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Cost Analysis of Type 2 Diabetes Mellitus Therapy in High-Income and Low and Middle-Income Countries: A Systematic Review

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Abstract

Introduction: Diabetes is currently a very serious health problem. There is an increase in the prevalence and incidence of type 2 diabetes mellitus, this disease causes suffering for sufferers and also causes the death of a person, which makes a large economic burden for both the community and health care facilities. This study aimed to analyze the total direct medical costs of type 2 diabetes mellitus therapy in high-income, low- and middle-income countries.

Methods: A systematic review was carried out following the PRISMA guidelines. The article search method was carried out by searching PubMed, ScienceDirect, and Springer for articles that analyzed the total direct medical costs of type 2 diabetes mellitus therapy. Nine articles are considered important to be discussed in this review, these nine articles were published between January 2014 and December 2023.

Result: The results showed that the two components that had the greatest impact on the direct medical costs of managing type 2 diabetes were inpatient services and medications. Direct medical costs ranged from the lowest to the highest at $343,93 for the Kenya study to $5.090,48 for the Spain study, while medication costs ranged from $34,23 for Indonesia to $645,52 for Bangladesh from the average annual direct costs per person. The most widely used drugs were oral hypoglycemic drugs, while the most expensive drugs were Combination of Oral and Insulin. Complications of diabetes resulted in increased expenditure of the total direct medical costs.

Conclusion: This review concludes that the studies reviewed indicate a considerable health financing burden in the care of type 2 diabetes mellitus. Efforts to prevent diabetes complications have the possibility of saving the cost of diabetes care.

Keywords: *Burden of Disease; Complications; Health Care Costs; Healthy Life-style; Medicines.*

Introduction

Diabetes mellitus is a widely used term to denote a heterogeneous metabolic disorder whose result is chronic hyperglycemia. It is caused by impaired insulin secretion or insulin effect, or usually both[1]. There has been a spread of the population with diabetes across countries, both in developed and developing countries[2]. The incidence of type 2 diabetes mellitus increases annually in prevalence and incidence, so it becomes a disease that causes suffering to sufferers and also causes the death of a person[3]. Type 2 diabetes dominates the incidence rate by 90% over type 1 diabetes. It has been predicted that the incidence of diabetes in the next few years, there will be 537 million people in all countries who are expected to suffer from diabetes, and predictions for 2025 will increase diabetics to 783 people worldwide. Many people with diabetes are undiagnosed and most of them live in countries with middle to lower-income levels, these people have a prevalence of around 90%[4].

Many factors lead to an increase in the prevalence of diabetes, including male gender, unemployment, a tendency to exercise lazily, obesity, and hypertension[5,6]. Individuals with a diagnosis of diabetes have a high risk of complications such as neuropathy, cardiovascular and kidney disease. Of the several complications that can be suffered by diabetic patients, the most common complication is cardiovascular disease with a prevalence of 32,2%. Diabetics who experience cardiovascular deaths account for 9,9% of individuals. Cardiovascular complications contribute a high percentage of the cost of type 2 diabetes mellitus therapy, reaching 42% of the total direct costs[7]. Diabetics with macrovascular and microvascular complications have therapy costs 3,14 times higher than patients without complications[8].Controlling the condition of diabetes is very important because it can prevent complications. By controlling the incidence of diabetes complications, there will be savings in therapy costs from various parties, namely from the payer side, the health system, and individuals with diabetes [9].

Research conducted in China stated that there was an increase in the number of cases of diabetes from 2009 to 2016 by 1,8% and the economic burden provided increased by 1,52 times along with the number of cases that also increased. The largest component of direct medical costs is influenced by the cost of hospital care which accounted for 66,2% in 2009, it then increased to 75,9% in 2016. The results of the study indicate that the government needs to

urgently allocate more financial resources for efforts to prevent diabetes and its complications[10]. Treatment therapy for diabetes mellitus is carried out continuously for life, which requires a lot of money. Cost analysis in the United States shows an increase in healthcare costs for diabetes and its complications. There was an increase in economic costs by 26% from 2016 to 2017 due to an increase in the rate of diabetes, and the cost per patient, especially in people aged 65 years and over, this caused Medicare to experience an increase in economic costs[11]. Factors that influence the direct medical costs of diabetes therapy are treatment class, severity, number of secondary diagnoses, and length of hospitalization[12]. Education, household income, and socioeconomic status also have a significant influence on direct medical costs[13].

Costs in diabetes health management include spending on resources used in the management of the condition, including consultation visits in outpatient services, diagnostic examinations, medications, emergency care, and hospitalization and treatment procedures. There has been no research on a systematic review of cost analysis in low- and middle-income countries (LMICs) and high-income countries (HICs). Research on economic costs has significant relevance to assist decision-makers in formulating policies and programs, to achieve higher levels of efficiency and effectiveness in the utilization of medicines. In addition to the adverse health effects of diabetes on society, individuals, households, and healthcare systems are also affected by the burden of diabetes[14]. Given this background, it aims to analyze an article that deals with the total medical costs of type 2 diabetes mellitus in high-income low-income, and middle-income countries.

Methods

This study uses an approach using the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) guideline.

Search Strategy

The study made an electronic search using the following keywords: Diabetes Mellitus AND (Costs AND Cost Analysis OR Direct Cost). The article search was run in three databases namely PubMed, ScienceDirect, and Springer. The search was conducted from August to October 2023. In this study, the articles discussed were articles published from 2014 to 2023. After the search is carried out, the file is downloaded in BIB format, then the file is uploaded in Mendeley.

