

An economic evaluation of diabetes mellitus management in South East Asia

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ABSTRACT

Background: In 2014, it was estimated that there were 422 million adults living with diabetes while there were 108 million ones in 1980. Since, 1980, the prevalence (age-standardized) of diabetes has almost doubled globally, increasing from 4.7% to 8.5% in the adult population. Diabetes caused 1.5 million death in 2012. According to WHO, in 2013, one of the world's most significant health expenditure was diabetes mellitus, about 612 billion dollars, or about 11% of the total direct health expenditure in the world. In 2014, there were 96 million adults with diabetes in 11 countries in the South East Asia region, with the prevalence of diabetes among adult patients increasing from 4.1% in 1980's to 8.6% in 2014. **Objective:**The aim of the study was to identify and review the original articles which evaluated the economic impact of diabetes mellitus management in South East Asia. **Method:** PubMed and ProQuest database were reviewed to identify the economic evaluation of DMT2 management in South East Asia. The inclusion criteria used in this study were all the original research articles published between 2005 and 2014 on the economic evaluation of DMT2 management in South East Asia, using cost-minimization analysis, cost-benefit analysis, cost-effectiveness analysis, as well as cost-utility analysis. The articles were assessed using the checklist of the Consolidated Health Economic Evaluation Reporting Standards (CHEERS). **Result:** 15 articles were potentially related to this study. The evaluation of the economic impact of DMT2 management in South East Asia included the cost, medical and non-medical cost-effectiveness, assessment and acceptance from the community. The uses of DMT2 single-drug or combination drugs could be used as a strategy to treat or reduce DMT2 disease and avoid complications caused by this disease, by providing better cost-effectiveness. The diabetic patients were expected to become more frequently disciplined in medical use and also in purchase of drugs. Quality-adjusted life year (QALY) was the main outcome to appraise the effectiveness of these studies. Incremental cost-effectiveness ratio (ICER) was computed in the range from \$93,896.52 to \$110,713.08 per QALY. **Conclusion:** Early DMT2 drugs treatment was a cost-effective alternative in the Southeast Asian countries. Complications have had a significant impact on the costs of managing type 2 diabetes mellitus. The prevention of diabetic complications would not only benefit the patients but potentially reduce the overall healthcare expenditure.

Keywords: Economic Evaluation, DMT2, South East Asia.

Introduction

Diabetes Mellitus is a group of metabolic disorders characterized by increased blood glucose concentration. Type 1 diabetes known as insulin-dependent or childhood-onset

diabetes is characterized by deficient insulin production in the body. Meanwhile, Type 2 diabetes is known as non-insulin dependent ^[1]. Type 2 diabetes is often less marked, and as a result, it may be diagnosed several years after onset when the complications have already arose ^[2]. It is generally associated with numbers of long-term severe complications which are a major cause of morbidity, hospitalization, and mortality for diabetic patients ^[3]. Both the economic expenditure for healthcare systems and the patients' risk for disability, death, and decreased quality of life are essentially enhanced by these complications ^[4]. Due to the direct medical costs and loss of work and wages which are the consequences of diabetes and its complications, people with diabetes and their families and

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also health systems and national economies have to deal with the remarkable economic loss^[1].

Globally, the prevalence of diabetes among adults has risen from 108 million people in 1980 to 422 million people in 2014. The most remarkable rises have been observed in East Asia and South Asia; and in 2014, the highest number of people with diabetes were found to be in these areas; 106 million and 86 million; respectively ^[5]. The global prevalence of this disease was estimated to be 151 million in 2000, 194 million in 2003, 246 million in 2006, 285 million in 2009, 366 million in 2011 and 382 million in 2013 by the International Diabetes Federation (IDF). The global diabetes prevalence in adult aged 20-79 years was estimated to be 8.8% of the total world population in 2015 including 415 million ^[6]. Western Pacific Region included the highest number of people with diabetes (153.2 million). And, more than half (56%) of all people with diabetes were found to be living the South East Asia Region or Western Pacific Region ^[6].

The high incidence of diabetes has been observed particularly in Southeast Asia's four most populous countries - Indonesia, Philippines, Thailand, and Vietnam- which collectively have over 500 million people. Indonesia alone has over 10 million diabetic patients, according to the data from the International Diabetes Federation (IDF). In Thailand, 4 million people reportedly had diabetes in 2015. In the same year, in Philippines and Vietnam, 3.5 million people were reported to have diabetes mellitus ^[5].

The region with the highest proportion of death from diabetes was the Western Pacific Region, about 16% of all cause of mortality in the region, and 75.5% of all diabetes death occurred in people aged up to 69 years. In low-income countries, diabetes deaths were in people under the age of 60, whereas this portion in high-income country was 29.6% ^[6]. South East Asia was the second highest number of deaths in 2015 after the western Pacific region, with 1.2 million of deaths (IDF).

Diabetes imposes a significant economic burden on the global health-care system. This burden can be measured through direct medical cost, indirect medical cost associated with productivity loss, premature mortality and negative impact on the national gross domestic product (GDP) ^[1]. Direct medical cost associated with diabetes include expenditure for preventing and treating diabetes and its complications. These costs include inpatient hospital cares, outpatient and emergency cares, medication and medical supplies, and long-term care ^[1, 7]. According to NCD-RisC report in 2016, the direct cost of diabetes was over \$825 billion per year on the global economy ^[5]. There are also some indirect costs related to diabetes which include health-related days absence from work and normal activities, free time loss, lost earning capacity from permanent disability and lost productivity from premature mortality. It also comprises of care in nursing home and informal care ^[7].

Health expenditure at a total of USD 7.3 billion to USD12.4 billion was spent on the 78 million people living with diabetes

in 2015, which amounted to 12% of the health budget of the region. In comparison with the other IDF regions, the lowest health expenditure was spent per person with diabetes (USD93 to USD158) in the Southeast Asia Region. In 2017, it was shown that the average cost per person with diabetes who lived in southeast Asia was accrued to be USD115.92. In the meantime, in North America and the Caribbean, diabetes cost per person stood over USD8000 (www.statista.com).

Researches on the cost-effectiveness has been done in several South East Asian countries. To obtain comprehensive information about the economic evaluation, community acceptance, and willingness to pay any intervention on diabetes mellitus management, a systematic review has been done. The result of this systematic review has been expected to be used as a consideration of diabetes mellitus program policy in South East Asia.

Objective

This study aimed to identify and review the original articles which evaluated the economic impact of diabetes mellitus management in South East Asia

Methods

Search Study

For finding the relevant studies for this review, a three-stage process was used to search through the titles and abstracts. At the first stage, the studies were chosen based on the abstracts and titles. Irrelevant titles, abstracts only papers and duplicates were rejected clearly. In the second stage, the results were cross-checked, and their results and retained candidate studies were collected for full paper screening. Finally, the full papers of the studies were read thoroughly.

Studies about the economic evaluation of diabetes mellitus in South East Asia were searched in PubMed and ProQuest. The terms used for this review search were: "economic evaluation (cost minimization, cost-benefit, cost effectiveness and cost utility)," and "diabetes mellitus management in South East Asia". The data was obtained online and filtered based on the inclusion and exclusion criteria. The inclusion criteria were all sources published between 2005 – 2014 in full text which were primarily written in English.

Inclusion criteria

The study selection was further guided by the following inclusion criteria: (i) The papers should have been original research articles published in peer-reviewed journals. (ii) The types of economic evaluation including: cost-effectiveness, cost-utility, or cost-benefit analyses should have been covered. (iii) The participants of the studies should have been the targeted population groups. (iv) The interventions such as: uses of oral antidiabetic, screening, government policy, and community program should have been included. (v) The outcomes should have included cost per QALY (Quality Adjusted Life Years), cost per life year, cost per DALY

(Disability Adjusted Life Years), cost per diabetes cases, and other related outcomes. And finally, (vi) Studies should have been published between January 2005 and December 2014.

Data Extraction

Data extraction using a standardized data extraction form was done according to the Consolidated Health Economic Evaluation Statement (CHEERS) [8]. The kind of economic evaluation, the subjects' features, the intervention details, the comparator, the analytical model which was used, the effectiveness data, the sensitivity analysis, and the reported results related to the review were all included in the obtained data. The extracted fields have been represented in Table 1.

Table 1. Criteria for article analysis

| | |
|-------------------------------------|---|
| Design Study | Setting and location |
| | Type of study |
| | Study perspective |
| | Time horizons |
| | Discount rate |
| | Choice of model |
| Information about Diabetes Mellitus | General information about diabetes |
| | Strategy of diabetes mellitus management |
| | Study of efficacy and effectivity in diabetes mellitus management |
| Cost Component | Direct medical cost, direct non medical cost, indirect cost |
| | Estimating resource and cost |
| | Unit cost in diabetes mellitus management |
| | Source cost |
| Outcome measurement | Cost effectiveness criteria |
| | Incremental cost and outcomes |
| Result | Sensitivity analyses |

Result

A comprehensive review of the related literature found original articles about the economic impact or economic evaluation and community acceptance, and the willingness to pay for any intervention in diabetes mellitus in the South East Asia region. Articles with predefined keywords were added with country names, namely Brunei, Myanmar, Cambodia, Timor Leste, Indonesia, Laos, Malaysia, Philippines, Singapore, Thailand, and Vietnam. Articles obtained complied with the inclusion criteria of the PubMed and ProQuest. All of them met the study criteria and were included in the systematic review. Data from the selected articles have been presented in figure 1.

