of the parameters on the incremental cost-effectiveness ratio in the same diagram. The horizontal length of bar is represented the sensitivity of study results to the variation of each parameter. The parameter that has the most influential shows at the top of the diagram and follows by less influence at the bottom [49].

3.10.2 Probabilistic sensitivity analysis (PSA)

Using for determining the effect of change in all parameters at the same time in the reasonable range such as standard error. To handle PSA, Monte Carlo simulation is the popular method to use in this sensitivity analysis.

In the Monte Carlo simulation, regarding drawing the value of all parameters, their distributions are derived from computer randomization at the same time. The process is repeated a large number of times e.g. 1,000 or 10,000 times. Once the stimulation is completed, the expected value of each arm of the decision analysis model will be associated with a distribution of incremental cost or effectiveness value [49].

CHAPTER IV RESEARCH METHODOLOGY

4.1 Research design

This study uses a decision analytic model to compare the cost-effectiveness of managed care and conventional care for osteoporosis. The target populations of this study were patients aged 50 years and over with fragility hip fractures. Conventional care was recruited from 2012 to 2013, managed care was recruited from 2017 to 2019.

Inclusion criteria

- Patients aged over 50 years with prior low-trauma hip fractures are admitted to the orthopedic ward (Low trauma fractures are defined as falls from standing height or less and not occurring because of road traffic accidents and secondary osteoporosis [50]).
- Osteoporotic hip fracture was defined as intertrochanter or femoral neck fracture (ICD-10 S72.1)

Exclusion criteria

- Patients with a fracture due to high energy trauma, secondary osteoporosis (e.g. chronic kidney disease, mineral and bone disorders; CKD-MBD), and bone tumors.

4.2 Data collection

Managed care includes patients from 2017 to 2019, the orthopedist who responses for fragility hip fracture allow accessing from the medical record. For the conventional care, the data collects from 2012 to 2013, the study receives data from hip fracture registry which is the data that orthopedist has collected for using in previous work Additionally, data of conventional care cannot access during 2014 to October 2017 both from medical record and orthopedist's record.

Cost data provides direct medical cost, managed care derives from the medical record and conventional care derives from orthopedics record and some

information both of intervention derives from interview orthopedist and previous cost study in KCMH.

Clinical data provides baseline patient characteristics: age, type of hip fracture, type of acute treatment, length of stay, outpatient department visit, adherence, and at 1-year follow-up consists of mortality rate, secondary fracture, rate of osteoporosis treatment, and BMD rate. Managed care derives from the medical record, secondary fracture derives from the medical record and is confirmed by the orthopedist. Conventional care derives from the orthopedic record.

In terms of using the decision analytic model to analyzing cost-effectiveness, some of the Markov state, parameters such as refracture rate derives from other previous studies or meta-analyses.

Ethical consideration

The study was conducted after the Institutional Review Board at Faculty of Medicine, Chulalongkorn university's approval (IRB No.482/63, COA No.1043/2020). The data collected and processed for this study had been managed by the investigator and confirmed by the orthopedic surgeon to ensure the accuracy of data under national and/or local laws and regulations on personal data protection (Annex 1).

4.3 Theoretical framework

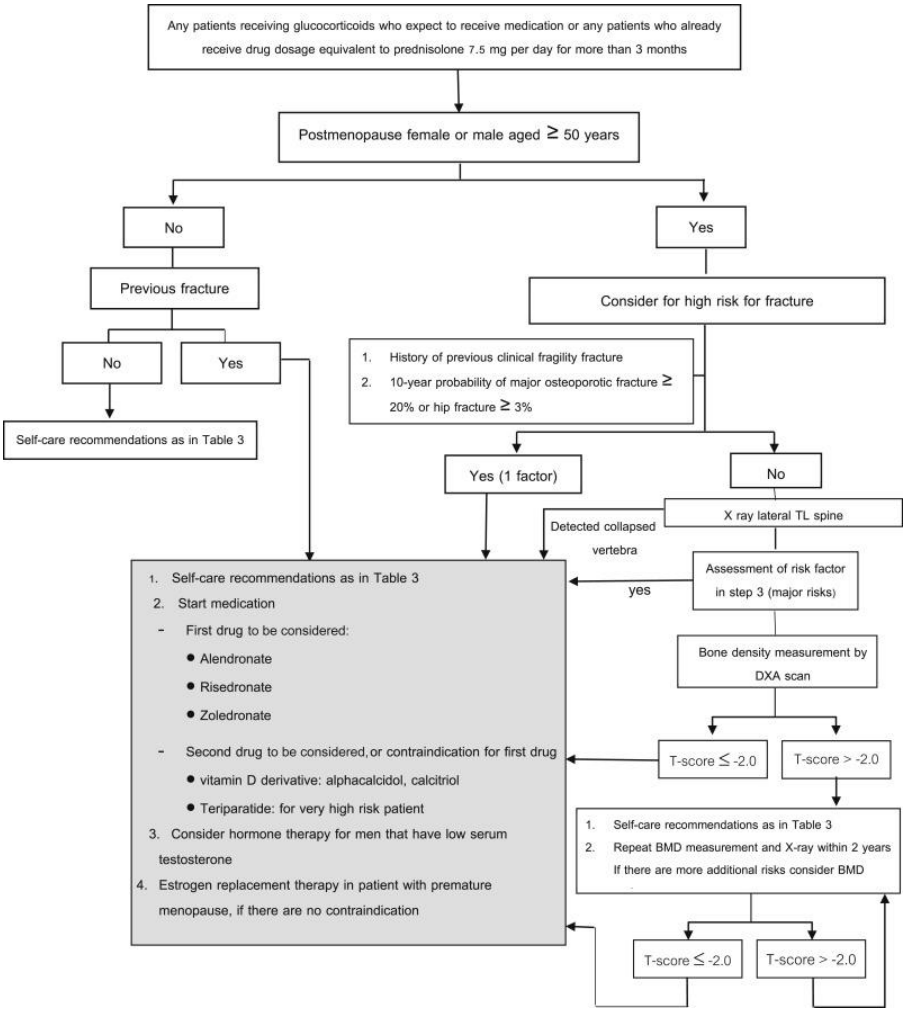


Figure 4 Algorithm for treatment of osteoporosis drug

According to the algorithm for osteoporosis drug treatment, it is a part of osteoporosis treatment guideline from the Thai Osteoporosis Foundation (TOPF), patients aged 50 or over should be considered for osteoporosis and called “high-risk group of fracture” [20]. In patients who sustained prior fractures are considered to start appropriate assessment and treatment, they have a high risk to experience recurrent fracture when compared to normal people. The investigation provides an assessment of risk factors by using X-ray, Bone density measurement by DXA. If the result of bone density that presents in T-score level is less than or equal to -2.0,

patients need to consider for initiated osteoporosis drug. Moreover, patients aged 50 and over should be provided self-care education for example how to choose high calcium food, raising awareness of fall prevention and exercising, etc.

Regarding the importance of case identify, osteoporosis drug treatment, and prevention, this study includes patients aged 50 and over who sustained a hip fragility fracture. In addition, compared the results in the rate of investigation, rate of osteoporosis treatment, and prevention between managed care and conventional care.

Moreover, this study provides perioperative management which focuses on expedited surgery and optimal management of fracture complications, to describe more effective management in perioperative management, the study also compared managed care and conventional care.

The aim of the study is not only to focus on the clinical outcome but also concern on the direct medical cost which occurred for osteoporotic hip fracture treatment from the provider perspective, so the result in this study provides cost-effectiveness analysis between two interventions.

4.4 Perspective

The provider perspective is used to estimate the costs incurred by the treatment of the osteoporotic hip fracture.

4.5 Decision analytic model

The retrospective study of patients with fragility hip fracture will enter to Markov model. Osteoporosis is a chronic disease, so Markov model is appropriate used in this study. The model allows patients to transition to another state that depends on patients' condition. Additionally, costs are accounted into the model and multiplied by the number of patients in each state. The results of the Markov model are represented by accumulative cost and life-year gained.

Cycle length of 1 year is chosen because it is closely to the time frame that can be capture progression of disease and resolution of disease state.

The time horizon of the analysis was lifetime from the time of occurred fragility hip fracture until patients aged 100 years or died. During a cycle, the patient may make a transition from one state to another.

The transitional probability of each state is accounted to the model to measure the probability to move from one state to another state. The probability from each Markov state is summated equal to 1. Besides, the life-year gained and the cost is also attached to each state. During model running. disease outcomes and costs will be occurring, the accumulated life years and costs are obtained at the end of the simulation.

4.6 Markov State

The figure demonstrates five health states in the Markov model and the details of each state are as follows.

