WORKING PAPER

Costing of Type 2 Diabetes Mellitus in Cambodia: Micro-costing, budget-impact and cost-effectiveness analysis

Summary

Type 2 diabetes mellitus (T2DM) is a major and growing medical, social and economic burden for Cambodia. This paper forecasts the epidemiological and economic consequences of T2DM and discusses the most cost-effective interventions against T2DM.

T2DM is a major public health challenge in Cambodia, but the economic simulations clearly indicate that prevention and treatment of this disease is highly cost-effective. However, not all interventions that are cost-effective are also feasible, given limited resources.

The introduction of a combined screening programme and full coverage of all patients requiring OAD or insulin therapy would result in nearly 600,000 years of life saved and 78,000 death cases averted within the simulation period. The number of diagnosed diabetic cases would increase from around one-third of all diabetes patients (37%) to nearly all (89%). Among diagnosed patients, the number with complications would decline from 68% to 51%. More patients would not require any medication (9% instead of 8%), but also more patients would require insulin (21% instead of 17%). Assuming implementation of this combined intervention in 2008, the annual budget for professional diabetes prevention and treatment that year would have been nearly USD 8 million.

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Abstract

Background: Type 2 diabetes mellitus (T2DM) is a major and growing medical, social and economic burden for the South-East Asian country of Cambodia. However, there has not yet been any economic modelling to predict the number of cases and the budgetary impacts of this disease.

Objective: This paper is written to support the German development aid organisations as well as the Royal Government of Cambodia in forecasting the epidemiological and economic consequences of T2DM, while at the same time enabling them to select the most cost-effective interventions against T2DM.

Methodology: A Markov model was developed to analyse the specific T2DM situation of Cambodia. Data for the model was retrieved from scientific and grey literature, as well as through key informant interviews.

Basic Model: The number of people living with T2DM is expected to steadily increase from 145,000 in 2008 to over a quarter of a million (264,000) in 2028; an increase of 82%. At the same time, the prevalence rate among people 35 years old or above will increase from 4.0% to 4.4%. The majority of T2DM cases (63-64%) will remain undiagnosed, exacerbating the disease. In 2008, some 59% of diagnosed patients had complications; in 2028 this will increase to 68%, with a higher share of the patient population requiring insulin. In 2008, around 2% of diagnosed patients did not require any form of treatment, 84% needed oral anti-diabetic (OAD) therapy, and 14% required insulin. In 2028, around 8% of diagnosed cases will not require medication, three-quarters (76%) will need OAD therapy, and 17% will need insulin therapy.

In 2008, diagnosed T2DM patients (around 54,000 individuals) incurred costs of USD 2 million for their diabetes treatments. Over half of this amount (57%) was spent for OAD therapy, with the remainder used for insulin therapy. By 2028, the costs of treatment will double to USD 4 million, and include nearly 100,000 patients. If all patients (including those that are undiagnosed) had to pay for treatment the respective costs would be USD 5.5 million and USD 11 million in 2008 and 2028, respectively. These calculations assume stable prices and no discounting.

Screening: We calculated a scenario for the case of an ideal screening programme (100% test sensitivity and 100% coverage) that detects every patient within one year after the onset of T2DM. The results of this test would be an increase in the number of people living with T2DM and a strong decline of the number of T2DM-related death cases. The incremental cost-effectiveness ratio (ICER) is USD 463.46 per year of life saved (LYS); i.e., screening the entire population over 35 years old annually for T2DM is cost-effective if the sensitivity and accuracy of the test is 100% (the tests accurately capture 100% of diabetes patients). However, these strict assumptions are not very realistic, and further simulations show that screening should be limited to risk groups.

Oral Anti-Diabetic Therapy: It is estimated that only one in eight patients (12.5%) requiring (OAD) medication had access to it in 2008. If 100% of patients requiring OAD therapy receive it, nearly 200,000 years of life will be saved and 25,000 death cases averted between 2008 and 2028. At the same time, the percentage of diagnosed diabetics receiving OAD therapy would increase from 76% to 78%, but the total number of diagnosed people living with diabetes at any stage of the disease would also increase. Consequently, the average cost per diabetes patient would increase from USD 42 to USD 53.

Insulin Therapy: It is also estimated that only one in eight diabetes patients (12.5%) requiring insulin therapy currently had access to it in 2008. If all patients requiring insulin were to receive it, around 43,000 years of life would be saved and nearly 6,000 death cases averted between 2008 and 2028. By 2028, the overall number of patients requiring insulin therapy will increase, and their proportion among all diagnosed patients will increase from 17% to 22%. Consequently, the total cost per diagnosed patient would increase from USD 42 to USD 63.

Combined Intervention: The introduction of a combined screening programme and full coverage of all patients requiring OAD or insulin therapy would result in nearly 600,000 years of life saved and 78,000 death cases averted within the simulation period; a decrease in death cases of 27%. The number of diagnosed diabetes cases would increase from around one-third (37%) to nearly all diabe-

tes patients (89%). Among diagnosed patients, the number with complications would decline from 68% to 51%. More patients would not require any medication (9% of patients instead of 8%), but also more patients would require insulin (21% instead of 17%). Assuming implementation of this combined intervention in 2008, the annual budget for professional diabetes prevention and treatment that year would have been nearly USD 8 million.

Discussion: Type 2 diabetes mellitus is a major public health challenge in Cambodia, but the economic simulations clearly indicate that prevention and treatment of this disease is highly cost-effective. However, not all interventions that are cost-effective are also feasible, given limited resources. External support will still be required to ease the growing burden of T2DM in Cambodia.

1. Introduction

Type 2 diabetes mellitus (T2DM) is a noncommunicable disease (NCD) with a high prevalence and an increasing incidence worldwide. The International Diabetes Federation (IDF) estimates that about 350 million people are affected by diabetes worldwide, and nine out of 10 diabetes patients live in low- and middle-income countries [1]. IDF also expects a large increase in diabetes cases, which will result in enormous costs of treatment, tremendous human suffering and death [2]. Thus, T2DM is a disease of high public health importance, and a good representative to analyse the economic impact of noncommunicable diseases on the health care system of Cambodia and other low-income countries.

The World Health Organization (WHO) estimates that around two-thirds (66%) of the 55 million death cases worldwide were caused by noncommunicable diseases [3].[1] However, the relative importance of NCDs varies greatly by world region. In Africa, for instance, around 61% of death cases are still caused by conditions classified in the first WHO category (communicable, maternal, perinatal and nutritional conditions);[2] in Europe only 6% of deaths are attributable to these same conditions. South-East Asia[3] has progressed quite far in the epidemiological transition [4], with around 29% of death cases caused by conditions in the first WHO category, 60% caused by noncommunicable diseases (WHO category 2 conditions), and 11% by injuries (WHO category 3) [5]. For the Western Pacific region, the respective figures are 9% (category 1), 83% (category 2) and 8% (category 3). Figure 1 shows the proportion of causes of death in the total death burden for all WHO regions.

As Table 1 shows, the leading NCDs in South-East Asia, the Western Pacific and worldwide are quite similar, but their relevance differs strongly between indicators. If we analyse the incidence rates, we realize that injuries, cancer and stroke are most frequent. If we focus on prevalence rates, deficiencies (of iron, iodine, and/or protein-energy) are most relevant. Worldwide and in South-East Asia, cardiovascular diseases and cancer are the two main causes of death. Injuries are the third leading cause worldwide, but in South-East Asia it is respiratory diseases. Worldwide, quality of life (expressed in disability adjusted life-years lost) is mainly affected by neuropsychiatric diseases, injuries and cardiovascular diseases, but in South-East Asia and the Western Pacific the order of importance for these diseases changes.

Consequently, the majority of countries in the South-East Asia and Western Pacific WHO regions have become very advanced, and noncommunicable diseases and injuries are the leading causes of death. However, there are wide variations between countries within each region. For instance, it is difficult to compare Laos and Cambodia with Australia and New Zealand, although they are in the same WHO region.

Diabetes is categorised by WHO as a category 2 condition; i.e., it is a noncommunicable disease with a subcategory of its own. In 2000, diabetes was the 10th leading cause of death, both worldwide and in the two target WHO regions of this paper [5]. In 2011, diabetes was one of the top eight causes of death worldwide, with 1.4 million death cases (2.6% of all death cases worldwide) and a mortality rate of 20 per 100,000 individuals. In South-East Asia diabetes also ranks as the 8th leading cause of death, with nearly 400,000 deaths (3% of all death cases), and a rate of 21 deaths per 100,000 individuals. In the Western Pacific WHO region, diabetes ranks the same, but is linked to 300,000 death cases (2.4% of all death cases), and a rate of 16 deaths per 100,000 individuals.[4] Thus, diabetes is of

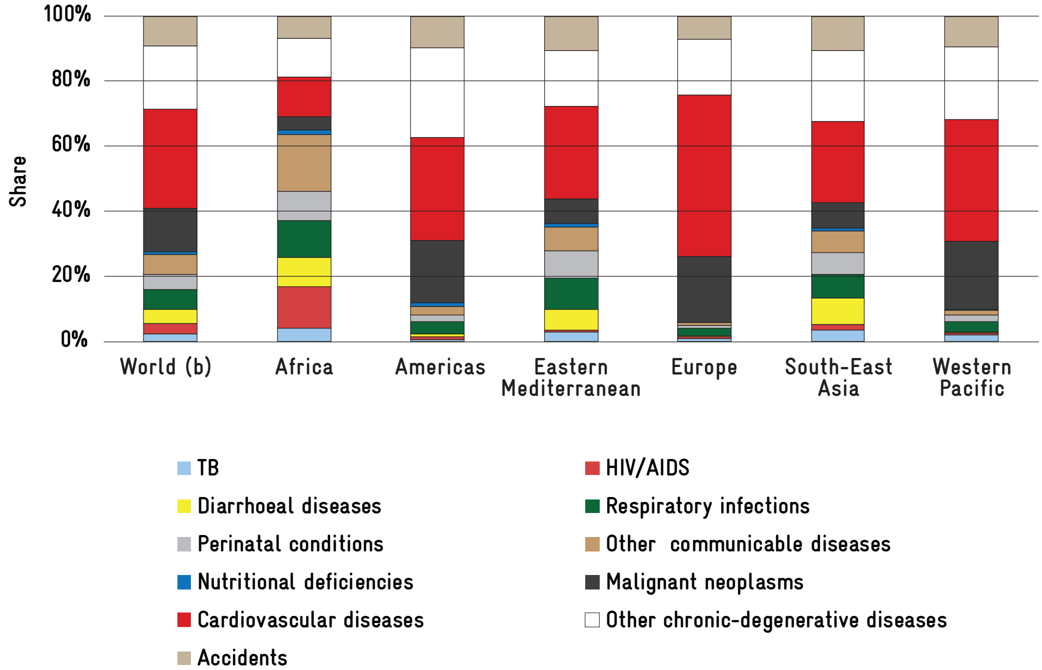
1 All data in this section is from 2011.