The results of the article screening were fifteen articles that satisfied the criteria which were relevant to the economic evaluation of diabetes mellitus. The articles were reviewed using CHEERS checklist covering the method (the study design) and the research results. The results of the review of the fifteen articles can be seen in Table 2 and Table 3.

The review yielded four studies that assessed the cost-effectiveness of oral antidiabetic drugs by different interventions.

The intervention included in this reviewed varied from preventing to treatment issues. The study in Waritchaphum Hospital with 30 beds found that the average public treatment cost per patient per year was 94.71 USD in 2008. Drug cost (25% of total cost), inpatient cost (24%), and outpatient visit cost (17%) were respectively the highest expenditures. Another investigation conducted in Warichaphum estimated the total cost of illness of 475 participants to be USD 418,696 USD in the financial year of 2008. 23% of the total cost included the direct medical cost, 43% was the direct nonmedical cost and 37 % was the other indirect costs. It was found that the average cost of illness for each diabetic patient was 881.47 USD in 2008, which equaled 21% of per capita gross domestic product of Thailand. Therefore the disease not only affected the individuals but also the family members, friends, and neighbors. The study discovered that the average time spent on informal caregiving was 112.38 hours per month. The estimated cost of informal caregiving was 110,713.08 USD using the opportunity cost approach and 93,896.52 USD using the proxy good method in 2008 [9-13].

Studies to compare the performance, cost and cost-effectiveness of the four screening method in identifying individuals with abnormal fasting on plasma glucose among Thai adults have been conducted at Chulalongkorn Memorial Hospital. The total cost screening per one newly detected patient was 59,12 to 69,62 US dollars. In comparison with the universal FPG test, all screening methods using questionnaires have been relatively more cost-effective. Moreover, their relative cost effectiveness was not notably different. The aim of using the screening program was identifying T2DM cases as early as possible, to avoid negative consequences. In Cambodia, the simulations of an ideal screening program that detected every patient within one year after the onset of T2DM have been conducted from the government's perspective. The cumulative number of T2DM related death cases from 2008 to 2028 was 462.000 instead of 476.000. Screening for T2DM was only cost-effective if the sensitivity of the test was high while the unit price was low [14].

Interventions by oral antidiabetic drugs (OAD) have been studied in some countries in Southeast Asia. Studies in Thailand and Malaysia showed that the use of irbesartan in the early stages had substantial clinical and economic benefits to reducing time in dialysis from 61% to 63% compared to the standard treatment, reducing the total cost by 9% in Thailand, and increasing life expectancy from 0.31 to 0.48 years. Researches to assess losartan have been done in

Malaysia and Singapore. Losartan plus CT (conventional antihypertensive therapy) reduced the number of days patients with ESRD (end stage renal disease) admitted in hospitals by 37.9 per patient over 3.5 years compared with CT alone. The reduction of ESRD days resulted in declining costs which ranged from 910 USD to 4346 USD per patient over 3.5 years. Pioglitazone has been administered in place of rosiglitazone in type 2 diabetic patients who could not control their blood glucose using the mixture of sulfonylurea and metformin. Pioglitazone had better clinical outcomes and higher lifetime cost. The incremental cost per QALY was 186,246 baht (5389 USD). The effect of pioglitazone on %HbA1c decrease was the most sensitive to the outcomes^[9, 10, 12, 15].

The complications of diabetes mellitus are often both macrovascular and microvascular. A study of these complication cases in Indonesia found that in total, 84.35 % patients T2DM had at least one of these complications, with 8.7 % having only microvascular complications, and 48.7% having only macrovascular complications, and 28.7 % of the total having both macrovascular and microvascular complications. The average cardiovascular was calculated to be 774.37 USD per patient in 6 months. It included the cost of medications, physician visits and monitoring cardiology tests^[3].

Screening programs to determine T2DM cases as early as possible have been conducted in some of the Southeast Asian countries to avoid all negative consequences^[4].

The successful management of diabetes includes the control of high glucose level (WHO, 2012). Some intervention has been done to manage diabetes Mellitus Type2 in South East Asian countries. The mostly used intervention provided in the T2DM treatment was the use of drugs, such as irbesartan and BIAsp 30. The use of irbesartan in the early stages has had broad clinical and economic benefits in increasing life expectancy from 0.31 to 0.48 years. Early irbesartan treatment had a 66% (Thailand) to 95% (Taiwan) success rate, which was dominant over late irbesartan^[9].

There is evidence that using BIAsp 30 as a cost-effective treatment option in some western and developed countries increased the life expectancy for more than 1 year, and was highly cost-effective, and as well, it reduced the risk of complications^[12]. Starting with BIAsp 30 in people with type 2 diabetes was found to be cost effective in all countries increasing the life expectancy at 1 – 30 years^[12].

There has been an immediate need for an intervention to develop an international policy framework for the prevention and control of non-communicable diseases. A most supportable strategy should include the interventions for preventing and controlling interventions such diseases and injuries that can be applied at the lowest cost in developing areas where there is a high prevalence of the disease. Most of the studied interventions were considered to be highly cost-effective, meaning that they generated one healthy year of life at the cost of <Int2000^[11]. Table 4 shows the results of oral antidiabetic drugs for T2DM treatment.

People with diabetes are prone to consequences in both short term and long term complications. The review yielded three studies about the cost for diabetic patients with complications, and one study about the cost of disability in diabetic patients. The presence of the late complications of diabetes has become a prime determinant of disability. Thus, disability and complications have become an economic burden for the countries, e.g., in this case Thailand and Indonesia^[3, 16, 17]. The chronic nature of the disease and its devastating complications have made it a very costly disease^[18].

The 2007 report revealed that most of the disabled patients had impaired vision in one or both eyes, hearing impairments, paresis, disability of limbs and amputations^[17]. The definition of disability and its severity of disability among the study participants used the Bartel index score. A person received a score based on whether they received help while carrying out these activities. The index of 100 indicated independence, 75-95 showed mildly disabled, 50-70 indicated moderately disabled, 25-45 represented severely disabled and 0-20 showed very severely disabled^[17].

The cost of informal caregiving which has been a cost component was never estimated in Thailand. Considering the economical perspectives, the costs related to the informal caregiving intensified the morbidity and mortality risk, because providing informal cares implies that informal care is not free. Informal care is the name given to the care provided by people from care recipients' social relations including family, friends, acquaintances and neighbors. Therefore, to formulate health policy, estimating the cost of informal care is necessary^[13]. Revealed preference method has been administered to determine the cost of informal care. For valuing informal care by opportunity approach, time cost approach was used as the based case. While valuing informal care using proxy good method, the earnings from household work and health and social workers were considered^[13].

Table 5 shows the cost of illness caused by diabetic complications, disability, and informal caregivers of diabetic patients. QALY and DALY were the popular outcomes used in 15 articles reviewed. In this review, eight studies were found using QALY and DALY as the outcomes, one study did not report, while the rest found different outcomes.

This review yielded three articles about the cost of diabetes mellitus, with two studies found in Thailand and one study found in Cambodia^[4, 18, 19]. In Thailand, diabetes was ranked fifth and third of top ten diseases among men and women; respectively based on the years of disability in their life^[18]. In Cambodia, diabetes caused 3,122 cases (2008) and 39.00 cases of disability adjusted year (DALY) per year in 2004^[4]. No economic modeling of T2DM was found in Cambodia^[4]. In Thailand, no economic modelling from provider perspective of diabetes mellitus was found. The component cost use in the treatment of diabetes has been shown in Table 6.

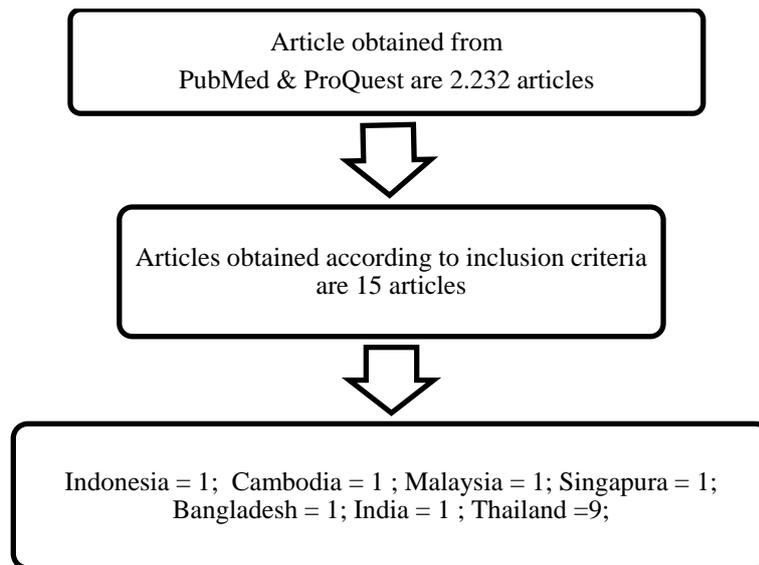


Figure 1. Study selection flowchart through literature search.