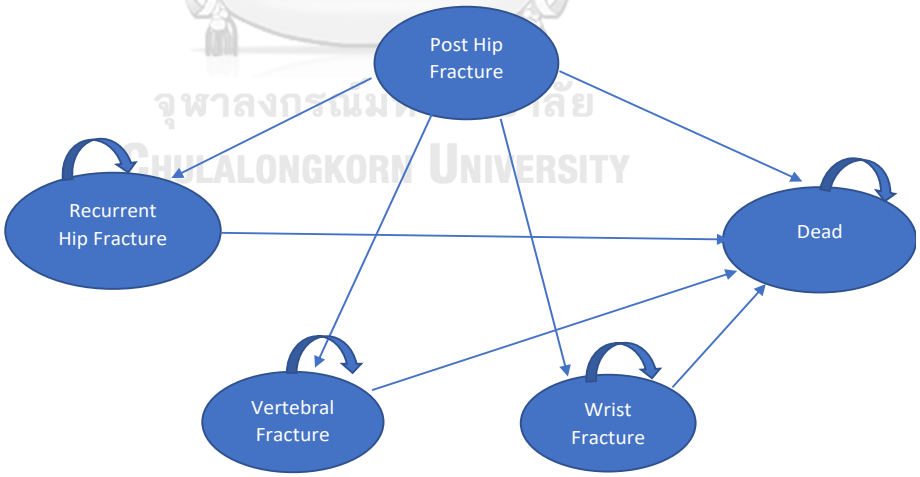


Figure 5 Health state in Markov model

State definitions

4.6.1 Post hip fracture state

Post hip fracture state is represented the state that represents patients who had fragility hip fracture.

4.6.2 Recurrent Hip fracture state

Recurrent Hip fracture state is represented the state that represents patients who had recurrent fragility hip fractures.

4.6.3 Vertebral fracture state

Vertebral fracture state is represented the state that represents patients with fragility hip fracture who have a new vertebral fracture.

4.6.4 Wrist fracture state

Wrist fracture state is the state that represents patients with fragility hip fracture who have a new wrist fracture.

4.6.5 Death state

Death state is represented all the patients who died from other states.

4.7 Parameter

4.7.1 Refracture rate

The risk of hip fracture recurrence is a function of time after hip fracture. Refracture rate is estimated from the retrospective cohort study. In this study, no limit on number of re-fractures is defined.

4.7.2 Effect of osteoporosis drug treatment

Effect of osteoporosis drug treatment uses in relative risk which means how drug reduced the risk of fracture when compared with no taking drug group. Based on a meta-analysis of denosumab, alendronate and teriparatide were assumed to reduce the rate of fracture under partial adherence. This study focuses solely on the relative risk of reductions to osteoporosis patients and assumes patients with normal BMD has no benefit of bisphosphonate treatment. In terms of treatment duration, a 5-year interval was used in taking the drug, after that drug holiday was used applied

to stop taking the drug for 5 years as well. During the drug holiday, the efficacy drug is still the same.

4.7.3 Mortality rate

The proportion of sustained osteoporotic hip fracture patients who died within one year is divided by the total of patients and calculated for each age-specific mortality rate.

4.8 Cost data

According to the retrospective study which focused on the direct medical cost that provided operation room, inpatient, and outpatient departments from the provider perspective.

Table 3 Costing that involved in Non-Revenue Producing Cost Center (NRPCC) and Patient Service (PS) of osteoporotic hip fracture

Costing category	Conventional care	Managed care
Operation room		
Labor cost	☑	☑
Capital cost	☑	☑
Inpatient department		
Labor cost	☑	☑
Capital cost	☑	☑
Medical care cost	☑	☑
Outpatient department		
Labor cost	☑	☑
Capital cost	☑	☑
Medical care cost	☑	☑

4.9 Transition probability

4.9.1 Transition probability Post hip fracture state to Recurrent hip fracture

This relative risk is obtained from a systematic review, the results shows in terms of the relative risk (RR) and 95% confidence intervals (CI).

PubMed database was searched with this query "(((((((exp OSTEOPOROSIS/) OR (OSTEOPOROTIC FRACTURES/)) OR (osteoporo*.mp,kw,jw.)) OR ((bone* adj5 (lost or loss* or lose or losing)).mp.)) OR ((bone* adj10 (postmenopaus* or post-menopaus* or menopaus*)).mp.)) OR ((bone* adj5 (break* or broke*)).ti,ab.)) AND ((((((liaison adj5 (service* or program*)).mp.) OR ((fracture adj5 (liaison or prevent*)).mp.)) OR (secondary fracture prevention.mp.)) OR (((program* or strateg* or intervention*) adj10 implement*).mp.))) NOT ((NONHUMAN/ or ANIMAL/ or ANIMAL EXPERIMENT/) not HUMAN/)" between 2010 and 2020.

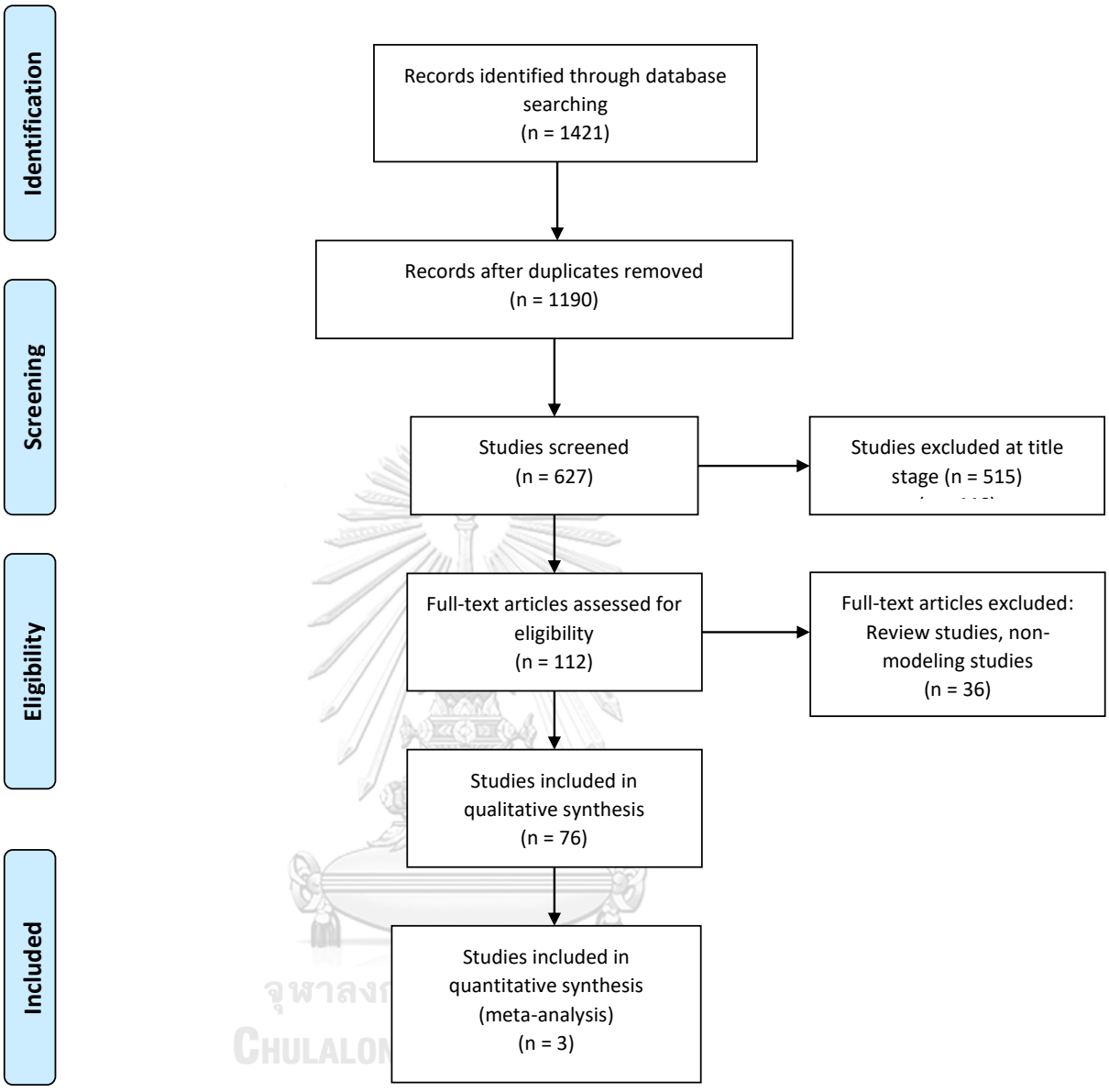


Figure 6 Flow diagram of the study selection for Post hip fracture state to Recurrent hip fracture state

Inclusion criteria

1. Clinical trial, randomized control trial, or observational studies which evaluated the clinical effectiveness of osteoporotic treatment.