2 This categorisation is a standard, although it might not be optimal for all analysis purposes. For instance, cervical cancer is categorised as a noncommunicable disease, although it is caused by an infection of the human papillomavirus (HPV). At the same time, nutritional deficiencies and maternal conditions are usually noncommunicable, although they are included with communicable diseases.

3 Geographically, Cambodia belongs to South-East Asia, but WHO counts Cambodia as a country of the Western Pacific region (with Australia, New Zealand and Tonga, among others). A comparison of the demographic and epidemiological figures of Cambodia with the averages from these two WHO regions indicates that Cambodia is indeed much more similar to countries in South-East Asia than those in the Western Pacific WHO region.

4 For comparison, in Africa diabetes is ranked 13th, with 172,000 death cases (1.8% of all death cases) and a rate of 20 deaths per 100,000 individuals.

Figure 1: Relative share of causes of death, by WHO region (2011; NCDs are in red). (Source: [3, 5])



	Worldwide	South-East Asia	Western Pacific
Incidence	1. Injuries 2. Cancer 3. Stroke	1. Injuries 2. Stroke 3. Cancer	1. Injuries 2. Stroke 3. Cancer
Prevalence	1. Iron-deficient anaemia 2. Iodine deficiency 3. Migraine	1. Iron-deficient anaemia 2. Iodine deficiency 3. Protein-energy malnutrition	1. Iron-deficient anaemia 2. Iodine deficiency 3. Protein-energy malnutrition
Death Cases	1. Cardiovascular diseases 2. Cancer 3. Injuries	1. Cardiovascular diseases 2. Cancer 3. Respiratory diseases	1. Cardiovascular diseases 2. Cancer 3. Respiratory diseases
Quality of Life	1. Neuropsychiatric conditions 2. Injuries 3. Cardiovascular diseases	1. Injuries 2. Neuropsychiatric conditions 3. Cardiovascular diseases	1. Neuropsychiatric conditions 2. Injuries 3. Cardiovascular diseases

Table 1: Top NCDs worldwide, in South-East Asia and the Western Pacific (Source: [3, 5]).

increasingly high public health relevance. It is one of the most prominent NCDs, and a major cause of morbidity and mortality in South-East Asia and the Western Pacific Region, as well as worldwide.

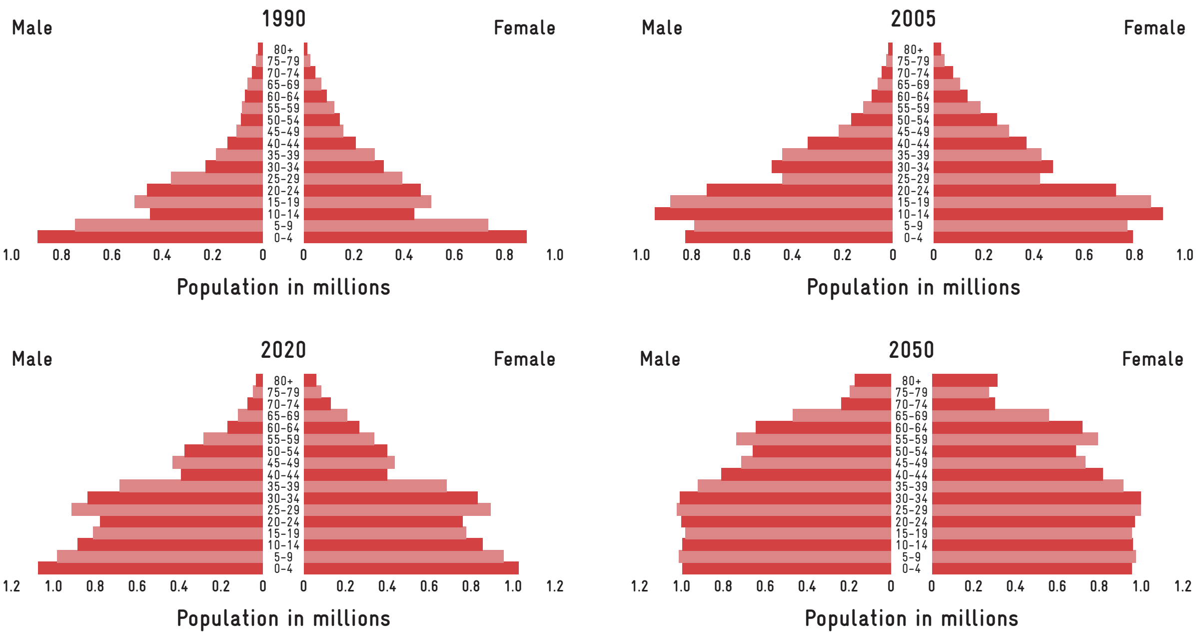
Cambodia has a unique modern history which led to a delayed epidemiological transition and a specific age structure. The Cambodian population pyramid from 1990 clearly shows the dramatic impact of the Khmer Rouge period (1975-1979). However, Figure 2 also shows that the population of Cambodia is rapidly ageing. As chronic-degenerative disease prevalence is mainly determined by age [4], it is extremely likely that the absolute and relative importance of NCDs in Cambodia will increase.

Currently the population is still young, so the share of morbidity and mortality caused by noncommunicable diseases is slightly lower than in other countries in the region. However, as Table 2 indicates, in 2010 NCDs were already the cause of at least one third (34%) of loss of quality of life (measured as disability-adjusted life years; DALYs) [6],[5] and nearly half (46%) of all death cases [7] in Cambodia. It is expected that the impact of NCDs will steadily increase with the ageing of the population.

The current situation and expected developments require the government's full attention on these diseases,

5 Data from 2004.

Figure 2: Cambodian population pyramids; 1990, 2005, 2020 and 2050. (Source: [11])



and an evidence-based nationwide strategy. Consequently, the National Strategic Plan for the Prevention and Control of Noncommunicable Diseases [8] puts strong focus on cardiovascular diseases, cancer, chronic respiratory diseases and diabetes. However, it is also obvious that a lot of work still has to be done. In particular, the Ministry of Health (MOH) of the Royal Government of Cambodia needs to conduct a health economic evaluation of NCDs in order to select the most appropriate intervention programmes. Furthermore, a budget-impact analysis is required to understand how much these programmes will cost. Currently, this analysis cannot be evidence-based because there is little information available on the costs of prevention and treatment of NCDs in Cambodia.

The national WHO STEPwise approach to Surveillance (STEPS) Noncommunicable Disease Risk Factor Survey conducted in 2010 [9] shows a T2DM prevalence rate among adult Cambodians (25-64 years old) of around 3% (approximately 170,000 people), but there are large differences between age groups, regions and genders. Younger adults (23-34 years old) have a lower prevalence rate (around 1%); older adults (55-64 years old) have a higher rate (6%). Assuming this function is linear, we can calculate an age-specific T2DM prevalence rate for the proportion of the population age 35 and older (which we will refer to later) of about 4%.

	Death Cases	Lost DALYs
Communicable, maternal, peri-natal and nutritional conditions	83	2,903
Noncommunicable diseases	58	1,724
Malignant neoplasms	11	169
Diabetes mellitus	3	39
Neuropsychiatric conditions	3	451
Cardiovascular diseases	24	361
Respiratory diseases	6	132
Digestive diseases	5	122
Other	9	376
Total	150	5,003

Table 2: Burden of disease in Cambodia, in thousands of cases. (Source: [6, 7])

The T2DM prevalence rate in the urban population is much higher than in the rural population (5.6% and 2.3%, respectively). At the same time, women are more affected than men (3.3% and 2.5%, respectively). Other surveys calculate slightly different prevalence rates [10], but confirm the general finding that T2DM is a major public health problem in Cambodia.

According to WHO calculations, diabetes causes around 3,000 death cases (2008) and a loss of 39,000 DALYS in Cambodia per year (2004; Table 2) [8]. This makes T2DM the fourth leading NCD for cause of death, and the sixth leading NCD for loss of quality of life in this country. Compared with other NCDs, however, these figures seem low. For instance, one-fifth of death cases (21%) are caused by cardiovascular diseases (for which T2DM is a major risk factor), 7% are caused by cancer and 5% by chronic respiratory diseases. However, the WHO figures may underestimate the real burden of diabetes in Cambodia. Due to various factors, explained below, we can assume that the majority of people dying from diabetes or diabetes-related complications are not properly recorded. T2DM is definitely a growing public health problem that causes tremendous human suffering, demands high resources and hinders the economic development of Cambodia.

Prevention and treatment of T2DM is limited in Cambodia. Although the risk factors of diabetes (e.g., unhealthy eating behaviour, overweight, physical inactivity, etc.) are well known, primary prevention measures can be improved. The MOH conducts primary prevention activities in cooperation with other ministries (e.g., the Ministry of Education, Youth and Sports), but the majority of people of Cambodia are most likely not aware of the risks of developing diabetes. This is in particular dangerous as there is some evidence that the risk of diabetes is higher in Cambodia than in many other regions due to genetic [12] and nutrition reasons [13].

The main objective of secondary prevention is to avoid complications of diabetes (e.g., diabetic retinopathy, nephropathy, cardiovascular comorbidities, and diabetic food syndrome), and the early development of the final stage of T2DM which requires insulin replacement therapy, by identifying early/asymptomatic disease stages and providing appropriate therapy. Thus, screening of high-risk groups is of utmost importance in order to detect the disease early before complications occur. It is estimated that around two-thirds (67%) of T2DM patients are not diagnosed, and thus have no chance to slow down the progression of the disease or prevent complications [10].

There is some discussion on how and where screening for T2DM should be done. MOH prefers a referral model with a high importance on specialised diabetes clinics. In this model, patients are first seen at their local health centre. Patients with risk factors are detected and transferred to the diabetes clinic for blood sugar testing. Currently, there are eight diabetes clinics in the country with 20 more scheduled to open soon. In areas without access to diabetes clinics, patients are sent to the nearest referral hospital where laboratory services are available to measure blood sugar levels.

There is also discussion about whether this strict referral system for diabetes diagnosis is efficient, and what role health centres should play. The main problem is that many patients referred to diabetes clinics or referral hospitals for testing never show up, so it would be more effective and efficient to perform the testing and diagnosis at the health centre level, or even at the community level. This diagnosis could be supported by urine glucose testing, which is easier than blood sugar testing but less reliable. There seems to be general agreement that mass screening of the entire population is not recommended, but the most appropriate secondary prevention instrument to screen high-risk groups in low-income countries has yet to be determined.

The standard first-line treatment is an oral anti-diabetic (OAD) medication (e.g., Metformin); the second-line treatment is insulin replacement therapy. Ideally, OAD medication, insulin and the respective equipment (e.g., syringes, needles, etc.) should be available from the MOH Central Medical Store. However, there are severe shortages of supplies. Treatment should be accompanied by regular laboratory examinations (e.g., semi-annual Hb1Ac testing) as well as examinations for retinopathy, nephropathy, neuropathy and cardiovascular diseases. In reality, only a small percentage of diabetes patients ever show up at the hospital for treatment (estimates were not available), and almost no regular examinations beyond a symptom-related diagnosis are performed in the public health system. Complications are not treated in the majority of patients, as chronic diseases are not included in the basic package of health care services subsidised by MOH and the majority of patients can neither afford treatment at referral institutions nor at private providers.