Table 2. Checklist item 15 articles using CHEERS instrument

| No. | STUDY (YEAR) | COUNTRY | 1 | 2 | 3 | 4 | 5 | 6 | 7 | 8 | 9 | 10 | 11a | 11b | 12 | 13a | 13b | 14 | 15 | 16 | 17 | 18 | 19 | 20a | 20b | 21 | 22 | 23 | 24 | SV | % | |
|-----|-------------------------------------|------------|---|---|---|---|---|---|---|---|---|----|-----|-----|----|-----|-----|----|----|----|----|----|----|-----|-----|----|----|----|----|----|----|----|
| 1 | Annemans <i>et al.</i> (2008) | Malaysia | V | V | V | V | V | V | V | V | V | V | V | V | V | O | V | V | V | O | V | V | V | V | V | V | O | V | O | O | 22 | 81 |
| 2 | WK Seng <i>et al.</i> (2005) | Singapura | V | V | V | V | V | V | V | V | O | V | O | V | O | O | V | V | O | O | V | V | O | O | O | O | O | V | O | O | 15 | 56 |
| 3 | Ortegón M <i>et al.</i> (2012) | Bangladesh | V | V | V | V | V | V | V | V | V | O | V | V | V | V | V | V | O | V | V | V | O | V | O | V | O | O | O | 21 | 78 | |
| 4 | Flessa S <i>et al.</i> (2014) | Cambodia | V | V | V | V | V | V | V | V | O | V | O | V | O | V | V | V | V | V | V | V | V | V | V | O | O | V | V | V | 22 | 81 |
| 5 | Riewpaiboon A <i>et al.</i> (2011) | Thailand | V | V | V | V | V | V | V | V | V | V | V | O | O | V | V | V | O | V | V | V | O | V | V | O | V | V | V | 22 | 81 | |
| 6 | Srichang N <i>et al.</i> (2011) | Thailand | V | V | V | V | V | V | V | V | O | V | V | V | O | V | V | V | O | O | V | V | V | O | O | O | V | V | V | 20 | 74 | |
| 7 | Chatterjee S <i>et al.</i> (2011) | Thailand | V | V | V | V | V | V | V | V | V | V | V | O | V | V | V | V | O | V | V | V | O | O | O | V | V | V | V | 22 | 81 | |
| 8 | Chatterjee S <i>et al.</i> (2011) | Thailand | V | V | V | V | V | V | V | V | O | V | V | V | V | O | V | O | V | V | O | O | V | O | O | O | V | V | V | 20 | 74 | |
| 9 | Chirakup S <i>et al.</i> (2008) | Thailand | V | V | V | V | V | V | V | V | V | V | V | V | O | O | V | V | V | V | V | V | V | O | O | O | V | V | V | 22 | 81 | |
| 10 | Riewpaiboon A <i>et al.</i> (2007) | Thailand | V | V | V | V | V | V | V | V | V | V | V | O | V | V | V | V | O | O | V | V | V | V | V | O | V | V | V | 23 | 85 | |
| 11 | Riewpaiboon A <i>et al.</i> (2011) | Thailand | V | V | V | V | V | V | V | V | O | V | V | V | V | V | V | V | O | O | V | V | V | O | O | V | V | V | V | 22 | 81 | |
| 12 | Sookaneknun P <i>et al.</i> (2010) | Thailand | V | V | V | V | V | V | V | V | O | V | V | V | O | V | V | V | V | V | V | V | O | V | V | O | V | V | V | 23 | 85 | |
| 13 | Chaikledkaew U <i>et al.</i> (2008) | Thailand | V | V | V | V | V | V | O | V | O | V | V | V | O | V | V | O | O | O | V | V | O | O | O | O | O | V | V | V | 17 | 63 |
| 14 | Shafie AA <i>et al.</i> (2014) | India | V | V | V | V | V | O | V | V | V | V | V | V | V | O | V | V | V | V | V | V | V | V | V | V | O | V | O | V | 23 | 85 |
| 15 | Andayani TM <i>et al.</i> (2010) | Indonesia | V | V | V | V | V | V | V | V | O | O | V | O | O | V | O | V | O | O | V | V | O | V | O | O | O | V | O | O | 15 | 56 |

Notes:

1 – 24 is checklist item from CHEERS
 V = Presence of statement

SV = Summary of statement
 % = Percentage

0 = Absence of statement

Table 3. Summary of 15 articles selected for the systematic review of metode economic evaluation of diabetes mellitus management in South East Asia, as published in the international literature (in PubMed & ProQuest) between 2005 and 2014 (PART 1)

| No | Study/ Years | Country | Title | Introduction | Target Population | Setting and Location | Study perspective |
|----|------------------------------------|--|--|--|---|---|---|
| 1 | (2008) Annemans <i>et al.</i> | China Malaysia South Korea Taiwan Thailand | An Asian Regional Analysis of cost effectiveness of early irbesartan treatment Versus conventional antihypertensive, late amlodipine and late irbesartan in patient with type 2 diabetics hypertention and nephropathy | Diabetic nephropaty is a common and serious implication of diabetes mellitus. Diabetic nephropaty was found in 51.7 % of all end-stage renal disease (ESRD) cases among patiens starting dialysis in Malaysia. ESRD is also expected to increase in Asian region. | Participant were man and woman who presented 59 years old patients with type 2 diabetes, and MAU (with UAE = Urinary albumin excretion 20 – 199 ug/minute) and presenting characteristic similar to the base line in IRMA-2 | Five Asian different setting - China - Thailand, - Malaysia, - Taiwan and - South Korea | Third party payer |
| 2 | WK Seng <i>et al.</i> (2005) | Hong Kong Korea Japan Malaysia Singapore Taiwan | Losartan reduces the cost of diabetic end stage renal disease an Asian perspective | The use dialysis services represent a significant healthcare budget around the world. In Taiwan government spends approximately 6% of their anual health care budget on the reimbursment of dialysis therapy. Health care programme aimed to preventing or delaying onset of ESRD in patients with type 2 diabetes might reduce the economic burden of ESRD in this region | Participant were 252 patients type 2 diabetic of asian ethnicity with age 31- 70 years with nephoropathy. | This study was setting on health care system responsible for all direct medical cost in : - Hongkong, - Taiwan, - Singapore, - Malaysia - Korea - Japan | third party payers and the national or regional health care perspective |
| 3 | Ortegon M <i>et al.</i> (2012) | Bangladesh Malawi Nepal India | Cost effectiveness of strategies to combat cardiovascular disease, diabetes, and tobacco use in sub-Saharan Africa and South East Asia mathematical modelling study | Cardiovascular disease is the single largest cause of mortality, This have an economic impact through loss income or labour productivity. Need a policy framework to prevent and control this disease. The management prevention efforts include population level and individual level | A lifetime population model was used to assess the cost effectiveness of 123 single or combined prevention and treatment strategies for cardiovascular disease, diabetes, and smoking | Two World Health Organization sub-regions of the world: countries in: - sub-Saharan - countries in South East Asia | The public health and population perspective. |
| 4 | Flessa Set <i>et al.</i> (2014) | Cambodia | Costing of diabetes mellitus type II in Cambodia | The Royal Government of Cambodia wants to address this rising disease and take care of its population, but for this purpose it urgently needs a prediction of the expected number of T2DM cases in Cambodia, determine the most costeffective intervention strategies, and estimate the budget impact of prevention and treatment of this disease. | For this study the sample was T2DM Patient, concentrate on the cohort ≥ 15 years in the year 2008. | The study was conducted at The Ministry of Health finances first-line (health centres) and second-line (hospitals) health facilities. | The Ministry of Health of Cambodia (Government) perspective. |
| 5 | Riewpaiboon A <i>et al.</i> (2011) | Thailand | Cost analysis for efficient management diabetes treatment at a public district hospital in Thailand | Only one study formulated a diabetes cost model from the provider perspective at a public hospital in central Thailand. Cost modelling determines a mathematical relationship between cost (dependent variable) and factors influencing the cost (independent variables) that can be used in both the prevention and treatment of diabetes. | Method The target population: 475 diabetic patients who were randomly selected from Waritchaphum Hospital's electronic database of 1415 diabetic patients who received outpatient and/or inpatient treatment | The study was conducted at Waritchaphum Hospital in Sakhon Nakhon province in northeastern Thailand. | provider's perspective |