2. Intervention comprised of osteoporosis identification, assessment, and treatment.

3. Physician-led intervention played an important role in the case coordinator.

4. Participant aged over 50 years with osteoporotic hip fracture

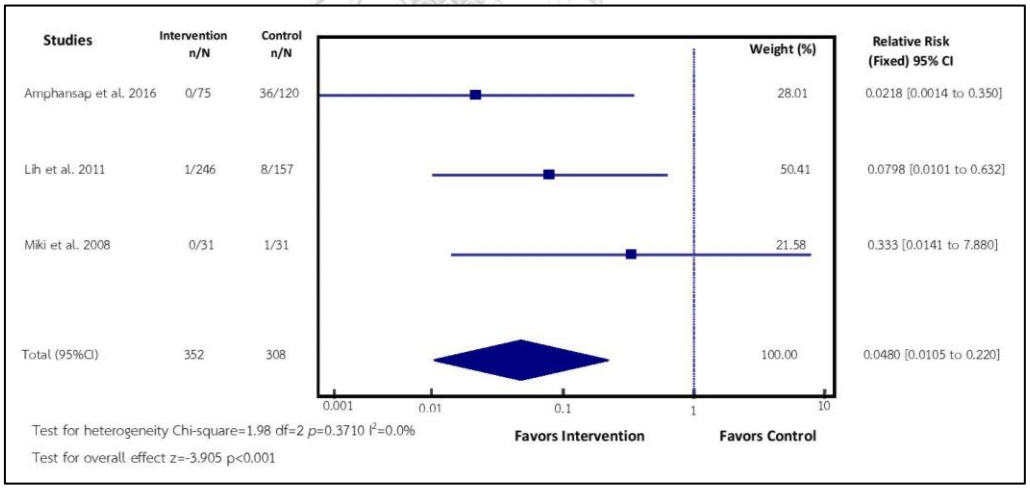
5. Included the articles from 2000 to 2020.

Exclusion criteria

1. Studies that included hip fracture from high-energy trauma or secondary osteoporosis.

The result of 3 studies reported that in terms of relative risk with 95% CI was 0.048 (0.0105-0.220).

Table 4 The relative risk of recurrent hip fracture



4.9.2 Transition probability Post hip fracture state to Vertebral fracture state

From the systematic review, no met inclusion criteria. Thus, the rate of vertebral fracture obtained from the study of the incidence of vertebral fracture in Thai women and men: a prospective population-based study [51]. Then, multiplying with the relative risk that represented the efficacy of osteoporosis drug treatment. In this study, the percent loss of drug interventions is 10% for managed care and 70%

for conventional care. Partial adherence as this formula = (1 - [1 - RR of fracture with osteoporosis drugs] × [100 % - percent reduction in efficacy] [13].

Table 5 Incidence rate of vertebral fracture

Age (year)	Incidence rate/1000
50-59	21.6
60-69	30.2
over 70	57.1

The RR of vertebral fracture is obtained from a published network meta-analysis which shows the effectiveness of different drug treatment for reduction of fragility fractures [52].

Table 6 The relative risk of vertebral fracture

Type of osteoporosis drugs	RR of vertebral fracture (95% CI)
Denosumab	0.32 (0.22-0.45)
Alendronate	0.57 (0.45-0.71)
Teriparatide	0.27 (0.19-0.38)

In terms of osteoporosis treatment, the orthopedist provides alendronate, teriparatide, and denosumab. The proportion of patients who are provided osteoporosis treatment following 4 types of drugs derived from the current study.

Table 7 The proportion of patients who taking osteoporosis drugs in each type

Type of osteoporosis drugs	Proportion
Denosumab (Prolia), a 6-monthly injection	0.469
Alendronate (Fosamax), a weekly pill	0.406
Teriparatide (Forteo), a daily injection	0.125

The proportion is derived from managed care and adjusted for the conventional care group by interviewing orthopedists, the proportion shows a similar type of drug that using inappropriate treatment.

Table 8 Transition probability of vertebral fracture for age-specific

Age (year)	Transition probability	
	Conventional care	Managed care
50-59	0.0180	0.0111
60-69	0.0250	0.0155
over70	0.0467	0.0289

4.9.3 Transition probability Post hip fracture state to Wrist state

From the systematic review, no studies meet the criteria. The study is used an incidence rate based on Japan's population [53].

Table 9 Incidence rate and transition probability in each age group

Age group (year)	Incidence rate	Transition probability
50-54	0.0018	0.0017
55-59	0.0032	0.0030
60-64	0.0033	0.0031
65-69	0.0034	0.0032
70-74	0.0036	0.0034
75-79	0.0033	0.0031
80-84	0.0038	0.0036
Over85	0.0042	0.0039

4.9.4 Transition probability Post hip fracture state to Dead state

This study uses mortality rate from previous study of osteoporotic hip fracture in Thailand. The study found that advancing age is tended to be a high mortality rate. The number of patients in this study is 367 [7].

Table 10 Mortality of osteoporotic hip fracture within 1 year (%)

Age groups (year)	Mortality of osteoporotic hip fracture within 1 year (%)
50–59	3.7
60–69	13.48
70–79	25.32
over 80	48.39

Table 11 Transition probability

Age groups (year)	First-year	Subsequent year
50–59	0.0363	0.0334
60–69	0.1261	0.0334
70–79	0.2237	0.0381
over 80	0.3836	0.0492

The relative risk is obtained from the systematic review, the results showed in terms of the relative risk (RR) and 95% confidence intervals (CI).

The result of 3 studies reported that in terms of relative risk with 95% CI is 0.750 (0.529 to 1.063).

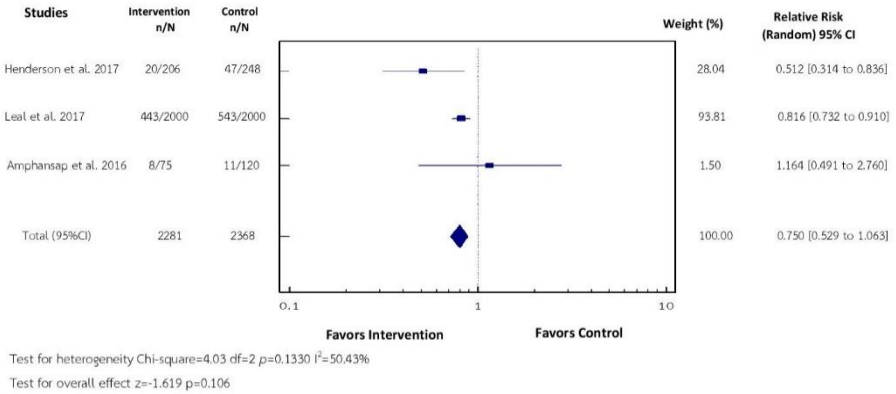


Figure 7 The relative risk of patients with osteoporotic hip fracture died at 1 year

4.9.5 Transition probability Vertebral fracture state to Dead state

The probability is derived from the study of mortality rate after vertebral fracture in Korea [54]. Following mortality rate in long-term care, from a systematic review, no studies met criteria and lack of evidence the clinical outcome in Thailand.

Table 12 Mortality rate of vertebral fracture at 1 year

	Mortality rate (/1000)	
Age group (year)	First-year	Subsequent year
50-54	0.0189	0.0047
55-59	0.0204	0.0075
60-64	0.0230	0.0099
65-69	0.0334	0.0139
70-74	0.0484	0.0238
75-79	0.0781	0.0411
80-84	0.1240	0.0629
85-89	0.1801	0.0930
90-94	0.2522	0.1417
95-100	0.3431	0.1507

Table 13 Transition probability

Age group (year)	First-year	Subsequent year
50-54	0.019	0.005
55-59	0.020	0.007
60-64	0.023	0.010
65-69	0.033	0.014
70-74	0.047	0.024
75-79	0.075	0.040
80-84	0.117	0.061
85-89	0.165	0.089

90-94	0.223	0.132
95-100	0.290	0.140

4.9.6 Transition probability Wrist fracture state to Dead state

The transition probability of wrist fracture to dead state in this study assuming similar to the general population. According to the data from the Health Information Group under the Ministry of Public Health [55].

Table 14 Mortality rate and transition probability in each age group

Age group (year)	Mortality rate (/1000)	Transition probability
50-54	6.5	0.006
55-59	7.7	0.008
60-64	8.5	0.012
65-69	9.4	0.017
over 70	48.9	0.049

4.10 Health outcome

To account for health outcomes, life-years gained were analyzed in terms of "person-years" which were obtained from the number of survivors in each age (51-100 years) and divided by 1,000 from Monte Carlo Stimulation.