Consequently, there is a need to predict the expected number of T2DM cases in Cambodia, determine the most cost-effective intervention strategies, and estimate the budgetary impact of prevention and treatment of this disease. The costing of diabetes follows a standard approach and will be done in three steps: literature analysis; costing of a particular service model (developed by the MoPoTsyo patient information centre, a Cambodian nongovernmental organisation which supports a peer-support approach and self-management of diabetes in poor communities); and a forecasting model for the cost of prevention and treatment of diabetes in Cambodia. Consequently, the next section presents findings from a literature review on the economic dimension of T2DM relevant to Cambodia. Afterwards, some results from a micro-costing are discussed. The fourth section analyses the results of a T2DM forecasting model in Cambodia. The paper closes with a discussion of the findings for the health care system in Cambodia.

2. Economic Burden of Type 2 Diabetes Mellitus

The economic burden of T2DM is tremendous and there are a number of papers on the cost of this disease and the cost-effectiveness of interventions worldwide. Zhang et al [14] published an estimate of global health expenditures for diabetes and concluded that 'global health expenditure on diabetes is expected to total at least USD 376 billion or PPP$ 418 billion in 2010'.[6] Consequently, '12% of the health expenditures and USD 1,330 (PPP$ 1,478) per person are anticipated to be spent on diabetes in 2010' [14]. North America, in particular the United Stated of America (USA), have the highest share of global health expenditures on diabetes (USD 214 billion), followed by Europe (USD 105 billion) and the West Pacific region (USD 38 billion). South-East Asia (USD 3 billion) and Sub-Saharan Africa (USD 1.4 billion) are still facing smaller burdens in absolute numbers, but these expenditures have to be understood in relation to national incomes.

The USA has the highest epidemiological and economic burden of T2DM. The Centers for Disease Control and Prevention (CDC) estimate the annual direct medical cost of diabetes in the USA at around USD 116 billion. In addition, the indirect costs (work losses and premature death) are estimated to be around USD 58 billion. Thus, this highly affected country suffers a loss of USD 174 billion per year due to diabetes [15].[7] Other estimates are even higher [16]. Considering that the average health expenditures for an American with diabetes (USD 11,700) were four times as high as for a person without diabetes (USD 2,900) [17], there is strong support to prevent the onset of diabetes, the progression of the disease and complications. A recent literature review demonstrated that most interventions against diabetes are expensive but cost-effective [18].

Other high-income countries are also highly affected. Waldeyer et al. [19] estimated the annual direct medical excess costs of T2DM in Germany at around €12 billion in 2010. They also calculated that costs would increase 79% by 2040 to €21.1 billion per year. This confirms an older study on the cost of diabetes in Germany, which shows that the average annual direct cost per diabetes patient was almost double the amount of an age- and sex-matched patient without diabetes [20]. The Eastern Mediterranean countries are also highly affected by this disease. Boutayeb et al. [21] estimated the cost of diabetes for 21 countries in this region at around USD 14 billion (ranging from USD 9 billion to USD 22 billion) with significant differences between countries. There is no doubt that T2DM is also a strong and increasing economic and public health problem in the Arab region.

For low- and middle-income countries, the evidence of the economic cost of diabetes is not as strong. Barcelo et al. [22] estimated the cost of diabetes in Latin America and the Caribbean in 2000. They calculated direct medical costs of USD 11 billion and indirect costs of USD 54 billion for the year. The major cost drivers were insulin and oral medications (USD 4.7 billion), hospitalisation (USD 1 billion), consultations (USD 2.5 billion) and care for complications (USD 2.5 billion). For Africa, Hall et al. [23] performed a systematic literature review. They concluded that the total annual costs of T2DM in Sub-Saharan Africa were approximately USD 67 billion. However, all these figures must be taken with caution, as some results are contradictory (e.g., the results for Sub-Saharan Africa between Hall et al. [23] and Zhang et al. [14]).

There is some literature on the economic burden of diabetes in South-East Asia. Soewondo et al. analysed the situation in Indonesia [24]. They concluded that 'at the time of writing there was no published evidence on the national direct costs of diabetes'. However, there is data from specific health care providers, which offers insight into the cost of diabetes in this country. One study from Kodya Hospital Yogyakarta calculated the monthly cost of T2DM per patient as nearly USD 20. Most of the direct medical costs identified were spent on drugs (96%) [25]. This data was confirmed in a study from another Indonesian hospital, Sardjito Hospital in Yogyakarta, where the average direct cost per month for diabetes treatment was USD 21 [26].

The conclusion of Soewondo et al. is also true for Malaysia as – to our knowledge – only limited data from specific facilities is available to assess the economic burden of T2DM for this country. Ezat et al. [27] calculated a cost of

6 The international dollar is widely used in economics to adjust costs for the purchasing power parity in different countries (PPP$).

7 All data is from 2007.

USD 102 per day for tertiary and secondary hospital inpatient services for diabetes patients. Primary hospitals were even more expensive (USD 116 per day) as their bed occupancy was lower (leading to a higher proportion of overhead per bed-day). The same study calculated outpatient costs for diabetes patients at around USD 51 for tertiary hospitals, USD 38 for secondary hospitals and USD 57 for primary hospitals. Another study on the costs of diabetes care in Malaysia was done by Ibrahim et al. [28]. They calculated the annual direct costs of a diabetes patient as USD 573. Medication made up the majority of these costs (USD 317), followed by laboratory services (USD 165).

Several articles from Higuchi (with co-authors) focus on the costs of diabetes care in the Philippines [29-31]. They calculated the monthly median costs for diabetes treatment as USD 20 (for insulin therapy) and USD 13 (for OAD therapy). Syringes were found to cost USD 0.22 per unit.

The costs of prevention and treatment of diabetes in Thailand are better understood. Chatterjee et al. [32] made a professional micro-costing and calculated the annual costs per diabetes patient at around USD 881. Of this amount, USD 203 was for direct medical costs, USD 353 went to direct non-medical costs (e.g., informal care and transport), and USD 326 was spent on indirect costs. These results confirm previous work done by the researchers for specific institutions [33]. For Thailand, we have also data on the cost of screening. Jiamjarasrangsi and Aekplakorn analysed the screening costs for abnormal fasting plasma glucose and came up with a range of around USD 5 to USD 7 per test.

Finally, for Vietnam, Beran and Higuchi [29] presented some cost estimates for insulin and OAD drugs. They calculated the cost of insulin as around USD 7 per month, the cost of OAD medicine as USD 31 per month, and the cost per syringe as USD 0.09. It should be noted that these findings are based on the same costing methodology as the authors' study from the Philippines (see above), but using country-specific figures.

In summary, there is quite a lot of data on the epidemiology [34] and the economic burden [35] of diabetes in South-East Asia. However, our knowledge of unit costs based on professional micro-costing is limited. At the same time there is a lack of data from Cambodia. It is obvious that costs cannot be easily transferred from middle-income countries (e.g., Indonesia and Thailand) to a least-developed country like Cambodia [36]. The first reason for this is that the absolute figures might be misleading, as the same resources (e.g., working hours) might be much cheaper in the poorer country. However, it is also wrong to assume that the costs between two countries have the same ratios as the per capita gross national product (GNP). Second, the share of certain cost categories might not be identical. For instance, the cost of drugs might be higher in Cambodia (due to a number of problems beyond the scope of this paper), whereas labour might be much cheaper. Third, the outputs are most likely not comparable; i.e., the scope and quality of services varies between different countries, as do the outcomes which depend strongly on the complete health care system, not only on the intervention against one specific disease. Finally, the frequency and severity of T2DM complications might differ from country to country. Consequently, there is a need to analyse existing costing studies specifically for Cambodia.

However, the number of studies examining the cost of prevention and treatment of diabetes in Cambodia is very limited, and their quality is usually not satisfactory. A very rudimentary approach comes from the World Diabetes Foundation [37], which financed a diabetes care project with costs of around USD 16 per patient annually, or USD 6 per consultation, including all treatment measures. It is obvious that this amount cannot be the base of a costing model for Cambodia. In some medical and epidemiological papers there is preliminary economic data on the subject. Raguenaud et al. [38] estimated annual costs of USD 48 for glibenclamide monotherapy and USD 192 for dual therapy with glibenclamide and metformin. However, these are very unreliable estimates.

Without assuming that this review is fully comprehensive, we can state that our knowledge of the economic burden of T2DM in Cambodia is as limited as our insights into the cost-effectiveness of certain interventions in this country. However, there is a need to base the decisions of MOH and its international health partners on evidence. Consequently, a micro-costing, budget-impact analysis and cost-effectiveness analysis of T2DM interventions must be made.

3. Micro-Costing Type 2 Diabetes Mellitus in Cambodia

No uniform and generally accepted model of prevention and treatment of patients with diabetes exists in Cambodia. Consequently, we will select one institution where the data is reliable, and which can serve as a model for the entire country, to analyse. This model is described in the next subsection. Afterwards, we present the methodology for this micro-costing and some results.

3.1. MoPoTsyo Model

In this section we will present the results of a costing of the services provided by the MoPoTsyo Patient Information Centre in Phnom Penh, the capital and largest city of Cambodia. This NGO has developed a model of managing two NCDs in Cambodia; hypertension and diabetes. Based on peer-educator networks, they produce preventive and curative services for patients and potential patients with diabetes and/or hypertension in a number of urban and rural districts. First, the MoPoTsyo Patient Information Centre is engaged in primary prevention by raising the awareness of risk factors for these diseases among the general population as well as public health authorities.

However, MoPoTsyo is much more engaged in secondary prevention; i.e., the identification of patients and follow-up therapy to avoid deterioration and complications of diabetes. They make peer educators out of patients by training them for six weeks (including a final exam). These peer educators are then able to screen for new patients and work with them to change their lifestyle and manage the disease. Peer educators are paid by MoPoTsyo Patient Information Centre.

In addition, MoPoTsyo supports and organises special consultation sessions at a local referral hospital. These happen regularly, around one to two days per month. On average, 30-40 members of the peer-educator networks (for both hypertension and diabetes) can meet a qualified doctor on each occasion.

One major element of the curative function of the MoPoTsyo Patient Information Centre is the revolving drug fund. It buys drugs, tests them, and distributes them to public and private pharmacies. Furthermore, MoPoTsyo Patient Information Centre monitors the adherence and prescribing behaviour of their patients. Thus, members of the peer-educator network can get their medicine at fixed prices, and these fees allow the institution to buy new drugs. This system has the advantage for patients of a reliable supply, and stable prices that are lower than in regular private pharmacies.

The curative function of the MoPoTsyo Patient Information Centre includes some laboratory diagnostics at the health centre level. For this purpose, laboratory teams come twice a year to health centres to perform procedures.