| | | | | | | | |
|----|-----------------------------|----------|---|---|---|---|--|
| 6 | Srichang Ner et al. (2011) | Thailand | Cost and Effectiveness of Screening Methods for Abnormal Fasting Plasma Glucose among Thai Adults Participating in the Annual Health Check-Up at King Chulalongkorn Memorial Hospital | Screening methods in thailand have been developed for detecting undiagnosed type 2 diabetes. These include the method which was proposed RMAT, the method proposed by (MOPH), a diabetes risk score for predicting incident diabetes and the method pro-posed by Keesukphan et al. The effectiveness of these methods has not been fully evaluated. | The target population: The study population included individuals between 35 and 60 years of age with no known diabetes or pre-diabetes who had participated in the annual health examination provided by the Preventive Medicine Clinic of the King Chulalongkorn Memorial Hospital. Between July and December 2008. | The study was conducted at King Chulalongkorn Memorial Hospital, Thailand | Societal perspective and a single payer perspective. |
| 7 | Chatterjee S et al.(2011) | Thailand | Cost of diabetes and its complications in Thailand: a complete picture of economic burden | Diabetes is a common metabolic disorder with increasing burede In Thailand, studies on the cost of diabetes estimated the cost either from provider or from patient . There is no study had yet been conducted in Thailand to explore the cost of illness of diabetes from societal perspective, the broadest viewpoint covering all costs irrespective of who incurs them. The present studywas an attempt towards this end. | The target population: total of 1415 diabetic patients (inpatients and outpatients taken together) received treatment from the study hospital and health centres in 2008. | The study was conducted at Waritchaphum hospital in Sakhon Nakhon province of Thailand | Societal perspective |
| 8 | Chatterjee Ser et al.(2011) | Thailand | Cost of informal care for diabetic patients in Thailand | Most studies had found that the cost associated with unpaid informal caregiver time account for a majority of the total cost of the disease. Given this backdrop, the objective of the present study was to estimate the cost of informal care for the diabetic patients at a public district hospital in Thailand. | The target population: For this study the sample size was fixed at 475 from a total of 1415 diabetic patients (inpatients and outpatients taken together) received treatment from the study hospital in 2008. | The study was conducted at Waritchaphum hospital, a public district hospital in Waritchaphum district of Sakhon Nakhon province in Thailand | Societal perspective |
| 9 | ChirakupSar et al.(2008) | Thailand | Cost-Effectiveness Analysis of Thiazolidinediones in Uncontrolled Type 2 Diabetic Patients Receiving Sulfonylureas and Metformin in Thailand | In Thailand only two studies compared the cost effectiveness between rosiglitazone and pioglitazone (thiazolidinediones groups) but both studies did not base their effectiveness on meta analysis | This project is a multicenter registry of 9419 diabetic type 2 patients receiving medical care in diabetic clinics of 11 tertiary centers in Bangkok and major provinces. The registry data were collected from April to December 2003. | The study was conducted at Buddhachinaraj hospital's, Thailand | the government hospital policymaker perspective. |
| 10 | Riewpaiboon A et al.(2007) | Thailand | Diabetes Cost Model of a Hospital in Thailand | Study about cost of illness is rarely conducted in Thailand. The researcher was aware of only one study conducted in seven government hospitals located in four regions of the country and in Bangkok. Another study just focused on patients' expenses as they used complementary and alternative medicine and not on that of the providers perspective. | The target population consisted of patients with diabetes (type 1 or type 2), defined as one who has plasma glucose at a level of at least 126 mg/dL by the fasting plasma glucose test, who receive treatment during fiscal year 2001 (October 1, 2000 to September 30, 2001) | This study was setting in Ampawa Hospital, a 30-bed public hospital in Samutsongkram, a central province of Thailand. | Third party payer perspective and government perspective |
| 11 | Riewpaiboon,A. et al.(2011) | Thailand | Disability and cost for diabetic patients at a public distric hospital in Thailand | Diabetic patients with disability use healthcare services more frequently than those not limited in activity. Estimated cost of disability among diabetic people aged 18-64 years to be US\$9.3 billion. In thailand, people with disability has also been raising from 0.5 in 1974 to 2.85% in 2007. | The present study covered 475 diabetic patients from waritchaphum hospital, 354 were female (75%) and 121 were males (25%). Age of all participants was 59,34. Most of them had primary education, dependent on farming and had type2 DM. | This study were doing during fiscal year 2008 (1 Oktober 2007 – 30 Sepetember 2008) at warichapuhum hospital in waritchapum district of sakhon nakhon province in northeastern Thailand | payer perspective and the social perspective cost of illness |

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|----|--------------------------------|------------------------------|---|---|---|--|--|
| 12 | Sookanekun Per et al. (2010) | Thailand | Economic analysis of the diabetes and hypertension screening collaboration between community pharmacies and a Thai government primary care unit | The sequential screening method is reasonable for cost and effectiveness in use. As community pharmacies in Thailand provide care in the private sector which is independent from the government sector the quality of the cognitive services, such as screening programs for diabetes and hypertension, are neither widespread nor standardized. | Person who age 40 years old or older in the area of kasieng pharmacy, chusak pharmacy and samukee PCU | This study was setting in two pharmacies ((Kasieng Pharmacy and Chusak Pharmacy) and seven communities in the area of Samukee PCU (Primary Care Unit) supervision. | provider perspective |
| 13 | Chaikledkaew Uer et al. (2008) | Thailand | Factors affecting health care cost and hospitalizations among diabetics patients in Thai public hospitals | The annual average cost per diabetic patient was 6.017 baht in seven government hospital, which was significantly higher than those without diabetes. The annual total healthcare cost per diabetic patient was 1.751 baht. The average medical cost per outpatient visit was about 1.206 baht per diabetic patient | This research is a retrospective study, conducted by using administrative databases obtained from four Thai government hospitals during october 1, 2002 and september 30, 2003. | Four Thai government hospitals. | Patient perspective and government perspective |
| 14 | Shahic, A A et al. (2014) | Arab Saudi, India, Indonesia | An analysis of the short and long term cost effectiveness of strating biphasic insulin aspart 30 in insulin naive people with poorly controlled type 2 diabetes | Analyse of randomised clinical trial and data from non interventional studies that beginning insulin analogues in people taking glucose lowering drugs alone is associated with improvements glucose control while improving quality of life. There is evidence that using BIAsp 30 as a cost effectiveness treatment option in a number of western and develop countries | Target Population : 1. Saudi Arabia, n=901 2. India, n=7546 3. Indonesia, n= 153 4. Nort Africa countries (Algeria, Tunisia and Marocco), n=279 | This study was setting in Saudi Arabia, Indonesia, India and North Africa (Algeria, Tunisia and Marocco, analysed using economic data from Algeria) | NR |
| 15 | Andayani TM et al. (2010) | Indonesia | Assessing The Impact of Complications on The Direct Medical Costs of Type 2 Diabetes Mellitus outpatients | These complications in type 2 dibabetes melitus substantially increase not only the economic burden for healthcare systems, but also the patient's risk for disability, death, and diminished quality of life | The target population were patients admitted into the Dr. Sarjito Hospital for treatment od Type 2 diabetes between may 2007 and august 2008. | This study was setting in Dr Sardjito Hospital in Yogyakarta province, Indonesia | Provider perspective |

Table 3. Summary of 15 articles selected for the systematic review of metode economic evaluation of diabetes mellitus management in South East Asia, as published in the international literature (in PubMed & ProQuest) between 2005 and 2014 (PART 2)

| No | Study/ Years | Comparators | Time horizon | Discount rate | Choice of outcomes | Single study-based estimates | Synthesis-based estimates | Measurement & valuation of preference-based outcomes |
|----|-----------------------------|--|--------------|---------------|--|--|---|---|
| 1 | Annemans, Let et al. (2008) | Late irbesartan, late amlodipine treatment and standard therapy. | 25 years | 3% | The outcome of each interventions was ability to reduced ERS, number of years patients lived free of ESRD, number days in dialysis and number of life years saved (QALY) | The result of two clinical trial, irbesartan in reducing microalbuminuria 2 and irbesartan in diabetic nephropathy trial were utilized as primary data to investigate the clinical and economical impact of different therapeutic strategies | Since ESRD management differed accros regional health care setting, the transition probabilities between the health states of disease progression were obtained from available local data for each setting and the treatment assumed after validation from local expert | The mortality rates for patients with MAU, were calculated by adjusting the age and sex specific all cause mortality values that were published in Malaysia, China, South Korea and Thailand and using officia statistic for Taiwan, by health state dependent relative risks |

| | | | | | | | |
|---|------------------------------------|---|---|---|----|---|---|
| 2 | WK Seng, <i>et al.</i> (2005) | The comparator of this study were placebo and conventional antihypertensive | 3.5 years | The outcome of each interventions was evaluated in ability the reduction of end point in NIDDM, reduce of creatinin concentration and reduce of blood pressure with RENAAL in patient with type 2 diabetes and nephropathy (free of ESRD) | NR | The RENAAL study design and result have been reported by Brenner et al. This study was to compared the renal protective effects of losartan plus CT with placebo plus CT in 1513 patients with type 2 diabetes. While the study result from 252 patients aged 31-70 years of Asian ethnicity with nephropathy and serum creatinin level of 115-265 µmol/L for men weighing > 60 kg have been reported by Chan JC et al. | NR |
| 3 | Ortegón M <i>et al.</i> (2012) | The majority of the of intervention analysed are drug base, ranges from 36% to 55% in low and middle income countries in the public and private sector respectively. Increase of taxation that would reduce smoking prevalence by 10% | over 100 years | The additional number of healthy years lived by population, equivalent to the number of disability adjusted life years (DALY's) | NR | Source data on tobacco taxation from previous WHO and World Bank Studies as reported by Asaria P, et al in 2003. The interaction in risk between CPS II cohort as Steenland K et al reported. Ischemic heart disease and stroke was modelled using estimates relative risk of stroke and visa versa from published epidemiological studies as reported by Mathers et al, Ezzali et al, WHO and Murray and Lopez. | Comparison between single or combined intervention with a baseline or null scenario. Null scenario was determined by back calculation incidence and case. Fatality rates using intervention effect sizes and current coverage rates |
| 4 | Flessa S <i>et al.</i> (2014) | The intervention include in this study were treatment with Antidiabetic oral and insulin and the role of peer educator network to search potential diabetic cases | 20 years (2008 to 2028) | The health outcome of each intervention are evaluated by disability adjusted life-years (DALYs) | NR | The epidemiology of T2DM simulated with Markov model. Basic parameters of this model used international data and adjusted it to Cambodia. | NR |
| 5 | Riewpaiboon A <i>et al.</i> (2011) | cost (dependent variable) and factors influencing the cost (independent variables) that can be used in both the prevention and treatment of diabetes. | the fiscal year 2008 (1 October 2007 to 30 September 2008). | The health outcomes of each intervention are evaluated in disability adjusted life-years (DALYs) | NR | Medical histories from Waritchapum hospital were reviewed for the study period (fiscal year 2008) to extract participants demographic characteristics and types and quantities of medical services received | NR |