4.11 Cost data

Health care provider perspective is accounted. The direct medical costs are used in the costing.

Cost for each 5 states

4.11.1 Post hip fracture state

- *Operation Room (OR)*

Two costs are related to operations such as labor cost and capital cost. Material care cost is not provided in this department because the operation room referres to Non-Revenue Producing Cost Center (NRPCC).

Resource requirements that occurred in this department were as follows.

1.1 Labor cost is derived from the operation room by interviewing the head of orthopedics operation room and orthopedist that providing the solely salary base.

Table 15 The health resources that distributed to provide operation

Group	Nurse	Orthopedic Surgeon	Anesthetist	Operation Hours
Conventional care	1	2	1	2.6
Managed care	1	2	1	2.6

Table 16 Labor cost of managed care at operation room

Surgeons		
Percentage of salary per month	40% of salary base (35,000 baht)	14,000
Salary cost per working day	8	1,750 baht/working day
Salary cost per hour	8	218.75 baht/hour
Operation duration per case	2.6	568.75 baht/case
Surgeons' salary cost	2	1,137.5 baht/case
Anesthetist		
Percentage of salary per month	70% of salary base (35,000 baht)	24,500
Working day per month	16	1,531.25 baht/working

		day
Salary cost per hour	8	191.41 baht/hour
Operation duration per case	2.6	497.66 baht/case
Anesthetist's salary cost	1	497.66 baht/case
Nurse		
Percentage of salary per month	100% of salary base	21,833.33
Working day per month	20	1,091.67 baht/working day
Salary cost per hour	8	136.46 baht/hour
Operation duration per case	2.6	354.79 baht/case
Anesthetist's salary cost	2	709.58 baht/case

Table 17 Labor cost of conventional care at operation room

Surgeons		
Percentage of salary per month	40% of salary base (35,000 baht)	14,000
Working day per month	8	1,750 baht/working day
Salary cost per day	8	218.75 baht/hour
Operation duration per case	2.6	568.75 baht/case
Surgeons' salary cost	2	1,137.5 baht/case
Anesthetist		
Percentage of salary per month	70% of salary base (35,000 baht)	24,500
Working day per month	16	1,531.25 baht/working day
Salary cost per hour	8	191.41 baht/hour
Operation duration per case	2.6	497.66 baht/case

Anesthetist's salary cost	1	497.66 baht/case
Nurse		
Percentage of salary per month	100% of salary base	22,846.15
Working day per month	20	1,142.31 baht/working day
Salary cost per hour	8	142.79 baht/hour
Operation duration per case	2.6	371.25 baht/case
Anesthetist's salary cost	2	742.50 baht/case

In terms of labor costs, there is no difference between intervention groups because patients underwent a similar surgical procedure.

1.2 Capital cost

In this study the data is derived from the study in cost analysis of patient services at King Chulalongkorn Memorial Hospital: a patient service area in 2001 [56] The data is provided medical care cost and building cost at 4,338,372 baht and converted to 2020 by using CPI, the result after adjusted is 1,807,655 baht [32].

Table 18 Capital cost for each intervention

Average capital cost per day	9,904.96
Average capital cost per hour	1,238.12
Average capital cost per hour per room	309.53
Capital cost for each intervention	804.78

- **Inpatient department (IPD)**

Inpatient department is provided patient service which is three costs such as labor cost, capital cost and medical care cost which involved in.

2.1 Labor cost is derived from the inpatient department in terms of salary base.

Table 19 Labor cost of managed care at inpatient department

Orthopedists		
Percentage of salary per month	10% of salary base (35,000 baht)	3,500
Salary cost per working day	2	1,750 baht/working day
Salary cost per bed	18 beds	97.22 bath/day/bed
Salary cost of orthopedists (Average salary cost/bed x Average Length of Stay)	12 days	1,167 baht/case
Nurse		
Percentage of salary per month	100% of salary base	282,484.17
Salary cost per working day	20 days	14,124.21 baht/working day
Salary cost per bed	18	784.68 bath/bed
Salary cost of nurse (Average salary cost/day x Average Length of Stay)	12 days	9,416.14 baht/case

Table 20 Labor cost of conventional care at inpatient department

Orthopedists		
Percentage of salary per month	10% of salary base (35,000 baht)	3,500
Salary cost per working day	2	1,750 baht/working day
Salary cost per bed	12	145.83 bath/day/bed
Salary cost of nurse (Average salary cost/day x Average Length of Stay)	15 days	2,188 baht/case
Nurse		

Percentage of salary per month	100% of salary base	233,780
Salary cost per working day	20 days	11,689 baht/working day
Salary cost per bed	12	974.08 bath/day/bed
The salary cost of a nurse (Average salary cost/day x Average Length of Stay)	15 days	14,611.25 baht/case

2.2 Capital cost

In this study the data is derived from the study in cost analysis of patient services at King Chulalongkorn Memorial Hospital: a patient service area in 2001 [56]. The data is provided medical care cost and building cost at 2,167,681 baht and converted to 2020 by using CPI, the result after adjusted is 903,200.42 baht [32].

Table 21 Capital cost at inpatient department

Steps	Results
Equivalent annual cost	903,200.42
Average capital cost per day	4,949.04
Average capital cost per bed	412.42

The capital cost for each intervention is the average capital care cost per day multiplied by the length of stay.

- Managed care: length of stay = 12 days, average capital cost per case = 4,949.04 baht.

- Conventional care: length of stay = 15 days, average capital cost per case = 6,186.03 baht.

- Medical care cost

There are provided treatment costs, medical equipment costs, and room costs. For conventional care, we can access implant cost and treatment cost, thus we adjusted for room cost at 492 baht per day and multiplied by the number of admission days.

Table 22 Medical care cost at inpatient department

Group	IPD	
	Annual cost/patient	SD
Managed care	64,795.00	37,129.00
Conventional care	57,960.36	42,914.19

Even though the length of stays of managed care is less than conventional care at 12 and 15 days, respectively, but the rate of room charge of managed care (2,480 baht/day) is higher than conventional care (492 baht/day) at 5.8 times.

This study converted charge price to cost by using an 18% of charge price reduction in each intervention Cost of medical care in both interventions in the year before 2020 is changed into the year 2020 by using the medical care Consumer Price Index (CPI).

- **Outpatient department (OPD)**

Outpatient department is provided patient service which is three costs such as labor cost capital cost and medical care cost involved in.

3.1 Labor cost is derived from the inpatient department, providing a salary base. The average labor cost per case is similar between both interventions. OPD visit times in managed care tended to be high rather than conventional care.

Table 23 Labor cost of managed care at the outpatient department

Orthopedists		
Percentage of salary per month	40% of salary base (35,000 baht)	14,000
Salary cost per working day	8	1,750 baht/working

		day
Salary cost per case	40 case/day	43.75 bath/OPD visit
Salary cost per case at 1 year (Managed care)	5 visits/case	218.75 baht/case
Salary cost per case at 1 year (Conventional care)	2.6 visits/case	113.75 baht/case
Nurses		
Percentage of salary per month	100% of salary base	22,666.67
Salary cost per working day	20	1,133.33 baht/working day
Salary cost per case	40 case/day	28.33 bath/OPD visit
Salary cost per case at 1 year (Managed care)	5 visits/case	141.67 baht/case
Salary cost per case at 1 year (Conventional care)	2.6 visits/case	74.25 baht/case

3.2 Capital cost

Table 24 Capital cost at the outpatient department

	Conventional care	Managed care
Equivalent annual cost	506,420.00	587,499.68
Average capital cost per day	4,220.17	4,895.83
Average capital cost per OPD visit	105.50	122.40
Capital cost for each intervention	274.31	611.98

3.3 Medical care cost

Table 25 Medical care cost at the outpatient department

Group	OPD	
	Annual Cost/patient	SD
Managed care	10,029	17,959
Conventional care	*2,188.30	-

*Based on interviewing orthopedists, conventional care should be provided calcium vitamin D, drug cost, and OPD service per visit.

Table 26 Costs of both interventions at 1 year in post-hip fracture state

Department	Conventional care			Managed care		
	LC	CC	MC	LC	CC	MC
OR	2,378	804.78	-	2,345	1,191.75	-
IPD	16,800	6,186.30	46,890.36	10,583.14	*4,949.04	64,795
OPD	188	274.31	*2,188.30	360.42	611.98	10,029
	19,366	7,265.39	41,064.89	13,288.56	21,122.13	75,164.75
Total cost	67,696.28 baht			109,575.44 baht		

4.11.2 Recurrent hip fracture state

The recurrent hip fracture state w similar to the post hip fracture state.

4.11.3 Vertebral fracture state

The data cost in this state is based on assumptions from interviewing orthopedists. The average length of stay was 7 days, operation time was 2 hours per case.