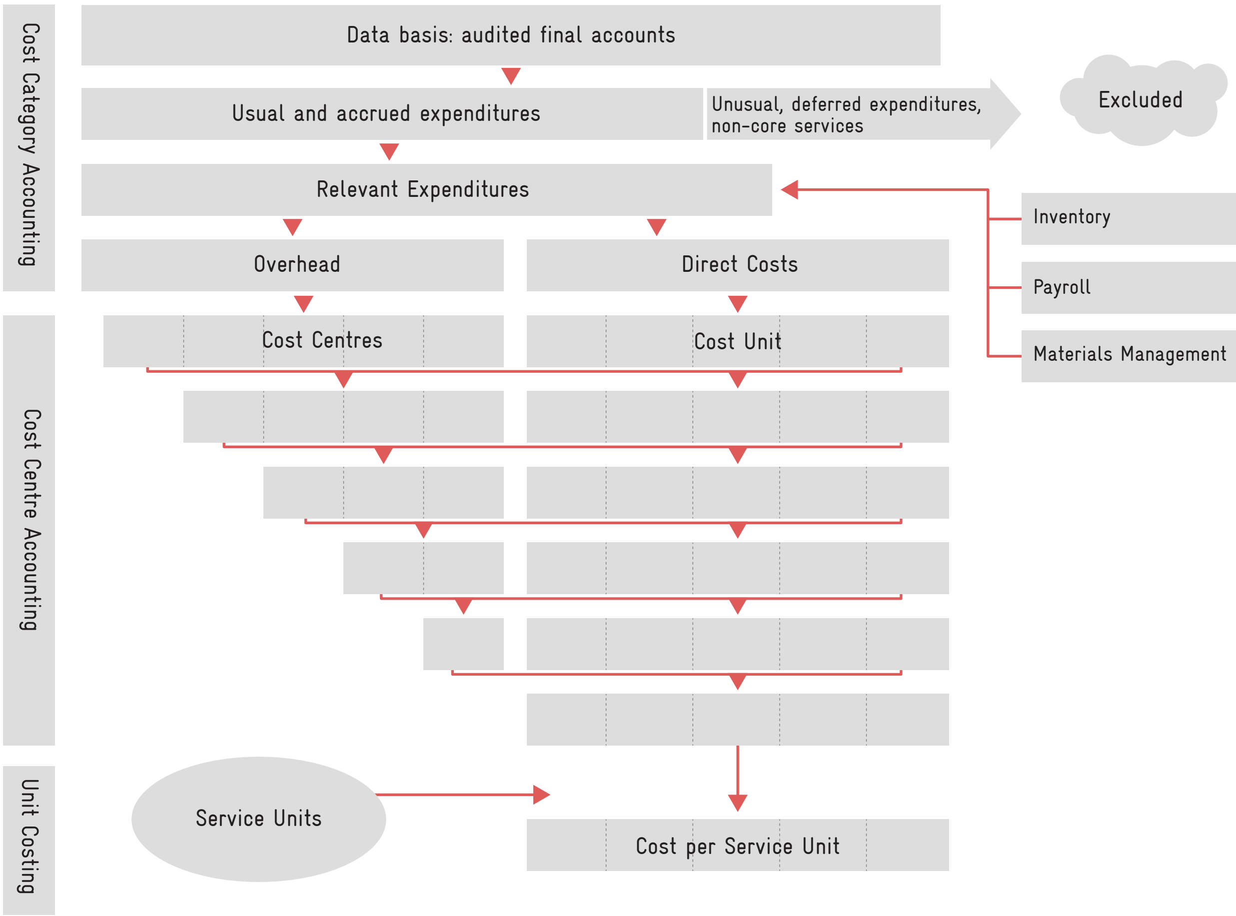
MoPoTsyo builds its support on the peer-educator network model – an instrument which is seen as a key approach in the government's national NCD strategy. Consequently, MOH is interested in ensuring that MoPoTsyo continues and expands its activities.

3.2. Methodology

The main objective of costing is the determination of a cost per service unit. The starting point is usually the expenditures recorded in the financial accounts, which are allocated in stages (also called 'steps') to the costing units. Most routine systems, such as the calculation handbook of the German Diagnostic Related Groups (DRG) system [39], as well as many costing studies in developing countries [40-42] use a step-down approach (sometimes also referred to as a stepping-stone method), which does not require exact figures on the resource consumption of each activity. In the absence of a detailed process analysis and comprehensive time studies of MoPoTsyo's activities, we chose this methodology to calculate reliable unit costs.

Figure 3 gives an overview of this methodology. The (audited) final accounts and the respective account books were the starting points of the costing. In the first step, all entries were analysed in order to exclude irrelevant expenditures, such as payments for costs for the last year or next

Figure 3: An overview of the costing methodology employed.



Cost centre	Distribution plan	Data requirements
Management and administration	Equally distributed between all other cost centres	-
Peer education department	Fully assigned to cost unit peer education	-
Laboratory	Distributed between diabetes treatment and hypertension treatment cost units, according to actual use of laboratory services.	Laboratory statistics
Medical consultations	Distributed between diabetes treatment and hypertension treatment cost units, according to actual use of consultation services; costs of glucose tests for diabetes patients during medical consultations were allocated exclusively to diabetes treatment.	Service records
Revolving drug fund	Distributed between diabetes treatment and hypertension treatment cost units, according to actual consumption.	Materials management records

Table 3: Allocation of costs for MoPoTsyo costing.

year, unusual payments, and activities outside the core functions of the organisation (e.g., World Diabetes Day events, research projects, etc.). In addition, all payments for stocks and investments were removed and compared with inventories. The depreciation of fixed assets and the costs of materials consumed within the year were taken from the actual inventory and materials management records.

In the next step, every cost item for the year in all cost categories (see Table 4) was analysed to determine whether it could be directly attributed to a final costing unit or whether it constituted an overhead expense. Direct costs were allocated to the cost units, whereas overhead expenses for each cost category were allocated to the respective cost centres.

Basic terms	MoPoTsyo model	Explanation
Cost categories	a. Personnel costs b. Training c. Materials (except drugs) d. Depreciation e. Rent f. Drugs h. Travel and delivery i. Peer educator allowances j. Other costs	
Cost centres	1. Management and administration (headquarters) 2. Peer education department 3. Laboratory 4. Medical consultation 5. Revolving drug fund	
Cost units	i. Diabetes screening ii. Peer education iii. Diabetes treatment iv. Hypertension treatment	i. Number of diabetes screenings performed. ii. Number of peer educators covering the catchment area of one heath centre. iii. Number of diabetes patients under treatment. iv. Number of hypertension patients under treatment. NB: A patient with diabetes and hypertension is counted as a diabetes patient.

Table 4: Basic characteristics of MoPoTsyo costing model.

In the next step, a step-down costing approach was followed. As Figure 3 indicates, headquarter costs were allocated to the other cost centres according to a specific distribution plan (see Table 3). Afterwards, the total of allocated and original costs of the peer education department were allocated to the other cost centres according to another distribution plan. This process continued until the direct and indirect costs of all cost centres were allocated to the costing units. Finally, the cost per service unit was calculated by dividing the total direct and allocated costs per service unit by the total number of service units.

3.3. Results

Table 5 presents the basic costs per service unit for MoPoTsyo between 2011 and 2012. Diabetes screening costs were around USD 0.07 per person screened, but this is urine glucose screening, not blood sugar testing (urine glucose screening is cheaper, but less accurate). Treatment costs per diabetes patient were around USD 42 per year, including medication. The table also shows that the unit costs per screening, peer educator and diabetes patient have decreased from 2011 to 2012. This is mainly due to the higher workload; i.e., MoPoTsyo has benefitted from some economies of scale. In 2011, 83,690 screenings were done; in 2012, 219,689 screenings were performed. The number of peer educators has also increased from 74 to 108, and the number of diabetes patients receiving treatment has risen from 3,159 to 5,420. That the workload has increased while the unit costs have gone down indicates that the majority of costs per service unit are actually variable costs.

	Diabetes screening	Peer education	Diabetes treatment	Hypertension treatment
2011	0.10	1,319	43.47	16.81
2012	0.07	1,278	42.13	18.37

Table 5: Annual unit costs for MoPoTsyo, 2011 and 2012 (in USD).

However, the unit costs for treatment of hypertension have increased. The management of MoPoTsyo explained that this was caused by better adherence of hypertensive patients to their treatment schedule (a major problem in any hypertension treatment). The cost for medication in this client category was USD 0.49 in 2011 and USD 2.42 in 2012, whereas the price per drug unit remained stable. Thus, the assumption of better adherence to the treatment seems to be correct.

If we assume that the personnel costs and all overhead for the headquarters remains stable for at least some variation of output, we receive the cost functions for the total costs of the Patient Information Centre as:

$C = 196475 + 0.07s + 954p + 27d + 9h$, where

- C is the total cost of MoPoTsyo services;
- s is the number of diabetes screenings;
- p is the number of peer educators;
- d is the number of diabetes patients;
- h is the number of hypertension patients.

The factors are also the marginal cost; i.e., one additional diabetes patient costs USD 27 if only variable costs occur and the administrative structure can be maintained. Based on the estimate of 170,000 people living with diabetes in Cambodia,[9], the costs of treatment would be around USD 5 million per year if the MoPoTsyo model were applied and the overhead costs remained unchanged. If we simply assume that overhead grows linearly with output, the total costs would be around USD 7 million.[8]

These figures indicate that the cost of secondary prevention and treatment of T2DM in Cambodia are much lower than for neighbouring countries. It would be wrong to transfer costing data from other South-East Asian countries without reflecting the purchasing power parity, the cost structure and the respective model of care in Cambodia. However, this result does not contain a proper forecast or a budget-impact analysis. Therefore, a prediction model has to be designed. It will be presented in the next section.

8 The discussion whether NGO overheads should be included in the analysis goes beyond the scope of this paper. In one perspective, overheads are real and increasing coverage could definitely increase overhead costs. However, the public provision of services also incurs overhead, but the operational expenses of public administrations (including MOH) are hardly incorporated into those analyses.

4. Diabetes Prognosis in Cambodia

This analysis follows the standards for health economic evaluations provided by Schulenburg et al. [43]. As a first step, we will present the methodology and the parameters of the model. Afterwards, we make some estimates of the number of diabetes cases and their impact on the budget. Finally, we will present some intervention scenarios and discuss their cost-effectiveness.

4.1. Model

As diabetes is a noncommunicable disease, the probability of developing diabetes or transitioning to another stage of the disease is constant. Consequently, the epidemiology of T2DM is frequently simulated with Markov models [44]. However, there are very few Markov models designed for resource-poor countries [45], and none represent the specific structure and parameters of the Cambodian demography and the health care system. Thus, it is necessary to design a specific model incorporating the relevant parameters for Cambodia.

Figure 4 shows the principle structure of the Markov model. The vector wt represents the number of individuals in specific health states in time *t*.[9] The respective vector *wt*+1 for the next period (t+1) is calculated by multiplying the vector with the matrix of transition probabilities A [46]; i.e.