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|---|------------------------------|---|---|----|--|---|---|--|
| 6 | Srichang, N., et al., (2011) | The study compare the performance, cost, effectiveness and cost-effectiveness of four screening methods for abnormal fasting plasma glucose. | July and December 2008 | NR | Reducing fasting plasma glucose (FPG) testing after the 12-hour overnight fast. | The participant with positive result from the screening questionnaires were followed up for fasting plasma glucose after 12 hour overnight fast. Universal venous FPG testing was also conducted and use as reference for comparisson with other screening methods | Detail about variable and the cutt off criteria for positive results dor each screening methods base on study that have been reported by suthijumron (methods 1), bureau of disease, ministry of public health (method 2), Aekplakorn (method 3) and Keesukphan (method 4) | NR |
| 7 | Chatterjee S et al.(2011) | The costs were compared for different types of complications as well as with and without complications.. | 1 year (2007 – 2008) | 3% | The health outcomes of each intervention are evaluated in disabilityadjusted life-years (DALYs) | Unit cost medical services measued directly from hospital record. Medical service utilization were collected by the study member by reviewing medical record participant during october 2007 to september 2008). Information about direct non medical cost and medical cost through direct personal interview method | NR | The severe of disability confirmed using Bartel Index score |
| 8 | Chatterjee S et al.(2011) | The intervention use in this study was informal care giver such as family, friends. Acquitances, or neighbours to be cost saving in diabetic patiens | During financial year 2008 till march 2009.; | NR | Time spent of informal care giver for activity daily livint (includes instrumental daily livinf) and house hold daily living, taken together under helath are activities | Information of informal caregiving was collected through direct personal interview method either from the patients or from the caregivers. The data on time spent for informal care were collected by using recall method. The participants aske to write down all their ativities during a specific time, in this study during financial year 2008 to march 2009 | The concept of ADL, HDL and IADL were followed from Van den berg et al. The ADL include personal care, moving around in the house, going to the toilet, bathing, dressing, eating and drinking. The HDL include preparation of food and drink, cleaning the house, dishes, washing, ironing. While IADL include making trips and visiting family or friends, health care contacs, going to the bangk, etc | Valuing informal care using proxy goods method. Earning defined as wage plus other monetary and non monetary. Earning for HCA and ADL USD 3.03 per day and earning for HDL USD 4.47 for sakhon nakhon hospital. Work time per week cannot be exceed 48 h. Total workin time per month 192 h. |
| 9 | Chirakup Set al.(2008) | The intervention in this study was use pioglitazone 45 mg orally once daily compared with the rosiglitazone 8 mg orally once daily in patients who cannot control their blood sugar with sulfonylureas and metformin. | Time horizon of the simulation was 40 years.. | 3% | The health outcomes of each intervention are evaluated in Quality adjusted life-years (QALYs). Cummulative od incidence in each diabetes complications and total lifetime cost of the diabetes | Most of diabetic complication cost were calulated from Buddachinaraj hospital's database (Pitsanukook Thailand). The government policymaker perspective were taken considering only direct medical cost for ech competing treatment | Baseline characteristic in this study based on Thai Diabetes Registry Report (TDRP). Other characteristic that not report in TDRP retrieved from other publication related with thai polulation. T2DM patients identified by ICD10. Complication cost that could not be calculated from the hospital were derived from thai published literature, expert opinioon and DRG's (Diagnosis Related Groups) | NR |

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|----|------------------------------|--|--|----|--|--|--|---|
| 10 | Riewpaiboon, Aet al. (2007) | The intervention in this study was medical services consist outpatient, visit, inpatient stay, pharmacy services, home health care visit, laboratory investigation, emergency services and surgical services | During fiscal year the fiscal year 2001 (October 1, 2000–September 30, 2001) | 3% | Formulation of cost model provider perspective | Data were collected by reviewing the medical record of each participant, both inpatient and outpatient. The acquisition cost of drugs collected from the pharmacy department and medical material department | NR | The total direct medical cost were calculated through a summation of medical service cost in the result of multiplying the number of services by their unit cost. |
| 11 | Riewpaiboon, A et al. (2011) | The intervention of this study were the presence of complication and disability among diabetic patients | During the fiscal year 2008 | NR | The outcome in each intervention are evaluated as disability adjusted life year (DALY's) | Data were collected from the hospital waritchapum hospital financial record, medical records of each participants to get the information of medical service utilization. Information on direct non medical cost and time and productivity cost collect by direct personal nterview | The severity level of impairment were checked by using the ThailandnMinistry of pulic helath check list for evaluation. To get comprehensive view, The Barthel index sore was used | The outcomes among group was difine by bartel index score consist duration of disease, age and fasting blood sugar level |
| 12 | Sookanekun Per et al. (2010) | The intervention in this study were screening diabetes and hypertension between community pharmacies and government | During July–September 2007; | ND | The outcome of this research was reduce of blood sugar | The Data collected by action study among the participant in two pharmacy and one PCU | The inclusion criteria of the participant followed the dibetes association of Thailand recommendationfor PCU routine task. | ND |
| 13 | Chaikledkaew U et al. (2008) | - | 30th September 2002 – 1st October 2003 | NR | Decreased of comorbidity and complicatios | Data source obtained from four thai government hospital. Data include demographic characteristics, medical history of illness, health care utilization and medical cost. | All variables both comorbidities and complications used in this study are presented in table 1 page 570, based on ICD-10 codes. | - |
| 14 | Shafie AAet al. (2014) | The intervention of this study was treatment with BIAsp 30 in people with type 2 diabetes | over 30 years time horizons | 3% | The outcome of this study were QALY, the reduction of diabetes related complication | A1chieve was a 24-week, international, non-interventional, Participants were asked to complete the EQ5D questionnaire, used for self-assessment of HRQoL, at baseline and week 24 | o evaluate the safety an clinical effectiveness of insulin analogue in people with T2DM use A1 chive data collection. Data were collected on clinical effectiveness and adverse events at routine clinical visits (baseline 12 an 24 weeks). | EQ-5D HRqol |
| 15 | Andayani, TM et al. (2010) | The intervention in this study were individual with complication in T2DM (include macrovascular, microvascular or both) | The study was done between May 2007 and September 2008. | NR | NR | The data collection was done by interviewing and reviewing the medicalRecords. people were classified into four broad categories of complication status. A written informed consent was obtained from all the patients. | NR | NR |

Table 3. Summary of 15 articles selected for the systematic review of metode economic evaluation of diabetes mellitus management in South East Asia, as published in the international literature (in PubMed & ProQuest) between 2005 and 2014 (PART 3)

| No | Study/ Years | Single study- based economic evaluation | Model- based economic evaluation | Currency, price date, & conversion | Choice of model | Model assumptions | Analytic methods | Study parameters |
|----|--------------------------------------|--|---|--|-----------------------|--|--|---|
| 1 | Annemans <i>Let al.</i> (2008) | NR | CEA | 2004 US\$ | Markov model | NR | The probabilistic sensitivity analysis was use to assess the effect of uncertainly around each input parameter using second order monte carlo simulation). | The model investigated the impact of the four treatment option on the cumulative incidence of ESRD, the number of patients live free ESRD and the number of days dialysis and the number of life years save |
| 2 | WK Seng <i>et al.</i> , (2005) | NR | CEA | 2004 US\$ | NR | NR | In this study,the cost calculate in two stages: -Estimation the mean relationship between cumulative cost & survival time- Weightingf this mean relationship by the kaplan meier probabilitis of survival | Tabel 2 (page 522) shows the mean number of days with ESRD by treatmen group and follow up by time |
| 3 | Ortegón M <i>et al.</i> (2012) | Costs included all resour-ces required for the im-plementation and main-tenance of interventions, such as administration and planning, media and com-munications, law enforce-ment activities, training, evaluation, and monitoring. | CUA | 2005 USD. | WHO-CHOICE | NR | This analysis follows the standardised methodology on cost effectiveness analysis set forth by the WHO-CHOICE project12-14 and builds on previous analyses of public health interventions to lower systolic blood pressure and cholesterol15 and of tobacco use. | Main epidemiological parameters used in analysis of cardiovascular disease, diabetes, and tobacco related disease rates in WHO sub-Saharan African sub-region AfrE and South East Asian sub-region SearD Shown on table 2 |
| 4 | Flessa Set <i>al.</i> (2014) | The ministry of health is obliged to include only new intervention into basic package of services if they are cost effective in comparison to other possible intervention | CEA | all values are expressed in 2013 US\$. | Markov-Model | 57% of insulin requiring T2DM patients receive a monotherapy the average cost of insulin therapy is 114 US\$ p.c. p.a. | are crucial so that detailed analysiswas done based on the data of MoPoTsyo, data from WHO-CHOICE, the international drug price indicator guide and additional research on market prices in Cambodia. | The parameter of this study shows on table 1 |
| 5 | Riewpaiboo A <i>et al.</i> (2011) | The directmedical cost of the study participants was calculated by adding the unit costs of medical services and costs of drugs and medical supplies. The cost of medical services was calculated by multiplying the | CEA | The total annual cost for the study hospital was US\$ 2008 prices (US\$ 1 = THB 32, or Thai baht). | NR | The Study Formulated a forecasting cost model with direct medical cost as a dependent variable. | Descriptive statistics were used to summarize dependent and independent variables. The stepwise multiple regression analysis was employed to calculate the relationship between the direct medical cost of illness and | The predictor variables are presented in Table 3. |