Table 27 Costs of both interventions in vertebral fracture state

Group	Conventional care			Managed care		
	LC	CC	MC	LC	CC	MC
OR	1,803.66	619.06	-	1,803.66	916.72	-
IPD	7,839.37	2,886.94	21,882.17	6,173.30	2,886.94	37,797.08

OPD	188	274.31	*2,188.30	360.42	611.98	10,029.00
	9,831.03	3,780.31	24,070.47	8,337.38	4,415.64	47,826.08
Total cost	37,681.81			60,579.10		

4.11.4 Wrist fracture state

The data cost in this state is based on assumptions from interviewing orthopedists. The average length of stay is 3 days, operation time is 2 hours per case.

Table 28 Costs of both interventions in wrist fracture state

Group	Conventional care			Managed care		
	LC	CC	MC	LC	CC	MC
OR	1,803.66	619.06		1,803.66	916.72	-
IPD	2645.70	1,237.26	9,378.07	2645.70	1,237.26	16,198.75
OPD	188	274.31	*2,188.30	360.42	611.98	10,029.00
	4,637.36	2,130.37	11,566.37	4809.78	2765.96	26,227.75
Total cost	18,334.36			33,803.49		

Table 29 Summary of state cost and transition cost of each disease state

Cost	Mean
Cost of Conventional care	
State cost	1,614
-Drug cost	1,094
-OPD Visit Cost	520
Transition cost	
- Hip Fracture cost	75,708.96
- Vertebral fracture cost	37,681.81
- Wrist fracture cost	18,334.36
Cost of Managed care	

State cost	9,144.5
-Drug cost	8,144.5
-OPD Visit Cost	1000
Transition Cost	
- Hip Fracture cost	94,865.07
- Vertebral fracture cost	60,579.1
- Wrist fracture cost	33,803.49

4.12 Model assumptions

1. All patients with osteoporotic hip fractures are enrolled in the model.

2. Patients are assessed at 1-year after sustained osteoporotic hip fracture.

3. State cost is provided health resource that using in the operation room (OR) and inpatient department (IPD). Transition cost is provided recurrent hip fracture cost, vertebral fracture cost, and wrist fracture cost.

4. Cost of death state is assumed to be zero.

4.13 Data Analysis and Statistics

The incremental cost-effectiveness ratio (ICER) is estimated by the difference in costs by the difference in mean effects for a given model of managed care compared to conventional intervention.

$$ICER = \frac{\text{Cost of managed care} - \text{Cost of conventional care}}{\text{Life-year gained of managed care} - \text{Life-year gained of conventional care}}$$

4.14 Dealing with uncertainty

To deal with uncertainty, this study is provided a Probabilistic Sensitivity Analysis (PSA) to measure model inputs. Probability distributions are available for cost and outcome variables in one-way sensitivity analysis. PSA is accounted to measure the uncertainty input variables. In addition, tornado diagram is used to measure varied across the possible range in each parameter at that time. One thousand samples are generated in a Monte Carlo Simulation to select a value of each parameter for randomization and calculate expected costs and outcomes. Results are reported in terms of cost-effectiveness acceptability curves. All analyses are conducted using the Tree-age pro-2019.

4.15 Discounting

Both costs and outcomes are happened at 1 year will be accounted into the present value of the base year. Discount rate at 3% per year are used in base-case calculated both cost and outcome. One-way sensitivity analysis is conducted, the discount rate at 0% and 5% are adopted.

CHAPTER V RESULTS AND DISCUSSION

5.1 Base-case characteristic

Conventional care

We obtained data of 110 patients who met eligibility between 2012 and 2013. There were 87 females (79.1%) and 23 males (20.9%) with a mean age of 80 years old. The main fracture sites were at the neck of the femur (57.0%), the intertrochanter (40.0%), and subtrochanteric (3.0%). Most of the patients underwent operations at 90%, surgical procedures were provided such as fixation (60.0%), followed by hemiarthroplasty (39.0%), and total hip replacement (1.0%). The mean length of stay during admission was 15 days (SD=6.13).

Managed care

A total eligible patient of 82 was included between 2017 and 2019 with the mean age at 79 years old. Most of the patients underwent surgery (96%). Their main fracture sites were at the neck of the femur (52.0%), followed by the intertrochanter (46.0%) and subtrochanteric (1.0%). For patients who underwent operations, fixation was the main method (55.0%), followed by hemiarthroplasty (44.0%) and total hip replacement (1.0%). The mean length of stay during admission was 12 days (SD=6.83).

At baseline characteristics, the study found that the length of stay between the two groups was statistically significant decreasing the hospitalization days from 15 days in conventional care to 12 days in managed care (P=0.003).

Table 30 Descriptive characteristics of the participants

Baseline characteristics	Managed care (N=82)	Conventional care (N=110)	p-value*
Age (years), mean ± SD	79.33 (10.32)	80.15 (9.19)	0.563
Female, N (%)	66 (80.5%)	87(79.1%)	0.812
Type of fracture, N (%)			0.490

Baseline characteristics	Managed care (N=82)	Conventional care (N=110)	p-value*
Neck of femur	42 (52%)	63 (57%)	
Intertrochanter	38 (46%)	44 (40%)	
Subtrochanter	1 (1%)	3 (3%)	
Type of treatment, N (%)			0.118
Conservative	4 (4%)	12 (10%)	
Operative	78 (96%)	98 (90%)	
Type of operations, N (%)			**0.506**
Fixation	43 (55)	59 (60)	
Hemiarthroplasty	34 (44)	38 (39)	
Total hip replacement	1 (1)	1 (1)	
Length of Stay (days), mean ± SD	11.84 (6.83)	14.63(6.13)	0.003

*P < 0.05 is significant.

At a one-year follow-up, the study found that the death rate was decreasing from 11.8% in conventional care to 3.7% in managed care (P=0.045). In addition, the rate of the initiated osteoporosis drug, rate of BMD test, adherence, and the number of OPD visits was a significant increase in managed care when compared to conventional care (P<0.001). In terms of subsequent fracture, it was no evidence which reported in this result, thus the result in managed care was derived from interview orthopedist who experienced in the treatment of the osteoporotic hip fracture. In contrast, conventional care had a limitation of prediction because, at that time period (2012-2013), there was no classified fragility hip fracture (low-energy trauma) from other causes of hip fracture (high energy trauma or secondary osteoporosis) which mean that orthopedists were less focusing on fragility hip fracture.

Table 31 Results in a follow-up time period of 1 year

Characteristics	Managed care (N=82)	Conventional care (N=110)	P-value*
Death, N (%)	3 (3.7)	13 (11.8)	0.045
Secondary fracture, N (%)	4 (4.9) (interview orthopedist)	NA	
Post-injury osteoporotic medicine, N (%)	N=46	N=62	<0.0001
- No	7 {15)	42 (68)	
- Yes	39 (85)	20 (32)	
BMD test post-injury	60 (73)	15 (14)	<0.0001
OPD visit (times), mean (SD)	5 (1.76)	2 (1.58)	<0.0001
Adherence, mean (95% CI)	0.82 (0.74-0.91)	0.30 (0.21-0.39)	<0.0001

******P < 0.05 is significant.

5.2 Base-case analysis

Using the provider perspective, the average cost and average life-year gained from managed care and conventional care.

Table 32 Costs-effectiveness results base-case analysis

Study group	Average cost (baht)	Average life-year gained
Conventional care	419,353	8.2
Managed care	263,474	12.3
Difference	-155,879	4.1
ICER/LY	-38,019 (Managed care is dominant)	

For base-case analysis was showed that over their lifetime, the average cost in conventional care was 419,353 baht and yielded the average life-year gained at 8.2

life-year gained. In addition, the average cost in managed care was 263,474 baht and yielded the average life-year gained at 12.3 life-year gained.

According to the base-case analysis, among osteoporotic hip fracture patients revealed that managed care would have a high life-year gained (4.1) more than conventional care. From the result of the incremental cost, the managed care was cost-saving at 38,019 baht for one additional life-year gained. Thus, the managed care was dominant because it cost less and had more life-year gained

5.3 Sensitivity analysis

Deterministic Sensitivity Analysis

A second-order Monte Carlo simulation is used to measure probabilistic sensitivity analysis. The scatter plots of incremental cost and incremental effectiveness are illustrated in Figure 8. Most incremental cost-effectiveness ratios scatter plots are in the right upper quadrant which means that managed care is more effective.