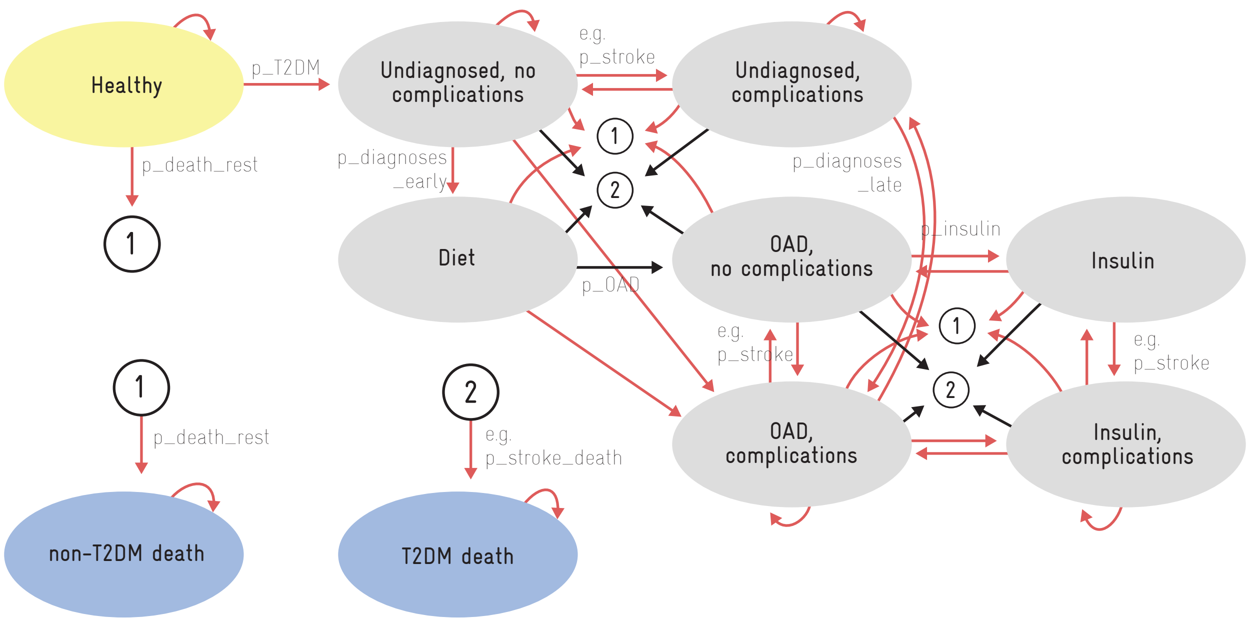
$$\underline{w}'_{t+1} = \underline{w}'_t \cdot A \text{, with}$$

$$\underline{w}_t = \begin{pmatrix} w_1 \\ \dots \\ w_n \end{pmatrix}; \quad A = \begin{pmatrix} a_{11} & a_{12} & \dots & a_{1n} \\ a_{21} & a_{22} & \dots & a_{2n} \\ \vdots & \vdots & \ddots & \vdots \\ a_{n1} & a_{n2} & \dots & a_{nn} \end{pmatrix}$$

Consequently, the number of individuals in the specific health states in time *t* is calculated as $\underline{w}'_t = \underline{w}'_0 \cdot A^t$ where w0 denotes the number of individuals in the conditions at the beginning of the simulation.

9 The health states used in our model are: healthy; undiagnosed, no complications; undiagnosed, complications; diet; OAD, no complications; insulin; OAD, complications; insulin, complications; non-T2DM death; and T2DM death.

Figure 4: Diagram of the Markov model for diabetes in Cambodia.



In addition to the conditions, the model conducts simulations for adults (everyone over 15 years old) in each five-year age group, and runs from 2008 to 2028. As the prevalence of T2DM in the proportion of the population under 35 years old is negligible, we concentrated on the cohort of Cambodians 35 years of age or older during the modelling period (everyone 15 years of age or older in 2008).

Table 6 exhibits the most important parameters of the Markov model, and their sources.[10] Where no country-specific data was available, we adjusted the available data according to the best estimates of Cambodian and international experts. For instance, it is estimated that diabetes manifests about 10 years earlier in Asian countries than in European ones [62]. The incidence rates were adjusted accordingly.

Parameter	Source	Comment
Prevalence rates	[1, 9]	
Demography	[47-49]	
Mortality	[50, 51]	
Age-specific incidence rates	[52]	Adjusted
Transition of stages	[53-57]	Adjusted
Diagnosis lag	[58]	Adjusted
Therapy options	[59]	Adjusted
Cost	[60, 61]	Own calculations, based on section 0.

Table 6: Basic parameters of the Markov model for Cambodian diabetes prognosis.

As the treatment costs are crucial to the model, a detailed analysis was conducted on the treatment data of MoPoTsyo, the international drug price indicator guide [60], and additional research on market prices in Cambodia. The costs of metformin and glibenclamide were estimated at around USD 25 and USD 3 per patient per year. With the assumption that 12% of patients use metformin exclusively, 10% use glibenclamide exclusively, and 79% use both drugs, the average cost per OAD patient is around USD 25. The cost per ml of insulin was estimated at USD 0.72 [60]. At an average consumption of 120ml per patient per month, we estimated annual costs of around USD 103 for insulin therapy (including insulin and syringe costs). Combined therapy was estimated to cost USD 129 per patient per year. Assuming the international standard that slightly more than half (57%) of insulin-dependent diabetes patients receive insulin monotherapy [60], the average costs of insulin therapy are USD 114 annually per patient.

10 For details on the model, please refer to: Flessa, S. and A. Zembok, Costing of diabetes mellitus type II in Cambodia. Health Economics Review, 2014. 4(1): p. 1-15.

Based on these parameters, we have forecast the epidemiological and economic impact of T2DM in Cambodia until 2028.

4.2. Basic Simulation

Figure 5 shows the development of type 2 diabetes in Cambodia from 2008-2028. The number of people with T2DM will steadily increase from around 145,000 in 2008 to over a quarter of a million cases in 2028 (264,000); an increase of nearly 82%). At the same time, the percentage of Cambodians age 35 and older will increase by two-thirds (67%), and thus the prevalence of diabetes among people in this age group will increase from 4.0% to 4.4%

The majority of T2DM cases will remain undiagnosed. The rate of undiagnosed diabetes is stable (63% to 64%), as the basic simulation assumes that no additional interventions are implemented. The number of diagnosed patients with complications, however, will increase at a greater extent than the number of diagnosed patients without complications. In 2008, slightly more than half (59%) of diagnosed patients had complications; in 2028 this rate will increase to two-thirds of diagnosed patients (68%). This is because the ageing population and longer duration of diabetes in patients will result in more patients with complications.

Figure 6 shows the number of diagnosed T2DM cases requiring different forms of therapy. 'Diet' means that a diagnosed patient does not receive any medication, managing the disease through a specific diet and modifications to their lifestyle. The use of oral anti-diabetes (OAD) drugs occurs at the next stage of the disease, followed by insulin injections. In 2008, only around 2% of patients did not require any form of medication, the vast majority (84%) needed OAD therapy, and around 14% required insulin. In 2028, around one out of every thirteen diagnosed cases of diabetes (7.6%) will not require medication, three-quarters (76%) will need OAD therapy, and around one-sixth (17%) will need insulin therapy. Thus, a higher share of the population will be in the severe state of diabetes, requir-

Figure 5: Basic simulation of type 2 diabetes cases in Cambodia, 2008-2028.

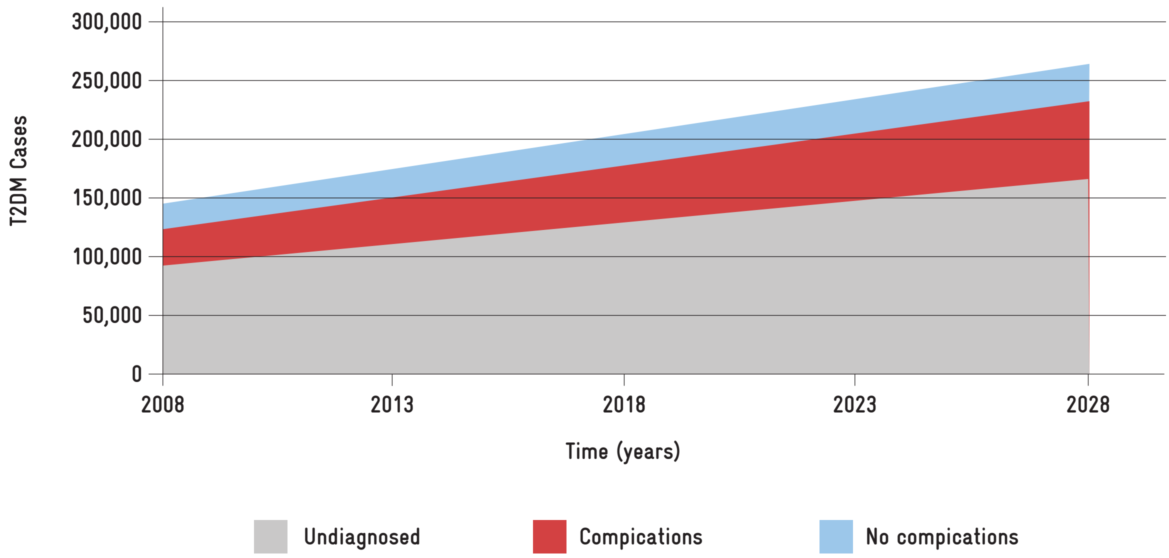
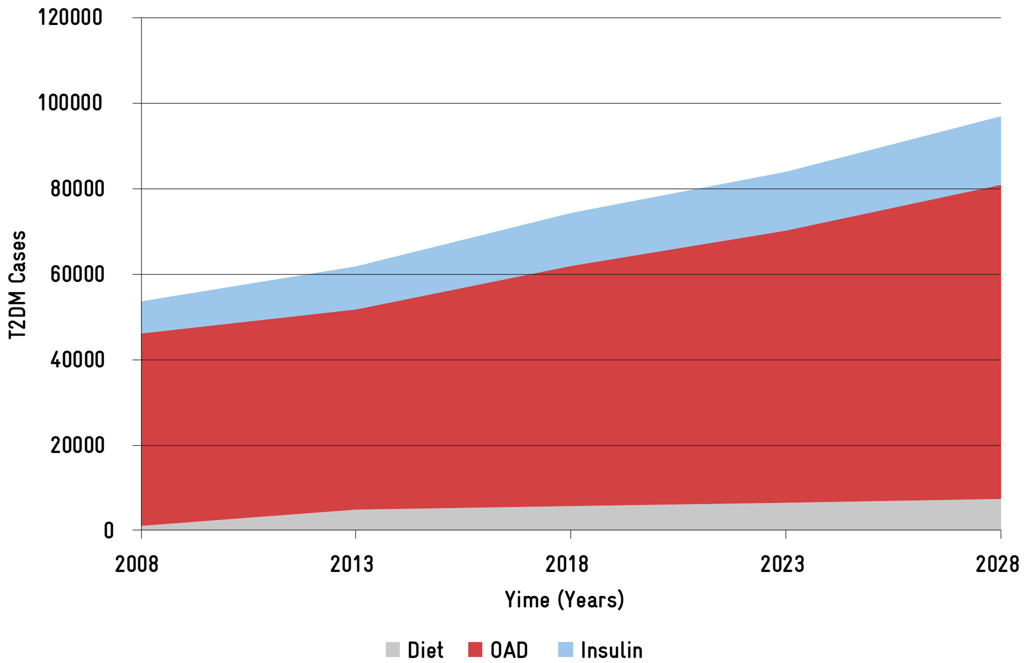


Figure 6: Basic simulation of T2DM patients in Cambodia classified by therapy types, 2008-2028.