| | | number of services by their unit costs. | | | | several potential explanatory variables | | |
|---|---------------------------|---|-----|---|-----------------------------------|--|--|--|
| 6 | Srichang N et al. (2011) | The full cost of a screening method was calculated from the sum of total direct medical and non-medical costs. The cost-effectiveness was then calculated as the total cost of a screening method divided by the total number of cases identified. | CEA | 2008Thai (exchange rate of 34.20 baht per dollar) | NR | NR | The receiver operator characteristic (ROC) curves were constructed by sensitivity plots against 1-specificity for each cut-off value as well as the area under the curve (AUC) to compare the impact of screening methods. | The overall sensitivities of all screening methods were high to very high and ranged between 71 and 92% for abnormal fasting plasma glucose screenings, while the overall specificities were low to moderate and ranged between 31 and 57% (Table 3) |
| 7 | Chatterjee S et al.(2011) | Cost components consisted of both direct and indirect costs. The direct costs reflected the resources used in treating or coping with the disease, including expenditures for medical care and the treatment of illness. Indirect cost included the societal cost of morbidity, permanent disability and premature mortality. | CBA | 2008 USD (1 USD = 32 THB) (Table 2). | NR | To check how the assumption of using minimum wage rate in mortality and permanent disability affected total cost | Statistical analyses were performed using SPSS Release 14.0. Descriptive statistics were used to summarise data on demographic characteristics, clinical status and costs. Cost comparisons between groups were analysed by the Kruskal-Wallis | Table 2 shows Cost of illness of diabetes (USD at 2008 prices |
| 8 | Chatterjee S et al.(2011) | For valuing informal care using proxy good method, from household work and from health and social work in 2003 were used. | NR | 2008 USD (1 USD = 32 Thai Baht) | - | disease characteristics of the study participants, the mean duration of the disease was 7.20 years, most of the patients had type 2 diabetes (99%) and the mean fasting blood sugar level was 156.06 mg/dl | For valuing informal care using proxy method. In proxy good method, one-way sensitivity analysis was performed by using the earnings for the country as a whole from the respective work, i.e. USD 4.78 per day for household work and USD 5.16 per day for health and socialwork. | NR |
| 9 | Chirakup S et al.(2008) | | NR | USD2007 (34.56 baht/US\$1) | Markov Model submodel Monte Carlo | The model can predict the long-term costs and outcomes in diabetes patients based on many large clinical and epidemiologic studies that are currently available. | HbA1c sensitivity analysed by the changes of e from baseline in pioglitazone group between -1.16 and -1.96 (upper bound and lower bound of the confident interval of %HbA1c changing in pioglitazone treatment report in the Chiquette's Meta-analysis | Nonspecific mortality probability values in the model were replaced by age-specific mortality data in Thai population. Probabilities values of death related to hemodialysis and peritoneal dialysis were derived from Thai renal registry project 2003. |

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|----|-------------------------------|--|-----|---|-----------|---|---|--|
| 10 | Riewpaibon A. et al. (2010) | Unit cost medical services calculated from the data given by hospital, composed in five steps | CMA | 2001 Thai baht (THB) (approximately 40 THB = US \$1). | - | - | The statistical analysis employed was the stepwise multiple regression. The statistic's assumptions and model checking were examined, i.e., normal distribution, multicollinearity, influential observations, and outliers. | Table 2 shows the unit cost of medical services and drugs commonly used by diabetic patients |
| 11 | Riewpaiboon P. et al. (2011) | Cost of illness estimates followed the prevalence-based approach and it measured the perspective of cost of illness of diabetes | CMA | 2008 USD (1 USD = 32 Thai baht) | - | - | Data analysis were performed using SPSS release 14 software, cost comparison between groups were analysed by Kruskal-Wallis Test | Total cost of illness for 475 study participants was estimated at USD 418,696. Of this 22.66% was direct medical cost, 39,887 was direct non-medical cost and 37,47 was productivity cost. Unit cost of inpatient stay, outpatient visit and dispensing (exclude drugs) at Waritchaphum Hospital were USD 74.33. |
| 12 | Sookaneknun P. et al. (2010) | The cost of the screening activities. Direct medical costs and direct non-medical cost in Model 1, 2 or combine from model 1 and 2 | CMA | In this study cost were expressed in 2007 US\$ after conversion from local currency THB | (Model 1) | (Model 2), shown as Fig. 2. | The sequential screening method is reasonable for cost and effectiveness in use | Table 2 Shows the screening results for each model of hypertension and diabetes. |
| 13 | Chaikledkaew U. et al. (2008) | Medical cost data were all charges of patients underpayments method such as capitation, free for service and out of pocket. Out of pocket means patients pay all healthcare cost by themselves | CMA | ND | NR | - | Multiple linear regression analysis and log transformation were used when a dependent variable was total healthcare cost. Logistic regression analysis was applied when the occurrence of hospitalization was a dependent variable. | Table 2 shows the result of the descriptive statistic of the sample. There were 24,051 patients with diabetes with average age 59 years old. Sixty six percent of patients with diabetes were female and 99% had type II diabetes. |
| 14 | Shafie A. A. et al. (2014) | NR | CEA | In this study cost were expressed in local currency, 2013 USD and GDP for each country | CORE | Short term analysis was conducted using the incremental cost of treatment and the incremental | Non parametric bootstrapping was used in each simulation to construct the confidence interval around data. | The significant improvements in surrogate clinical outcomes following change in therapy to BIASp in people with T2DM were associated with improvement in life expectancy, diabetes |

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|----|-------------------------|---|----|--|----|--|--|
| | | | | | | effect on EQ5. This assumption based on data collected from A1chieve (shown in table1) | related complication, cost and cost effectiveness shows in table 2 page 4 |
| 15 | Andayani TMet al.(2010) | Only direct medical costs, those directly related to delivery of the health care service, are included in the estimates reported here. Average per-patient total costs were estimated by applying unit costs to the likely course of treatment for each complication. | NR | In this study cost were reported in 2008 US dollars. | NR | - | Descriptive statistics was done to analyze the demographic details. Median with range was reported for cost details.. The macrovascular complications considered in this analysis are hypertension, hyperlipidemia, hypertension heart disease, congestive heart failure, angina pectoris, and ischemic heart disease. |

Table 3. Summary of 15 articles selected for the systematic review of metode economic evaluation of diabetes mellitus management in South East Asia, as published in the international literature (in PubMed & ProQuest) between 2005 and 2014 (PART 4)

| No | Study/ Years | Incremental costs and outcomes | Single study-based economic evaluation | Model-based economic evaluation | Characterizing heterogeneity | Study findings, limitations, generalizability, and fit with current knowledge | Source of funding and support | Conflicts of interest |
|----|------------------------|---|--|---|------------------------------|--|-------------------------------|-----------------------|
| 1 | Annemans Let al.(2008) | The incremental cost effectiveness ratio (ICER) of given treatment projected 25 years cost, expressed in 2004 US\$ | Summerized result of model operated in a 25 years an 3% discount rate for both costs and outcomes in all setting was discribed in figure 2, page 360 | Both increasing of MAU mortality and decreasing diabetic nephropathy mortality, reduced the beneficial effect of early irbesartan treatment in terms of decreased life years gained compare to base case. | - | The model exclude the cost of comedication for disease other than diabetic nephropathic | Not Found | Not Found |
| 2 | WK Senget al.(2005) | | - | - | - | The economic analysis did not include all countries in Asia, the six countries not be considered a representative sample of all Asian countries. | NA | NA |
| 3 | Ortegón M et al.(2012) | ICER provided for each cluster of interventions, which give the additional cost needed to secure one extra healthy life year as successively less cost effective strategies are entered into the mix. | | The probabilistic uncertainty analysis depicted in figures 3 and 4 also show that these interventions remain highly cost effective (cost effectiveness ratio < \$Int2000 per DALY averted) even after allowing for plausible variations incosts and effects | - | These results were obtained by means of a dynamic population model, using consistent demographic and epidemiological data of the populations studied, allowing a more precise prediction of the behaviour of the disease and consequently of the health and economic impact of the strategies studied. | Not Found | Not Found |