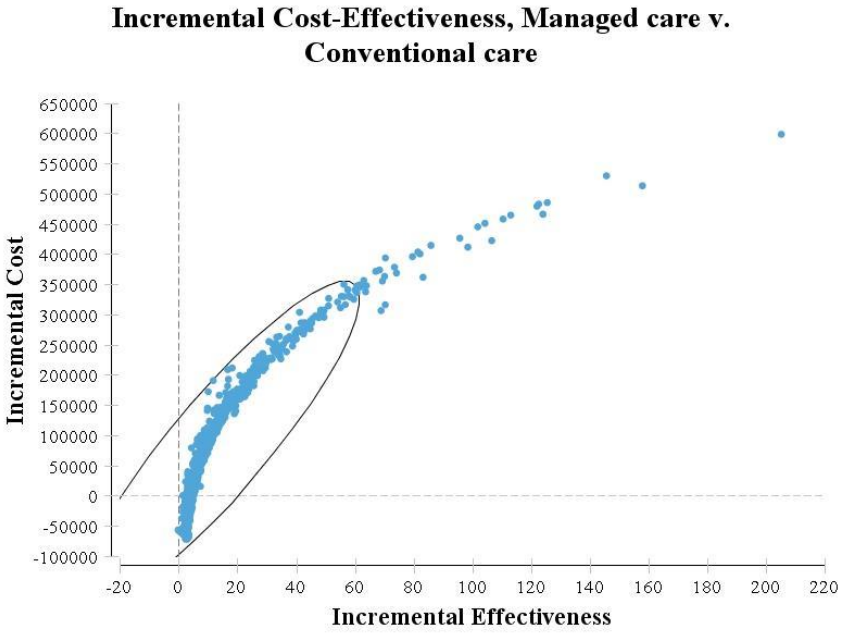


Figure 8 The cost-effectiveness acceptability curve

One-way sensitivity analysis

In one-way sensitivity analyses, the parameter is varied one by one in the range of 95% Confidence interval.

The Cost-Effectiveness Acceptability Curve (CEAC) is represented in Figure 8. The CEAC shows the probability of cost-effectiveness of each intervention for willingness to pay or decision threshold. The results illustrate managed care is preferable when willingness to pay is higher than 25,000 baht. At the willingness to pay at 160,000 and 480,000 baht (one- and three-times GDP per capita), the probability showed that managed care was cost-effective at 89%.

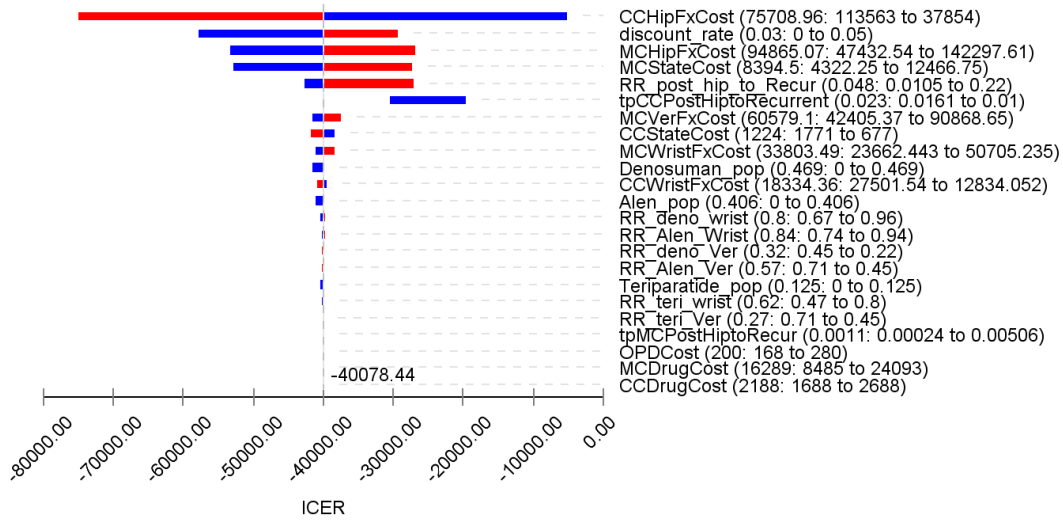


Figure 9 Tornado diagram of one-way sensitivity analyses

Abbreviation of parameters in Tornado diagram

Redline = High value

Blueline = Low value

CCHipFxCost = Hip fracture cost of conventional care.

Discount_rate= Discount rate

MCHipFxCost= Hip fracture cost of managed care

MCStateCost= State cost of managed care

RR_post_hip_to_Recur= The relative risk of recurrent hip fracture in patients who were provided managed care.

CCStateCost= State cost of conventional care

MCWristFxCost = Wrist fracture cost of managed care

Denosumap_pop = The proportion of patients who received denosumab.

CCWristFxCost = Wrist fracture cost of conventional care

Alen_pop = The proportion of patients who received alendronate.

RR_deno_Wrist = The relative risk of wrist fracture in patients who taking denosumab.

RR_Alen_Wrist = The relative risk of wrist fracture in patients who taking alendronate.

RR_deno_Ver = The relative risk of wrist fracture in patients who taking denosumab

RR_Alen_Ver = The relative risk of vertebral fracture in patients who taking alendronate.

Teriparatide_pop = The proportion of patients who received teriparatide.

RR_teri_Wrist= The relative risk of wrist fracture in patients who taking teriparatide.

RR_teri_Ver= The relative risk of vertebral fracture in patients who taking teriparatide.

OPDCost= OPD Visit cost

MCDrugCost= Drug cost of managed care

CCDrugCost= Drug cost of conventional care

According to the Tornado diagram (Figure 8), the two most sensitive parameters are hip fracture cost of conventional care and discount rate. The incremental cost per life-year gain is changed in the opposite direction which means that when the baseline of hip fracture cost in conventional care changes from 37,854 baht to 113,563 baht but the incremental cost per life-year gain is decreasing. In addition, the incremental cost per life-year gain is changed in the same direction on the discount rate which means that when the discount rate changes between 0% and 5%, the incremental cost per life-year gain is increasing.

The next three parameters which affected the incremental cost per life-year gain are hip fracture cost of managed care, state cost of managed care, and the relative risk of recurrent hip fracture. These parameters are changed then the incremental cost per life-year gain changed in the same direction.

For other transition costs such as vertebral fracture cost and wrist, fracture cost has little impact on the results of the incremental cost per life-year gain in the present study.

5.4 Discussion

According to the definition of managed care which provides perioperative management and secondary fracture prevention (patient identification, assessment, and treatment initiation) in a high-risk group of osteoporosis patients, there is no study focusing on these processes in Thailand. Although there are a few studies of cost-effectiveness analysis of osteoporosis medicines [48], most of the studies are used societal perspective and just provided medical care cost in direct medical cost (the current study includes labor cost, capital cost, and medical care cost). In terms of the study at the hospital level, there are two studies from the Ramathibodhi hospital such as the study of cost-utility analysis of osteoporotic hip fracture in Thai and the study of a cost analysis of osteoporotic hip fracture from, the results report cost per QALY and cost of hip fracture treatment that occurs in one year and both existing studies has no comparator to compare the outcomes. In addition, the studies are not performed the Markov model to evaluate the progression of the disease and the sensitivity analysis to conduct the robustness of variables. From the different methodology, the results of existing studies cannot apply to managed care which provides perioperative and post-fracture care directly.

This is the first study to evaluate cost-effectiveness analysis of managed care for osteoporosis compares to conventional care by using a Markov model from a provider perspective and patient perspective. Patients who sustained osteoporotic hip fractures will have low bone mass density and have a high tendency to face recurrent fractures. In the evaluation, a Markov model is used to handle the chronic disease which has progress to move from one health state to another health state during the remaining lifetime. The outcomes of a Markov model are accumulative cost and life years. According to the results, we can compare across different programs and can address the issues or the opportunity of adding more intervention in existing managed care programs.

Effectiveness data are obtained from the hospital database, the study provides a cost that occurs in the operating room (OR), inpatient department (IPD), an outpatient department (OPD). In detail for each department, labor cost, capital cost,

and medical care cost are included in the calculation. The clinical outcomes of a one-year follow-up in this study represent the current situation in the hospital after adding more attention to managing fragility hip fracture patients. The results of the study can be distributed to other hospitals that have the similar cost structure and service levels as King Chulalongkorn Memorial Hospital.

According to World Health Organization, the cost-effectiveness of an intervention is represented by the value between one and three times GDP per capita. The present study shows that the result in base-case analysis managed care is cost-effective (cost-saving) when compares to conventional care in King Chulalongkorn Memorial Hospital. The cost-effectiveness acceptability curve illustrates that at the willingness to pay at 160,000 and 480,000 baht (one and three times GDP per capita), the probability efficacy of managed care is cost-effective at 89% when compares to conventional care.

The results of the base-case analysis report that managed care was cost-saving when compared to conventional care. There were the reasons as follows.

1. Managed care has high efficacy of recurrent fracture reduction and decrease.
2. The survival of patients in managed care is longer than conventional care.