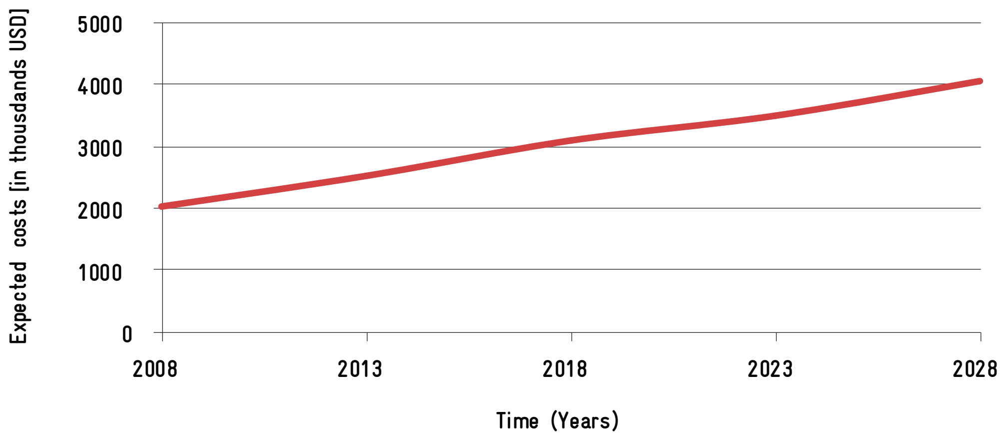


ing insulin. The increase in severe diabetes of over 110% is much higher than the increase in the total number of diabetes cases in Cambodia. The decision-makers in Cambodia can expect that the worst medical and economic consequences of T2DM are still to come.

This transition is also reflected in the steadily increasing cost of treating patients with T2DM in Cambodia. In 2011, it was estimated that only one in every eight people (12.5%) in Cambodia that required OAD or insulin therapy actually received it [63, 64]. The estimates in this model assume that this ratio remains stable until 2028. A scenario that accounts for increasing treatment coverage is presented in section 4.3.

In 2008, the 54,000 diagnosed T2DM patients incurred costs of around USD 2 million to pay for their diabetes treatments. More than half (57%) of this amount was probably spent for OAD therapies, and the rest for insulin therapy. By 2028, this amount will grow to around USD 4 mil-

Figure 7: Basic simulation of the budgetary impact of T2DM in Cambodia, 2008-2028.



lion to cover nearly 100,000 patients. The expected average cost per diagnosed diabetes patient per year was USD 38 in 2008, and is expected to be around USD 42 in 2028. If all patients (including those that are undiagnosed) were treated, the treatment costs in 2028 would be USD 11 million. Based on these estimates, the costs of treating diabetes will double by 2028 due to a shift in patients towards those with complications and those requiring insulin. These calculations assume stable prices and no discounting.

The estimated budgetary impact of diabetes greatly depends on the precision of the parameters. The most important budgetary parameter is the estimate of hospital costs. A 50% increase in these costs leads to a 40% increase in cumulative costs, whereas a 50% increase in OAD medication costs would only result in a 6% increase in total costs. Another important parameter is general and T2DM-related mortality. When diabetes patients die at a younger age, they have lower treatment costs. If T2DM-related mortality increases by 20%,cumulative treatment costs will decrease by 16%. If general mortality increases by 20%, cumulative treatment costs will decrease by 17%. However, even assuming the most cost-effective situation for all parameters (according to estimates from Cambodian experts and the literature review), the costs of treating diabetes will still increase through 2028.

In summary, Cambodia is facing an increasing number of diabetes patients that will require OAD and insulin therapies. Compared with the actual budget of MOH, the costs of treating these patients does not seem high, but these costs are in addition to existing expenditures for health care. Thus, there is a need to analyse the cost-effectiveness of interventions and determine the best use of scarce resources.

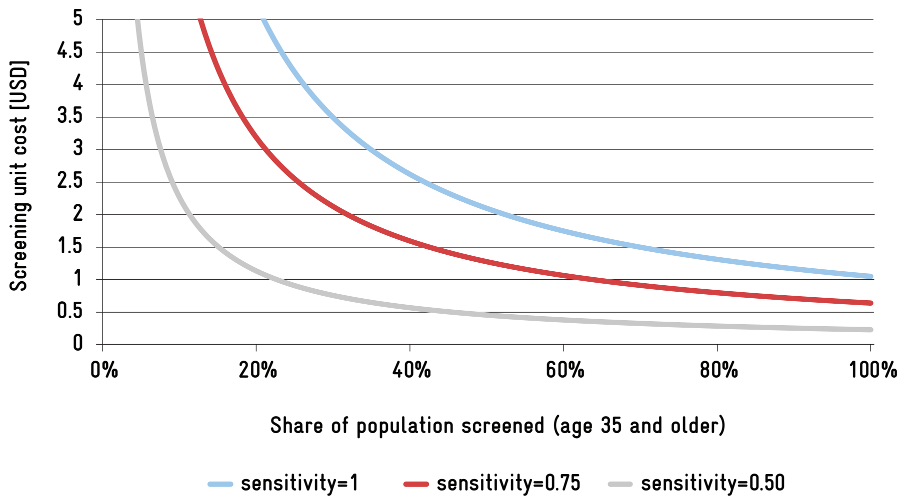
4.3. Cost-Effectiveness Analysis

4.3.1. Screening Programmes

The basic simulation assumes that diabetes patients in Cambodia are undiagnosed for an average of seven years [58]. Consequently, treatment of diabetes is also delayed, which leads to increased diabetes complications, earlier transitions to more serious treatment states, and higher diabetes-related mortality. The purpose of screening programmes is to identify T2DM cases as early as possible, ideally at the onset of the disease, in order to avoid these negative consequences. The impact of screening on the epidemiology and costs of diabetes depends on the share of the population screened (i.e., only high-risk groups, or the total population) as well as the sensitivity of the test. Ideally, every diabetes patient would be detected within one year. Although not technically possible, we present this ideal scenario of diabetes screening initially, and then we analyse the consequences of lower screening sensitivities and reduced coverage rates.

The consequences of an ideal screening scenario (the detection of every patient within one year after the onset of T2DM) are an increase in the number of people living with T2DM, and a strong decline of the number of T2DM-related death cases. By 2028, for instance, 275,000 people would be living with T2DM instead of 264,000. The cumulative number of T2DM-related death cases from 2008 to 2028 would be 462,000 instead of 476,000. The share of diagnosed diabetics with complications would decrease from 68% to 48%, and more diabetics would

Figure 8: Cost-effectiveness curve for diabetes screening.



be able to control their disease through diet and lifestyle (12% versus 7.6%). The total cumulative treatment costs would increase from USD 61 million to USD 68 million. However, the average cost per diagnosed diabetes patient in 2028 would decline from USD 42 to USD 33.

The incremental cost-effectiveness ratio (ICER) compares the cost of an intervention with the effect (e.g., years of life saved, reduced mortality). An intervention is usually assessed as cost-effective if the cost per life-year saved (LYS) is less than the annual gross national product per person. In the case of Cambodia, an intervention is cost-effective if ICER is less than USD 1,000 per LYS. If we assume the cost of urine sugar screening done by MoPoTsyo (i.e., USD 0.07 per person, plus USD 1 for the confirmation test) the corresponding ICER for screening the entire population is USD 463.46 per LYS. Thus, screening the entire population over 35 years old annually for T2DM is cost-effective if the sensitivity of the test is 100%.

In the second stage of the analysis, we vary the coverage (share of population tested) and the sensitivity of the test. If we assume that 100% of the population are screened, the cost per screening would be USD 1.05 if the screening was 100% sensitive, USD 0.64 if the sensitivity was 75%, and USD 0.23 if it was 50% sensitive. If the sensitivity of the test goes below 36%, screening will not be cost-effective at all.

If we focus on high-risk groups and reduce the coverage of the population, the cost per screening would be higher. In Figure 8, every combination of coverage (x-axis) and screening unit cost (y-axis) under the curves is cost-effective. For instance, if we limit screening to 33% of the adult population over 35 years old, the cost per screening could rise to USD 3.18 (sensitivity 100%), USD 1.93 (sensitivity 75%) or USD 0.69 (sensitivity 50%) and still be cost-effective. Limiting screening to groups at higher risk of diabetes (such as obese individuals) would allow for even higher unit costs while still safeguarding the cost-effectiveness of the intervention. In the discussion section we will address this issue again.

4.3.2. Oral Anti-Diabetic Therapy

Oral anti-diabetic (OAD) medication is not currently available at public health centres and district hospitals in Cambodia. Consequently, these drugs are only accessible to the very few individuals covered by private health insurance or those who can afford to pay for these drugs out-of-pocket in private health care institutions. Consequently, it is estimated that only around one in eight (12.5%) diagnosed diabetics requiring OAD therapy comply with the treatment [63, 64]. In this section we will analyse the consequences of improved access to OAD therapy. This would be possible if the Royal Government of Cambodia provided free or highly subsidised access to these drugs at rural health centres; i.e., if OAD medication became an element of the basic health care package in Cambodia.

Figure 9 shows the consequences of improved coverage of OAD therapy on LYS and death cases averted. As expected, more OAD-therapy patients receiving medication leads to a higher number of LYS and reduced mortality. This increase is almost linear. If 100% of patients requiring OAD therapy were to receive it, nearly 200,000 life-years

Figure 9: Impact of different coverage scenarios for OAD therapy in Cambodia , by patients requiring OAD therapy.