| | | | Standard approach | | | | | |
|---|---------------------------|---|---|---|---|---|---|---------------------------|
| 4 | Flessa Set al. (2014) | In this study of Cambodia, an intervention is cost-effective if the ICER is less than 1,000 US\$. Corresponding ICER is 464 US\$/YLS, i.e., | of disease modelling under uncertainty calls for a set of sensitivity analyses which are presented in section Sensitivity analyses. | - | - | The study finding : confirmed the general finding that T2DM is a major public health problem in Cambodia. | This research has been partly financed by (BMZ) through (SHP) Project implemented by (GIZ) GmbH. | No conflict Of interest |
| 5 | Riewpaiboon et al.(2011) | | The predicted treatment cost for hospitalized patients was more than 10 times higher than that of non-hospitalized cases. The treatment cost of diabetic foot complications was 665% higher than the treatment cost without complications, while the treatment cost with nephropathy was 259% higher. | - | - | A cost forecasting model showed that length of stay, hospitalization, visits to the provincial hospital, duration of disease and presence of diabetic complications (e.g. diabetic foot complications and nephropathy) were the significant predictor variable (adjusted R2 = 0.689). | The study was a part of the research project under the fellowship programme 'Asia Fellows Awards 2008–09 | No conflict Of interest |
| 6 | Srichang Net al.(2011) | Total cost and cost-effectiveness of screening methods for abnormal fasting plasma glucose per 1000 persons from the societal perspective and the single payer perspective showed in table 4. | - | - | - | Limitations of the present study included two repeated FPG of > 126 mg/dl was used as the gold standard instead of the 75 gm oral glucose tolerance test (OGTT). This might have resulted in the underestimate of type 2 diabetes prevalence. | supported by a grant from the National Research Council of Thailand (NRCT) | No conflict of interest |
| 7 | Chatterjee S et al.(2011) | - | - | - | the cost centres producing heterogeneous products (e.g. laboratory, radiology, emergency room), a micro-costing approach was used | the cost of outpatient visit and inpatient days at the health centres and provincial hospital were calculated on the basis of approximate results of some previous studies. | This study funded by the Ford Foundation. We express our gratitude to the Asian Scholarship Foundation for providing this opportunity.. | No conflict of interest |
| 8 | Chatterjee S et al.(2011) | - | sensitivity analysis and proxy good method country average earnings from household work and from health and social work used as a cost approach | - | - | that maximum time was spent for HDL. the informal caregivers spent maximum time on HDL and that time was significantly higher than times spent for all other activities. | The present study was a part of the research project under the fellowship program "Asia Fellows Awards 2008–09 | No conflict of interest |
| 9 | Chirakup S et al.(2008) | The incremental cost per QALY gained was 186,246 baht (US\$ 5389). | - | - | - | the use of pioglitazone 45 mg fell in the cost-effective range recommended by World Health Organization (one to three times of GDP per capita) on average, compared to rosiglitazone 8 mg. | Source of financial support: A grant from Thailand Research Fund. | No conflicts of interest. |

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|----|--------------------------------|---|--|--|---|--|---|--|--|
| 10 | Riewpaiboo A. (2007) | - | <p>The major cost was in pharmacy, because it included drugs and pharmaceutical services (an average of 2804 THB per person per year), followed by outpatient services (an average of 1528 THB per person per year).</p> | <p>Drug prices in Thailand were highly varied among brand-name drugs and local-made generic drugs. So the maximum and minimum drug prices from the referent drug list in the fiscal year 2001 of the Ministry of Public Health were used for the sensitivity analysis.</p> | - | <p>The treatment cost for a patient with type 2 diabetes without complication was approximately 4000 THB. The patient with hypertension consumed an additional 16% of cost of the patient without complication. The cost increased up to 232% for the case of gangrene.</p> | <p>The highest proportion of the treatment cost was related to pharmacy services (45%), and the proportions of outpatient services, inpatient services, and laboratory investigations were 24%, 16%, and 11%, respectively.</p> | <p>funded and supported by Faculty of Graduate Studies, Mahidol University, Bangkok, Thailand.</p> | <p>No conflicts of interest.</p> |
| 11 | Riewpaiboon, Aet al. (2011) | - | <p>The predicted treatment cost for hospitalized patients and those who visited the provincial hospital were significantly higher. The diabetic patients with complications incurred 145% higher treatment cost of compare to those without complication. While those who were disabled incurred 351% higher cost as compared to those who were independent.</p> | - | - | <p>The cost were found to increase progressively with the increase of number of complication. On average, the study participants had to spend USD 351.44 as direct non medical cost and lost USD 330.28 from being unable to work due to illness (table 4). At the present Thai government provides USD 187.5 per annum (500 bath per month) to registered disabled diabetic person as a disability living allowance</p> | <p>The cost of illness estimate ignored intangible costs such as pain and suffering from the disease. Productivity cost calculation did not take into account reduced earning or productive capacity due to disability. Productivity cost may be overestimated if the human capital approach is used to calculate such cost, which is why the frictional cost approach is preferred</p> | <p>funded by the Ford Foundation (grant number 08253)</p> | <p>There is no relevant conflict of interest to disclosure</p> |
| 12 | Sookaneknun P et al. (2010) | - | <p>The sensitivity analysis was emphasized on operational cost, including only labor costs, material costs and travel costs of the screening campaign. It was found that the unit cost of Model 1, 2 and the Combined Model were 322.0 (\$8.9), 125.5 (\$3.5), and 147.5 Bahts (\$4.1), respectively as shown in Table 5.</p> | <p>This study was able to contribute valuable benefits to PCU, including (1) the protocol of screening, (2) service advertisement to encourage the awareness of health issues, (3) the referral system and (4) the fast track service of referral for high risk clients.</p> | - | <p>The fast track had been developed after the study, so during the study there was very low GP visit by those referred and the method of recording those who visited GP which the results might not be recorded if the clients presented with normal level of blood glucose or blood pressure because of the busy circumstance of the PCU visit.</p> | <p>This study was supported with grants by the Thai FDA, the Health Promotion Project of the Faculty of Pharmacy, Mahasarakham University and the Pharmacy Network for Health Promotion</p> | <p>The authors state that they have no conflict of interest.</p> | |
| 13 | Chaikledkaew U et al. (2008) | - | - | - | - | <p>there has been no standardized claims data obtained and collection system and standardized data coding excluding ICD 10 code across hospitals yet, so different hospitals have different type of claims data collected and data coding.</p> | <p>Grant from the Thailand research fund</p> | <p>There is no conflict of interest</p> | |

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|----|---------------------------|---|--|---|---|--|-----------|--|
| 14 | Shafie AA et al. (2014) | The projected differences in glucose lowering treatment cost, management related cost, and overall cost after switching therapy to BIA Sp was shown in table 3 page 5 | The series of sensitivity analysis revealed that there was little or no impact on ICER. This was true for extending the time horizon to 50 years if no deterioration with time in HBA1c was factored into model. If the median HBA1c treatment effect was used in place of the mean value. The result was shown in figure 1 page 6 | Some uncertainties remain around health care cost while some were obtained from published and official resource for each country, local diabetes specialist were requested to provide values when no published data were available. For this reason in the sensitivity analysis explored the increase in potential overall cost that would still allow the intervention to be cost effective at an ICER of 3 times GDP per capita | - | The limitation of this study, there was different in term economic resources, development and culture. But nevertheless when adjusted to GDP using the WHO CHOICES criteria starting insulin with BIA Sp30 was highly cost effective by the base case in all term | Not found | The author receive funding from all major international pharmaceutical companies including from novo nordisk. Eva hamerby is an employee of novo nordisk |
| 15 | Andayani TM et al. (2010) | - | The strategy should address risk factors for cardiovascular disease such as smoking, high blood pressure, and hypercholesterolemia; it is not yet certain that improved glycemic control will also help, but recent epidemiological evidence suggests that macrovascular disease is related to postprandial glucose. | - | - | The average state costs of cardiovascular complications were calculated to be \$774.37 per patient for 6 month. to direct medical costs. The costs did not include patient out-of-pocket costs, direct non medical costs, indirect costs and intangible costs (eg. cost due to suffering). | Not found | Not found |

ND = Not Determined, NA = Not Applicable; NR = Not Reported

Table 4. Outcome and cost effectiveness of using oral antidiabetic drugs

| NO | Study/Years | Intervention | Outcome | Cost effectiveness |
|----|--------------------------|---|---|--|
| 1 | Annemans Let al. (2008) | Early irbesartan Late irbesartan Standard Late amlodipin | Use of irbesartan: - Days in dialysis reduce 245.3 days/patient - Years free of ESRD ranging between 10.5 – 12.4 years - Life expectancy 4%- 6% higher than other intervention (10.8 – 12.8 years) | Use of irbesartan : - Initially higher cost than other treatment (due to higher cost of irbesartan) - Cost saving after 11 -20 years, differ of each setting in time horizon 25 years - Cost of early irbesartan between USD8,455 to USD 2,990 or USD8,200 to USD29,732 higher than other treatment (with 3% discount rate) |
| 2 | WK Seng et al. (2005) | Losartan placebo conventional antihypertensive | Use of losartan : - In time horizon 3.5 years, the years free of ESRD was 37.9 days per patient - Life expectancy and quality adjusted life expectancy in the use of pioglitazone was 0.16 (9.62 years) and 0.14 (6.69 years) higher than rosiglitazone | Use of losartan by 3.5 years of follow up : - ESRD related cost saving ranged from USD910 to USD 4346 per patient - Reduced total cost from USD55 to USD515 - Total cost of pioglitazone were higher than rosiglitazone - ICER for one life year gained was USD4681 or USD5389 perQALY |
| 3 | Chirakup S et al. (2008) | Pioglitazone Rosiglitazone | | - Pioglitazone treatment was cost effective for any particular willingness to pay with willingness to pay value 110,000 bath and 33,000 bath per QALY |

| | | | | |
|---|--------------------------------|------------------------|--|--|
| 4 | Shafie AA <i>et al.</i> (2014) | BiAsp 30 +OGLD OGLD | <ul style="list-style-type: none"> - The time free of any complication in people with T2DM was greater with BiAsp30. The difference between treatment range between 0.18 years(Saudi Arabia) to 2 years (Indonesia) - The estimated QALY gains were range between 2.65 (Algeria) to 277 (Saudi Arabia) | <ul style="list-style-type: none"> - Total cost treatment with BiAsp 30 was lower than OGLD alone. It range between USD7399 (India) to USD49,263 (Saudi Arabia) - Treatment cost range between USD3876 (India) to 11,941 (Indonesia) - Management cost range between USD992 (India) to USD10285 - Complication cost range between USD2531 (Indonesia) to USD29,144 (Saudi) - ICER per QALY per years was estimated to be cost effective between 0.14 of GDP per capita in Saudi to 1.2 of GDP per capita in Indonesia |
|---|--------------------------------|------------------------|--|--|