Even though transition costs and state costs of managed care are costly but the transition probability from a post-hip fracture state to another state is lower than conventional care. According to the results in managed care, rate of BMD test, rate of drug treatment, and the number of OPD visit increases, these factors affect high efficacy of reduction in recurrent fracture. After admission, patients need to follow their surgical wound with an orthopedic surgeon, thus it is easier to inform BMD tests and educate how important it of taking drugs if they have low bone mass density. In the past, patients just follow their surgical wounds, orthopedists are not paying attention to whether patients sustain fragility hip fracture from osteoporosis or not. For these reasons, patients in managed care groups have a high tendency to stay cheap. The chance of transferring to other states was low because of its low recurrent fracture rate. In addition, the efficacy of reduction in death after sustained hip fracture at one year in managed care was higher than conventional care so patients in this group are likely to yield more life-year gained.

The results of one-way sensitivity analysis report that the cost of hip fracture in conventional care and the discount rate are the most sensitive parameters. The incremental cost per life-year gain was changed in the opposite direction when baseline of hip fracture costs in conventional care increase, the incremental cost per life-year gained decrease. Cost of hip fracture related to the recurrent fracture. Another parameter is the discount rate, when it changes from the value at base-case then the incremental cost per life-year gain changes in the same direction. The discount rate has more impact in the current study because the rate of mortality at subsequent years after sustained fracture is not different from the general population, therefore, during the remaining lifetime, both costs and outcomes are measured with discounting.

Moreover, hip fracture cost of managed care, state cost of managed care, and the relative risk of recurrent hip fracture are affected on the incremental cost-effectiveness ratio. For hip fracture cost of managed care, it is related to the transition probability of recurrent hip fracture and this cost is the highest when compared to other fracture costs, state cost of managed care is provided drug cost and OPD visit cost which occurs at the outpatient department. These costs are important because they refer to the cost of management in long-term following up. In addition, the relative risk of recurrent hip fracture is sensitive to incremental cost-effectiveness because it represents the efficacy of reduction in recurrent hip fracture and is related to the transition probability of recurrent hip fracture directly.

The results of this study should be contributed to the setting of the hospital which has orthopedists, similar cost and service level.

CHAPTER VI CONCLUSION AND SUGGESTION

6.1 Conclusion

Fragility fracture is the most severe complication of osteoporosis and causes the burdens of morbidity, mortality, and finance. The most fracture site is an osteoporotic hip fracture that can cause more chronic pain, morbidity, and mortality. In addition, more than half of patients who sustained prior hip fractures are likely to have more incidence of recurrent fracture. Even though fragility fracture patients will occur a high incidence of recurrent fracture, but post-fracture management is still unrecognized.

According to the gap of subsequent fracture management, two major models of care are widely established worldwide such as the Fracture Liaison Service and Orthogeriatric Service. The objectives are provided how to maximize profit in implementation program, by adapting their practice based on an appropriate structure in each health service.

In terms of managed care at King Chulalongkorn Memorial Hospital, we follow an indication for treatment of osteoporosis (figure 4) in a high-risk group who have a prior osteoporotic hip fracture. Orthopedist follows protocols from International Osteoporosis Foundation (IOF) and Thai Osteoporosis Foundation (TOPF) that using in osteoporosis management have been already implemented. In this study, there is a comparative group as the conventional care, the definition of conventional care is defined scope of responsibility only perioperative care (the pathway of taking care patient in the past). The situation at that time has no identification, assessment, and treatment initiation in fragility hip fracture. The osteoporosis assessment and treatment initiation depend on the orthopedist's decision, at that time there are a few orthopedists who are interested in this matter.

The methodology that using in this study is a Markov model, it is appropriate to perform this method in evaluating chronic disease. Osteoporotic hip fracture is likely to occur refracture, from the low bone mass density, patients will sustain not only hip fracture but also vertebral fracture and wrist fracture as well. The Markov state consists of Post hip fracture, Recurrent hip fracture, Vertebral fracture, Wrist

fracture, and Dead. The outcomes of the Markov model are accumulative cost and life-year gained. A cycle length of 1 year was chosen to measure the disease progression. The time horizon of the analysis was lifetime from the remaining their lifetime to aged 100 years old or died. As a result, outcomes and costs will be obtained in terms of the accumulated life years and costs at the end of the evaluation.

According to the results show that managed care has a statistically significant outcome at a one-year follow-up compared to conventional care. The death rate is decreasing from 11.8% in conventional care to 3.7% in managed care (P=0.045). In addition, the rate of the initiated osteoporosis drug, rate of BMD test, adherence, and the number of OPD visits are a significant increase in managed care when compared to conventional care (P<0.001). In terms of subsequent fracture, the study derives from meta-analysis, the result shown in relative risk with 95% Confidence Interval. For base-case analysis was showed that over their lifetime, the average cost in conventional care was 419,353 baht and yielded the average life-year gained at 8.2 life-year gained. In addition, the average cost in managed care was 263,474 baht and yielded the average life-year gained at 12.3 life-year gained.

According to the base-case analysis, among osteoporotic hip fracture patients revealed that managed care would be had a high life-year gained (4.1) more than conventional care. From the result of the incremental cost, the managed care was cost-saving at 38,019 baht for one additional life-year gained. Thus, the managed care was dominant because it cost less and had more life-year gained

In conclusion, managed care is post-fracture recurrent prevention which can be closed the osteoporosis treatment gap and decrease fracture complications after sustained osteoporotic hip fracture and is suggested to be cost-saving.

6.2 Limitations of the study

1. Costs of osteoporosis treatment are derived from the database of hospital and data collection from orthopedics department by interview orthopedist or review orthopedics record, these data sources provide medical care cost that occurred in

inpatient and outpatient department. Capital cost is obtained from the previous study of patient service in King Chulalongkorn Memorial Hospital and adjusted to 2020 by using Consumer Price Index (CPI). According to CPI that using cost adjustment, based on health care service cost, the inflation rate of this product was not changed rapidly when compared to other products. In addition, labor costs and some costs of treatment in conventional care were based on the orthopedist's assumption. Moreover, this study was not provided the cost of complications from fracture and the cost of an adverse event from osteoporosis drugs. According to limitations, the costs of treatment are an underestimation.

2. Cost to charge ratio was used at 0.8 from the general administration information of the hospital because King Chulalongkorn Memorial Hospital was not available.

3. Lack of some clinical data in existing such as recurrent rate of fracture, history of other fracture sites has not been provided in medical record yet.

4. This study was conducted in only the orthopedics department at King Chulalongkorn Memorial Hospital. Cost and clinical effectiveness might be the difference in other hospital service levels. Therefore, it was difficult to generalize to other hospitals that had different cost structures and service levels.

6.3 Policy suggestion

The results show that managed care is cost-saving, the key factor is recognizing the risk of refracture through identification, assessment, and enhancing bone healthy by initiating drug treatment. At the willingness to pay one to three times GDP per capita, managed care is cost-effective compared to conventional care.

Cost of the osteoporosis drug, the current situation, patients in Universal Coverage Scheme (UCS) and Social Security Scheme (SSS) cannot reimburse the cost of osteoporosis (denosumab, this kind of drug is the highest efficacy of fracture reduction). The results from this study, the National Health Security Office (NHSO) and Social Security Scheme (SSS) should consider including this drug in the benefits package.

The results of this study should support policymakers at King Chulalongkorn Memorial Hospital to consider expanding the special clinic as the Metabolic Bone Clinic to treat osteoporosis patients which provides not only hip fracture but also other fracture sites.

6.4 Suggestion for further study

The results of managed care show effective management of osteoporotic hip fracture patients by orthopedist role. In terms of the study of clinical and cost-effectiveness by a dedicated coordinator need to provide further study and also provides a multidisciplinary team that comprises family physicians, nurses, physical therapists, nutritionists, and other health personnel who respond for taking care of osteoporosis patients. Further study could be evaluated more both cost and clinical outcome on primary fracture prevention program such as assessment on BMD screening in people who aged 50 and over.

ANNEX

COA No. 1043/2020

IRB No. 482/63

INSTITUTIONAL REVIEW BOARD

Faculty of Medicine, Chulalongkorn University

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Certificate of Approval

The Institutional Review Board of the Faculty of Medicine, Chulalongkorn University, Bangkok, Thailand, has approved the following study which is to be carried out in compliance with the International guidelines for human research protection as Declaration of Helsinki, The Belmont Report, CIOMS Guideline and International Conference on Harmonization in Good Clinical Practice (ICH-GCP)

Study Title : Cost-Effectiveness Analysis of Managed Care for Osteoporosis.

Study Code : -

Principal Investigator : Miss Benchaporn Kotnarin

Affiliation of PI : Faculty of Economics, Chulalongkorn University.