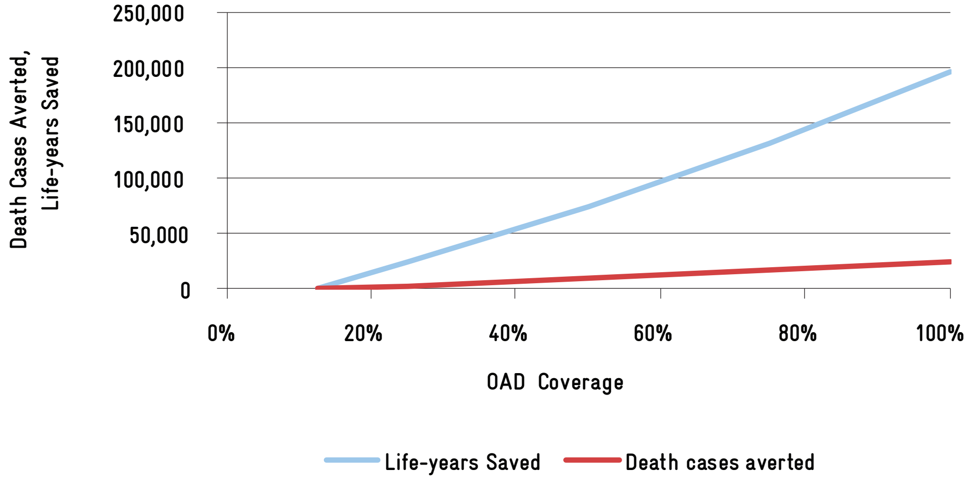
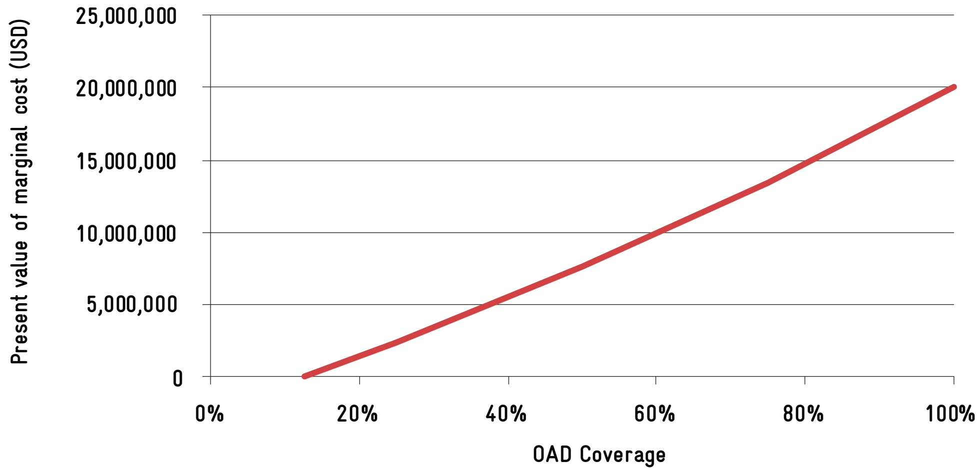


Figure 10: Marginal cost of different coverage scenarios for OAD therapy in Cambodia , by patients requiring OAD therapy.

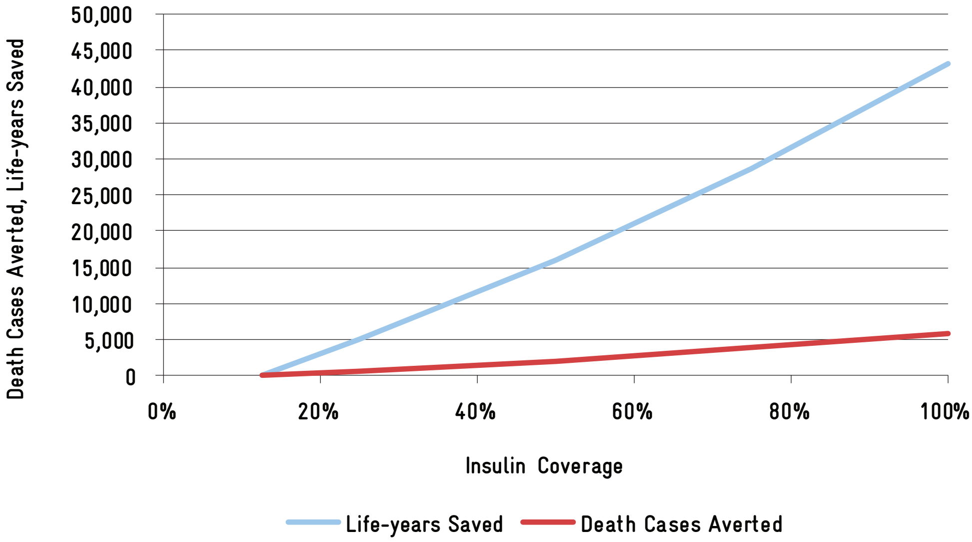


would be saved and over 25,000 death cases averted from 2008 to 2028. The percentage of diagnosed diabetics receiving OAD therapy would increase from 76% to 78%, but the number of people living with diabetes would increase across all patient spectrums (diet, OAD therapy and insulin therapy). Thus, more diabetics would require insulin, as more of them are living with the disease for a longer time. Consequently, the cost of diabetes treatments would strongly increase. That is, improving coverage of the population by OAD therapy not only requires more resources to purchase OAD drugs, but also to finance the costs of insulin therapy for the higher number of patients who survive OAD therapy and transition into insulin therapy. Consequently, the costs of treatment per diabetes patient would increase from USD 42 to USD 53.

Figure 10 shows the current marginal costs of improved OAD-therapy coverage. It is obvious that the costs increase linearly with increased coverage of the OAD-therapy patient population. However, the ICER for this figure is almost stable. An increase in coverage from the current situation (12.5%) to 25% of patients would result in an ICER of USD 101.74 per LYS; an increase to 100% would result in an ICER of USD 102.20 (discounted by 5%). The ICER for death cases averted are USD 840.61 (for 25% coverage) and USD 799.65 (for 100% coverage) per death case averted; i.e., higher OAD-therapy coverage improves the cost effectiveness of the intervention.

An ICER of around USD 100 per LYS is highly cost-effective in Cambodia, and this result is not generally dependent on the interest rate. Even at a rate of 7.5%,

Figure 11: Impact of different coverage scenarios for insulin therapy in Cambodia, by insulin-dependent patients .



ICER only increases to USD 105.39 per LYS. However, cost-effectiveness does not imply feasibility, as the budget constraints have to be respected. In 2028, Cambodia would have to spend USD 6.7 million to provide all OAD-therapy patients with access to this medication, instead of USD 4 million at the current coverage rate. USD 2.7 million would constitute a considerable increase in the national health budget.

4.3.3. Insulin Therapy

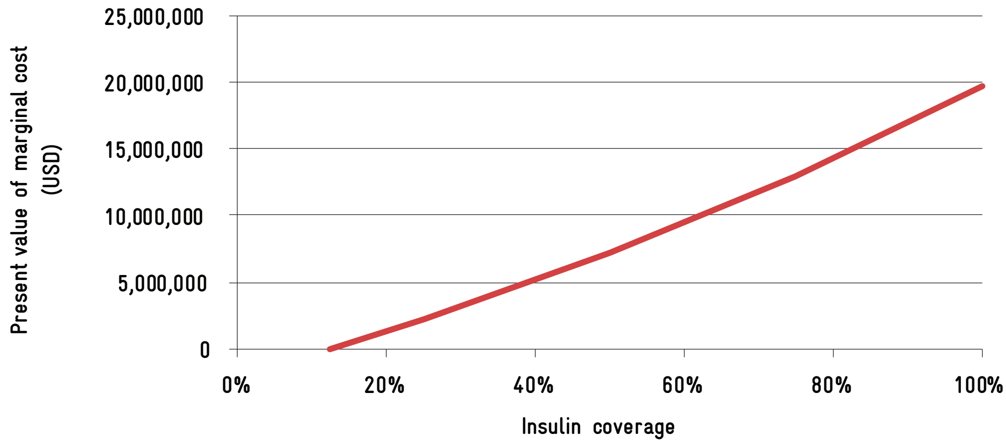
Insulin therapy in Cambodia is quite expensive and difficult to administer. Consequently, it is estimated that only around one in every eight patients (12.5%)requiring insulin therapy have access to it [63, 64]. In the following section, we will analyse the consequences of improved access to insulin therapy.

Figure 11 shows the impact of different insulin-therapy coverage rates on the number of death cases averted and life-years saved. As expected, many death cases will be averted and many years of life saved if more diabetes patients requiring insulin have access to it. If all patients requiring insulin receive it, around 43,000 life-years would be saved and nearly 6,000 death cases averted between 2008 and 2028. The number of people living with insulin therapy would also increase, so the share of insulin-dependent patients among all diagnosed diabetes patients would increases from 17% to 22%. Consequently, the total treatment costs would increase from USD 42 to USD 63 per diagnosed patient.

Figure 12 shows the present value of additional costs caused by improved access to insulin therapy from 2008 to 2028. If insulin coverage increases from the current baseline of 12.5% of insulin-dependent patients to 25%, additional costs will be around USD 2.3 million. If the entire insulin-dependent patient population is covered, it will cost an additional USD 19.7 million. Insulin therapy is quite expensive per person, so improving access to insulin is less cost-effectiveness than improving OAD-therapy coverage. The ICER is USD 451 per LYS if insulin-therapy access improves from 12.5% to 25%. For an increase n coverage from 12.5% to 100%, the ICER is USD 457.30 per LYS (discounted by 5%). If we calculate the cost effectiveness of increased insulin-therapy coverage in averting death cases, the respective ICERs are around USD 3,600 (25% coverage) and USD 3,400 (100% coverage) per death case averted.

Consequently, improved access to insulin is cost effective in Cambodia, but not as effective as improved access to OAD therapy. From a purely economic perspective, improving access to OAD therapies would be a higher priority than improving insulin-therapy access. However, patients requiring insulin are most likely suffering more than patients who can still manage their diabetes with OAD therapy. Thus, insulin therapy must be a high priority. However, the cost of improved access to insulin is considerable. If all patients requiring insulin were to receive full insulin coverage, the additional costs in 2008 would have been USD 2.5 million; i.e., a total of USD 6.5 million instead of USD 4 million. To meet this additional demand, Cambodia will have to find additional funds.

Figure 12: Budget impact of different coverage scenarios for insulin therapy, by insulin-dependent patients.



4.3.4. Combined Intervention

It is obvious that screening, OAD and insulin therapies should not be solitary interventions. A combined approach would best reduce the burden of T2DM in Cambodia. Consequently, the last scenario analyses the consequences of introducing an ideal screening programme and fully covering all patients requiring OAD or insulin therapy.

The consequences of this optimal prevention and treatment approach are impressive: nearly 600,000 life-years would be saved and around one-quarter of death cases (27%; 78,000 deaths) would be averted within the simulation period. The proportion of diabetes cases diagnosed would increase from the current level of one-third (37%) to nearly all (89%) patients. Among diagnosed patients, the proportion of those with complications would decline from two-thirds (68%) to half (51%). More patients would not require any medications (9% instead of 7.6%), but more patients would also require insulin therapy (21% instead of 17%).