Table 5. Outcome and costeffectiveness of complication, disability and informal caregivers of diabetics patients

| NO | Study/Years | Intervention | Outcome | Cost |
|----|------------------------------------|---|--|--|
| 1 | Chatterjee S <i>et al.</i> (2011) | Complication in T2DM patient No complication | <ul style="list-style-type: none"> - Diabetic complications found in 37% of study participants while 65% had comorbidity - Thirteen (3%) of participant died during the study period (1 year) - 5 participants found permanently disabled measured using BI score - The age with the complication 62.5 years old | <ul style="list-style-type: none"> - Cost of illness of diabetes estimated in Thai to be USD418,696 - Cost of illness with complication in this study was USD479.93 with number of people 148 people. while without complication was USD115. 12 with number of participants 327 - Cost of illness according to number of complication followed USD261.32 for one complication, USD 758 for two complications and USD 2131 for three or more complications |
| 2 | Riewpaiboon A <i>et al.</i> (2011) | Disability Non disability | <ul style="list-style-type: none"> - Diabetic complications were found among 31% of the study participants. - 9.68% of study participants had physical impairment and 9.26 5 had sight impairment. From BI score found that 13.5% of the study participants was disabled | <ul style="list-style-type: none"> - Unit cost at waritchaphum hospital for inpatients stay, outpatients were USD74.33, outpatients visit were USD 3.58 and dispensing excluding drug were USD1.69 respectively - Cost of illness associated with physical impairment were USD1716.03 (level 1), 3464,69 (level2) and USD4376 (level3). - Cost of illness associated with sight impairment were USD 763.83 (level1), USD1141 (level2), and USD2025 (level3) - Cost of illness according to BI score were USD598.24 for independent of study participant while disabled were USD2700.29 - Productivity cost due to disability and direct non medical cost were USD1222.95 and USD1052.37 |
| 3 | Chatterjee S <i>et al.</i> (2011) | Informal care | <ul style="list-style-type: none"> - The informal caregivers spent maximum time in performing HDL (Household daily living). Time spent on HDL was 42.21 hours per month - Time spent on IADL (Instrumental activities of daily living 6,71 hours per month. - Time spent on ADL (Activities daily living) 6.79 hour per month - Time spent on HCA (healthcare activities) 5.80 hours per month | <ul style="list-style-type: none"> - The value opportunity cost approach of informal caregivers was USD37.17 per month, while as per proxy gold method was USDD33.54 per month |

Table 6. Cost componen in diabetic treatment

| No | Study/Year | Componen of cost |
|----|-------------------------------|---|
| 1 | Flessa Set al.(2014) | - Direct medical cost include medication using oral antidiabetic therapy and insulin therapy or both |
| 2 | Riewpaiboon Aet al (2007) | - Direct medical cost consisted of the cost of outpatients services, inpatient services, pharmacy, laboratory, emergency, surgery services and home healthcare - Unit cost of inpatient include capital cost (11%), labor cost (60%) and material cost (29%) - The unit cost of outpatient and hospitalization, health care visit. |
| 3 | Chaikledkaew U. et al. (2008) | - All healthcare cost consumed by patient with diabetes were used instead of the cost related to diabetic-related treatment only. Cost component consist : |
| 4 | Chatterjee S et al. (2011) | - direct cost, reflected the resources used in treating or coping with the disease including expenditures for medical care and the treatment of illness. direct cost dived into : a) direct medical cost include cost of hospitalization, outpatient visit, drugs, laboratory tests, materials, emergency services and traditional medicines services and dental services. B) direct non medical cost include transportation to healthcare providers, time loss of the patient and the accompanied person for visiting healthcare providers, coast of meals and accomodation during visit and cost of informal care - indirect cost, includesocietal cost of morbidity, permanent disability and premature mortality |

Discussion

Considering the oral antidiabetic drugs treatment in several countries in South Asia, it was found that to be related with GDPs in each country. In early irbesartan treatment, the cause of such variations in the results of this intervention was compared to GDPs of the countries involved in the analysis expressed in USD in 2004. Malaysia had the lowest costs among the lowest GDP, while Taiwan had the highest costs and GDPs^[9].

The reduction in the number of days with ESRD for losartan was based on the Asian subgroup for RENAAL. The precision of the estimate for days with ESRD was substantially reduced compared with an analysis based on the full number enrolled in RENAAL. The studied countries should not be considered as a representative sample of all Asian countries^[10].

Because of its better lipid profile and glycemic control, Pioglitazone has been found to be more clinically beneficial over Rosiglitazone. The higher cost of pioglitazone group was mostly due to the medication cost. When the effect of glycemic control of pioglitazone was inferior to rosiglitazone, the ICER per QALY was USD 27,523 or five times higher than the ICER per QALY in the based case analysis. The ICER might be lower if the societal perspective was considered. The intervention with ICER less than one or falling between one to three times GDPs was highly cost effective and potentially cost-effective. The costs of treatment, management and complications were much higher in Saudi Arabia than the other countries in using BIAsp 30 due to the economic circumstances of the country. The finding was that a whole year estimate using only first-year cost and improvement in health utility based on ED5Q data was also cost effective perhaps indicating that the improvement in HRQoL made a large contribution to the model outputs, thus reducing the impact of long-term gains and costs. The increase in the potential overall costs would still allow the

intervention to be cost-effective at ICER of 3 times GDP per capita^[12].

The contribution of direct cost in total cost of illness on diabetic patients with complications was higher than that of indirect cost of illness as compared to the direct cost because of the cost component included in this study. The patients with complications had to spend substantially more money than the ones without complications, and it was found that the costs rose progressively when the number of complications increased. It can be related to other studies that showed diabetic complications and co-morbidities had a significant positive impact on the healthcare costs. In 2008, the average cost of illness for each diabetic patient was estimated to be USD 881.47 which equaled 21% of per capita GDP of Thailand. Informal caregiving contributed 28% of the total cost of illness of diabetes. In this study, a comparison was made between independent and disabled diabetics patients. Disability was defined by the Barthel index score considering the duration of the disease and fasting blood sugar level. Statistically, there was a significant difference between disabled and independent diabetic people in terms of age and disease durations. It means that the higher disease duration and age were responsible for disability among diabetic patients. On average, study participants had to spend USD 351.44 as direct nonmedical cost and lost USD 330.28 from being unable to work due to the illness. Some of the study participants had become very severely disabled within a short disease duration of diabetes. It was probably because they had gone undiagnosed and untreated for a long time^[3, 16, 17].

The characteristics of the informal caregiving were quite similar to the informal caregiving of the disabled stroke supervision. There were more female caregivers than males, not only in Thailand but also in different parts of the world. As the onset of disability among the diabetic patients increased progressively, they mostly needed help for HDL

followed by IADL tasks. According to the Thai culture, the sick or older adults have been generally taken care of by their family members. Regular HDL tasks were not entirely separated from additional HDL tasks. The cost of informal caregiving was lower in case of a good proxy method. It was because the study calculated only the cost of informal caregivers' leisure time foregone paid, unpaid and leisure work^[13].

The prevention and treatment of diabetes has not been an only financial problem in several countries in Southeast Asia. For example, Cambodia has had no safeguard of a stable supply of OAD medications and insulin (including syringe). The majority of the healthcare workers were not well trained in the detection of cases and treatment of patients. Cambodia has to invest in training doctors, nurses and other professionals in preventing and treating NCD^[14]. In Thailand, the primary cost was in pharmacy because it included drugs and pharmaceutical services (an average 2804 THB per person per year) followed by outpatient services (an average 1528 THB) per person per year. The total direct medical cost was 6311 THB per person per year. For home healthcare, the average cost per person per year was less than its unit cost. It was because of the reason that the average service utilization per patient per year was less than one. The finding might still be useful for healthcare providers and health policymakers because significant factors in this analysis were able to explain 54% of the variations in total health care cost.

Conclusion

In order to detain the complication and comorbidity caused by diabetes, healthcare providers should make use of some interventions like counseling, pharmaceutical care or disease management. Patients with complications had to spend substantially more money than the ones without complications. The disabled condition was more costly than the independent conditions on diabetic patients. The unrevealed cost related to the informal caregiving was a burden for Thai society since the informal caregiving was the most costly including (28%) of the total cost of illness of diabetes and about 40% of the contribution of the direct non-medical cost. Moreover, 23% and 37% were allocated for the direct medical and indirect costs.

The results obtained from the simulations represented that the prevention and treatment of T2DM can be economical even in the least developed countries. Differences in facility characteristics resulted in different patterns of resource utilization.

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