Review Method : Expedited

Continuing Report : At least once annually or submit the final report if finished.

Document Reviewed :

1. Research proposal Version 2.0 Date 11 August 2020
2. Protocol Synopsis Version 2.0 Date 11 Aug 2020
3. Case Record Form Version 1.0 Date 08 June 2020
4. Curriculum Vitae and GCP Training
   - Miss Benchaporn Kotnarin
   - Prof. Dr. Siripen Supakankunti, M.S., M.A.

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Vice-Chairman, Acting Chairman

The Institutional Review Board

Signature .....

(Assistant Professor Prapapan Rajatapiti MD, PhD)

Member and Secretary

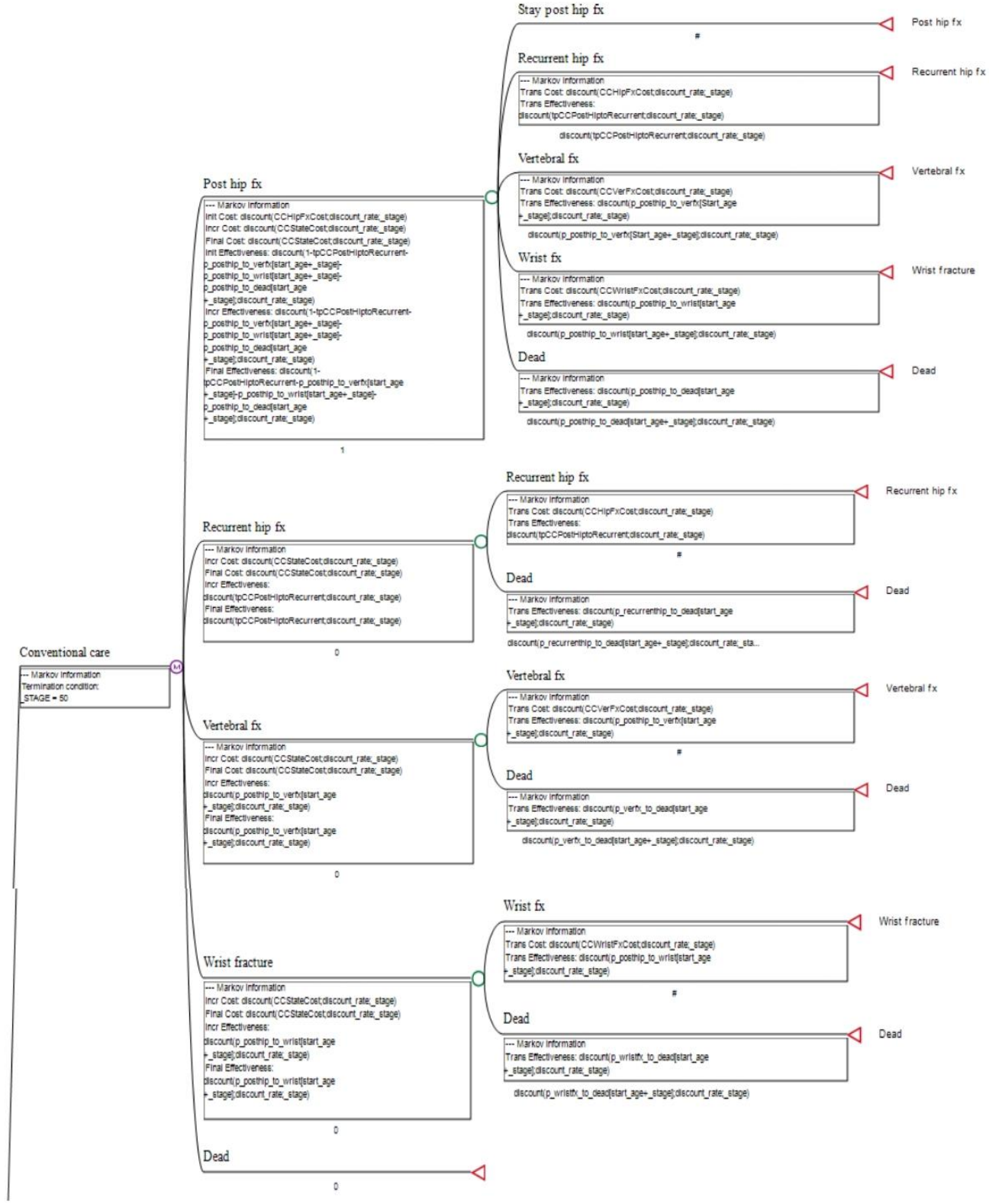
The Institutional Review Board

Date of Approval : August 19, 2020

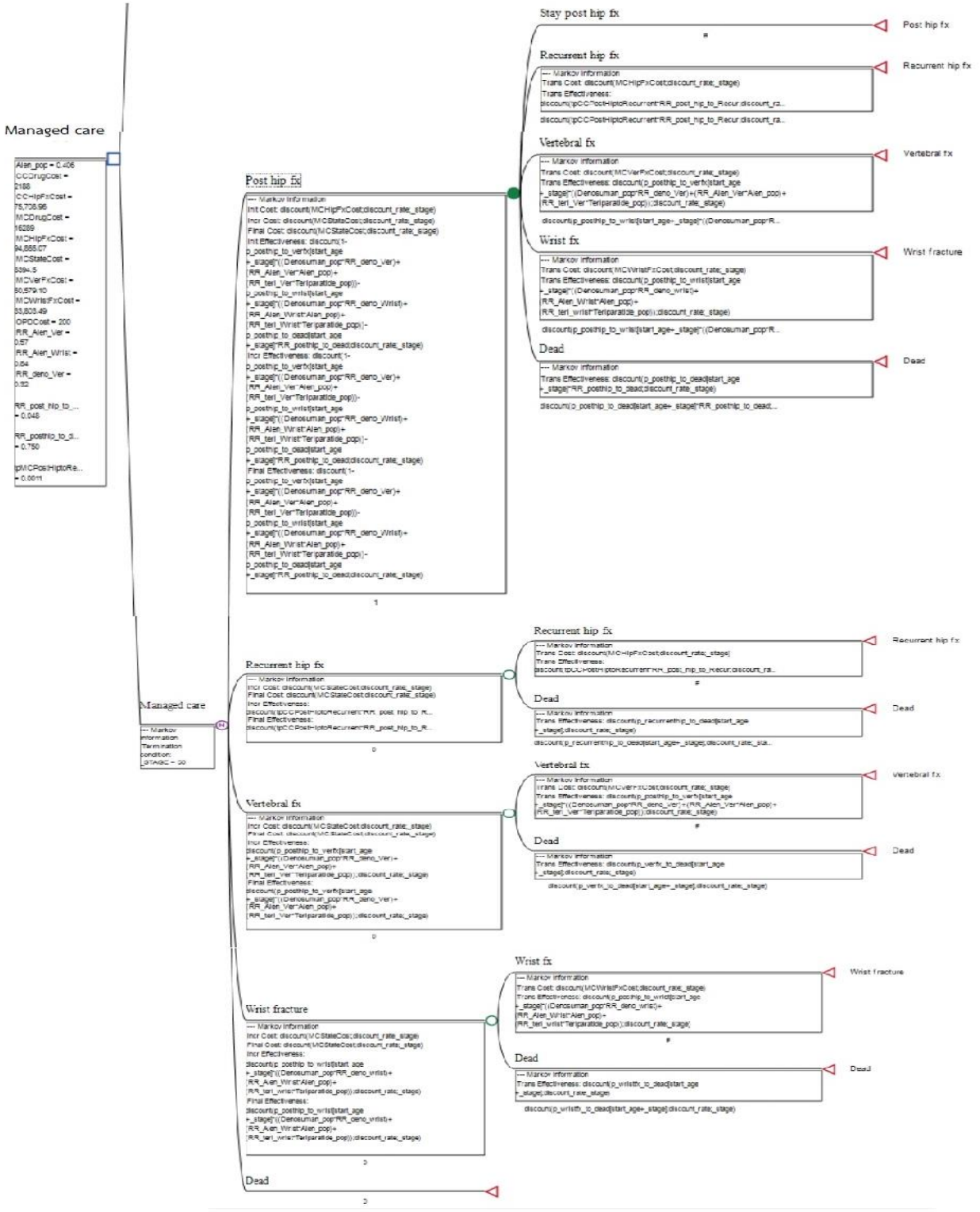
Approval Expire Date : August 18, 2021

Approval granted is subject to the following conditions: (see back of this Certificate)

Annex 1 Certificate of Approval



Annex 2 Example of Markov Decision tree in Tree-age Pro (Conventional care)



Annex 3 Example of Markov Decision tree in Tree-age Pro (Manage care)

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