However, substantial resources would be needed to achieve these results; the annual budget for professional diabetes prevention and treatment in 2008 would have been around USD 8 million, or nearly double the actual budget. This does not include the cost of mass screening. The model calculates that 6 million Cambodians aged 35 and older will be living in Cambodia by 2028, so the costs of mass screening will be substantial. Assuming that the unit costs calculated for the MoPoTsyo model (see section 0) are representative of the entire country (USD 0.07 per screening unit), screening the entire target population would add around USD 400,000. However, the ICER for these combined interventions is still quite favourable. Without the costs of mass screening, ICER is around USD 204 per LYS (discounted by 5%); with mass screening ICER would be around USD 215 per LYS. Consequently, diabetes prevention and treatment is highly recommendable from a health economics perspective.

5. Discussion

Type 2 diabetes mellitus is a major public health challenge in Cambodia. Currently, around 170,000 Cambodians are estimated to have the disease [9], but health planners should expect higher rates in the future. The Markov model showed that the number of T2DM cases will grow from 170,000 in 2013 to over a quarter of a million (264,000) in 2028. Based on the proportion of the population over 35 years old, this corresponds to a prevalence rate of 4.4% in 2028. There is no doubt that MOH, civil society and health partners (e.g., GIZ) will have to invest in efforts to prepare for this epidemic of T2DM in Cambodia.

IDF [65] estimates 364,000 diabetes cases in Cambodia by 2030, but their model is rather simplistic in comparison to the Markov model employed here. However, we have to accept that our forecast might underestimate the actual number of cases, as we assumed that transition probabilities will remain constant. For instance, we assumed that the likelihood of developing T2DM at a certain age would remain stable throughout the simulation period. This assumption might be wrong if nutritional and physical exercise habits change. With the increased availability of processed foods, even in rural areas, and the declining share of the population engaged in physical labour, it might be that our estimates are too conservative.

However, even with our conservative estimates the economic burden of T2DM in Cambodia is tremendous. Chronic complications are the main reason for increased costs, and the number of patients with complications will only increase with time. The model calculates that around 66,000 diabetes patients will require additional treatment for chronic complications in 2028. This will result in a doubling of treatment costs from USD 2 million to USD 4 million between 2008 and 2028.

Prevention and treatment of T2DM are not only financial problems. Currently, the majority of health care workers in rural health centres are not well trained in the detection of diabetes and treatment of patients. Cambodia will have to invest in additional training for their doctors, nurses and other health professionals in the prevention and cure of diabetes and other NCDs, which are also expected to increase in prevalence by 2028. As these patients increase, there will be an urgent need to intensify existing training programmes and allocate more time to NCDs.

At the same time, Cambodia has to ensure a stable supply of OAD medications and insulin, including related equipment such as syringes. This is also not only a financial challenge, but also a logistical one. Insulin requires uninterrupted cooling (below 15° Celsius), which is difficult to provide in a tropical country such as Cambodia where temperatures easily go up to 40° Celsius. For most people in rural areas, refrigerators are an unaffordable luxury and power supplies are intermittent. Providing community cooling systems for people living with diabetes (e.g., one refrigerator per village) could be discussed. However, logistics will remain an issue.

As shown in section 0, the cost estimates for diabetes treatment differ widely between studies in South-East Asia. Andayani & Imaningsih came up with a figure of USD 240 annually for one Indonesian hospital; Andayani [26] calculated annual costs of USD 252 for another hospital in the same country. The direct costs which Ibrahim et al. [28] calculated for Malaysia (around USD 573 per year), and Chatterjee et al. [32] calculated for Thailand (USD 555) are even higher. However, Martin [66] found in her cost study of Cambodian public health services that the average cost of a health centre outpatient visit was USD 1.00, and the average cost of an inpatient case in the medical department of a district hospital (CPA-1) was USD 20. This is only a fraction of what similar services would cost in Thailand, Malaysia or Indonesia.

The low cost of Cambodian health services and the low financial resources required to prevent and treat T2DM in Cambodia reflect the different economic parameters of South-East Asian countries. Thailand and Malaysia are upper-middle income countries [67], with national incomes per capita (in USD) that are 6 and 11 times higher than Cambodia's.[11] It is expected that treating patients in those countries would be much more expensive. Vietnam, Indonesia and the Philippines are lower-middle income countries. However, their GNPs per capita are also much higher than those of Cambodia (Table 7). Laos and Myanmar would be much more comparable countries, but to our knowledge there is no data on the cost of diabetes in these countries.

11 Respectively 4 and 7 times higher in international dollars (PPP$).

	Income Classification	GNP (USD)	GNP (PPP$)	Annual cost estimates (USD)	GNP/cost
Cambodia	Low	944	2330	42	22.5
Thailand	Upper-middle	5210	9280	555	9.4
Malaysia	Upper-middle	10432	16270	573	8.2
Vietnam	Lower-middle	1755	3620	-	-
Indonesia	Lower-middle	3557	4730	240-252	14.1-14.8
Philippines	Lower-middle	2587	4380	-	-

Table 7: Economic data and diabetes cost estimates for specific South-East Asian countries, 2012. (Source: [68])

As demonstrated in section 0, our simulation is highly sensitive to changes in the cost per service unit in hospitals. The model was developed using the average cost per patient in medical departments of Cambodian hospitals, as presented by Martin [66]. To our knowledge, no cost analysis exists analysing the exact cost per diabetes inpatient cases in Cambodia. Further research is needed in this area.

In addition, the cost estimates of Martin only examine public health care providers. The costs for treatment at private providers are much higher. If we assume that private providers are included in diabetes care in Cambodia, treatment costs will increase considerably and the cost effectiveness of interventions will decrease. The Royal Government of Cambodia could consider public-private partnership agreements, in order to safeguard professional diabetes care nationwide while containing the costs.

The economic development of the country until 2028 will have two consequences. First, it is likely that prices and wages will increase, making some of the cost estimates in this paper obsolete. Second, the public budget will also increase. It is unknown how prices and wages in the health care sector will increase relative to the national budget. If prices and wages increase at the same rate as the gross national income, but the national budget grows at a slower rate, it is possible that the cost-effectiveness of these interventions would remain constant, but the ability to finance them would decline.

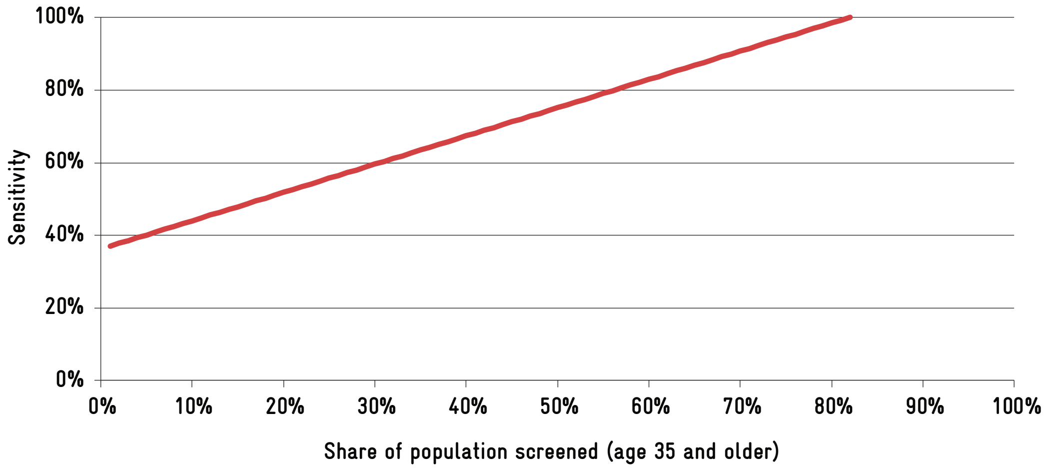
Our simulations clearly show that improved access to OAD medications and insulin therapy are cost effective in Cambodia. The Royal Government of Cambodia should be advised to include treatment of T2DM patients in its basic package of health care services. Even a slight increase in coverage (from the current level of 12.5%, to 25% of diabetes patients) would have a tremendous impact on mortality and quality of life (DALYs).

The cost effectiveness of screening for T2DM depends on two parameters. First, screening is cost effective only if the sensitivity of the test is high enough. Urine glucose tests are very cheap, but they might not be sufficiently precise. Urine tests have a high number of false negatives, especially if the test is only conducted once. If the sensitivity is not at least 37% they will not be cost-effective, even if the screening population was limited to 1% of adults. Estimates of the sensitivity of urine glucose tests in the literature do not provide a clear answer. Davies et al. estimated a sensitivity of 43% [69], Hanson et al. of 64% [70], and Friderichsen and Maunsbach of 21% [71]. Other authors showed that the sensitivity differs considerably when the test is done before and after glucose intake [72]. Employed in rural Cambodian health centres, a urine glucose test might turn out to be quite unreliable. However, as the WHO advises, 'Despite its low sensitivity, urine glucose testing may have a place in low resource settings where no other procedure is possible. This is particularly so, of course, when the prevalence of undiagnosed diabetes is likely to be high' [73].

Second, screening should focus on high-risk groups in order to ensure that it is cost-effective. The risk factors of obesity and low physical activity predict a large proportion of diabetes patients. However, even focusing on only 10% of the population with a test of 50% sensitivity, blood tests would have to cost less than USD 2.26 per test in order to be cost-effective. Figure 13 shows the cost-effectiveness of screening with blood glucose tests, assuming that one test costs USD 1.28 [61]. All combinations of sensitivity and screening populations under the diagonal line are considered cost-effective.

However, providing preventive and curative health care services at the provider level is only one component of managing diabetes. Frequently, undiagnosed diabetes cases will not go to health centres, either because they live too far away, have no transport or no time, or do not recog-

Figure 13: Cost effectiveness of diabetes screening with blood glucose tests.



nise any symptoms which would compel them to visit a health care provider. At the same time, diagnosed patients might not comply with the treatment instructions of professional health care workers. Consequently, community-based approaches will be required that identify potential patients, help them to seek professional care, and encourage them to follow through with their treatment. The peer-educator network supported by MoPoTsyo is such a community-based system, which has already shown that it is capable of improving the situation of people living with diabetes. The National Strategic Plan for the Prevention and Control of Noncommunicable Diseases [8] foresees a nationwide expansion of similar networks to assist in diabetes prevention and care. Thus, MOH could benefit from the experiences of MoPoTsyo.

Diabetes is a great challenge to all stakeholders of the Cambodian health sector. It has financial, medical, demographic and social implications. However, the main challenge now may be changing how decision-makers address this chronic-degenerative disease. Until now, the entire Cambodian health care system has been based on infectious diseases. One agent (e.g., plasmodium) causes one disease (e.g., malaria), and the connection between both is almost linear and deterministic. Consequently, finding, preventing and treating the single cause has been sufficient to provide proper health care. Chronic-degenerative diseases such as T2DM, however, have multiple causes and multiple effects. They are almost never caused by only one agent. Instead, many risk factors and conditions contribute to their development, including genetic factors. At the same time, no easily determined relationship between causes and effects exists; the same set of risk factors might cause none or very different NCDs in different people. Consequently, a new focus on NCDs will require a new thinking about medicine, health care and the engagement of health partners, such as GIZ. Type 2 diabetes mellitus may be the beginning of a different health care paradigm in Cambodia.

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