Inclusion and Exclusion Criteria

Articles discussed in this study are articles that meet the criteria of inclusion and exclusion. Inclusion criteria include articles that evaluate direct medical costs and drug costs of diabetes mellitus, articles written in English, and articles that can be accessed in full text. The exclusion criteria include articles that discuss type 1 and 2 diabetes but do not distinguish both costs and articles that did not cite direct medical costs and drug costs in the results section.

Data Extraction and Analysis

Once the articles were transferred to Mendeley and duplicates were removed, we checked the titles for relevance to the study objectives, then we identified eligibility for inclusion or exclusion based on the study abstracts. To determine whether an article met the inclusion criteria, we looked at the abstract and then reviewed it for completeness.

Articles that have been searched are then selected based on inclusion and exclusion criteria which are then explained based on PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) rules. The initial search resulted in 10.655 articles, of which 76 duplicate articles were identified and removed. Of the remaining 9.342 articles, 9.071 were excluded through abstract and title screening, leaving 29 articles that were then thoroughly analyzed. After the analysis, two articles were excluded, leaving only nine articles retained. These 9 articles will be discussed in this review (Figure 1).

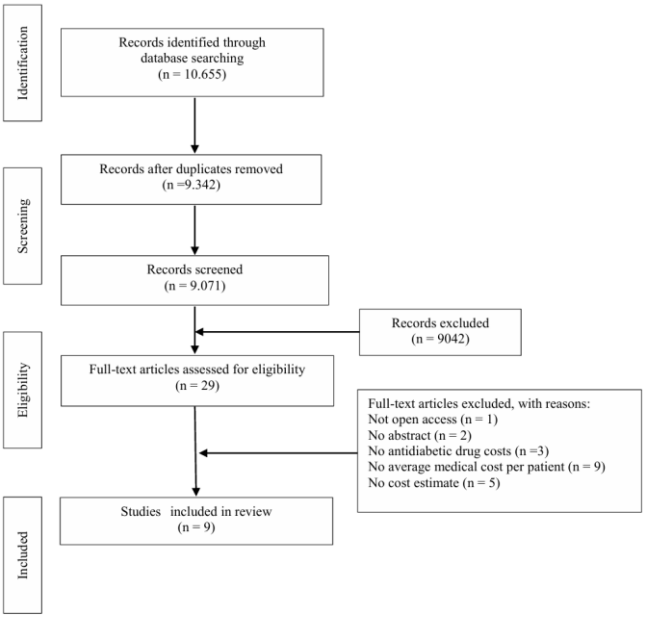

Figure 1. PRISMA flowchart

Quality Assessment Reporting

Quality assessment of the article being discussed using the Consolidated Health Economic Evaluation Reporting Standards (CHEERS). Each study domain was assigned a score of 0 (not reported) or 1 (reported). The results of the quality assessment of all articles are shown in Table I. Nine studies in this

review showed high quality according to the CHEERS checklist, scoring 22 out of a total of 24. All studies did not report the discount rate and model choice used in the study.

Table 2. Characteristics of included studies

Country	Setting for study recruitment	Study design	Methods	Study duration (year)	Sample size (n)	Funding body	Inclusion criteria	Mean age (years)
Lithuania[15]	Primary healthcare centers	Top-down approach	Database	2011	762	Privately financed	Diagnosed diabetes mellitus type 2 (ICD-10 diagnosis codes E11.0-9), age 18 years and older (gestational diabetes mellitus was excluded)	67,07
Singapore[16]	Hospital and clinic	Cross-sectional study	Medical records	2010	500	Publicly financed	Diagnosed T2DM	69
Spain[17]	Primary care	Retrospective study	Medical records	2011	126.811	Publicly financed	Diagnosis of T2DM	67,6
China[18]	Tertiary hospitals	Cohort study	Medical records and Interview	2015	871	Publicly financed	Diagnosed with type 2 diabetes according to the 1999 world health organization diagnosis criteria; (i) aged ≥18 years; (ii) living in the city for at least 1 year; and (iii) willing and being able to give written informed consent and complete the study.	58,1
Pakistan[19]	Clinic	Multi-center study	Medical records and Questionnaire	2021-2022	1.839	No financed	Diagnosed with T2D, age was ≥ 18 years, did not have any malignancies, and did not have other chronic diseases or drug abuse	N/A
Bangladesh[20]	Primary, secondary and tertiary care units	Cross-sectional study	Medical records and interviewed	2017	1253	No financed	Registered adults of either gender with a minimum one-year duration of T2DM	55,1
Kenya[21]	Primary care	Cross-sectional study	Interview	2017	234	Publicly financed	Self-reported DM diagnosis, had received treatment for a minimum of 6 months after diagnosis and were more than 18 years of age	58,9
Vietnam[22]	Tertiary hospitals	Cohort study	Database	2017	1.395.204	Publicly financed	Diagnosed with T2DM if they were aged 30 years or above, and either (1) had at least one international classification of diseases, 10th revision (ICD-10) code E11 or (2) had been prescribed with oral antihyperglycemic medication on two separate visit records.	60,8
Indonesia[23]	Secondary and tertiary care	Cohort study	Database	2016	812.204	Privately Financed	Above 30 years of age and had T2DM-related claims between January 1, 2016, and December 31, 2016.	N/A

Age

In this review, the average age of patients with type 2 diabetes mellitus ranged from 55-69 years (Table II). These data are consistent with the fact that age above 45 years is one of the factors that increase the risk of developing type 2 diabetes mellitus[24].

Cost Perspective

In analyzing health economic studies, various perspectives are used. Some of them include the government perspective, health system perspective, employer perspective, community perspective, and patient perspective. In this review, five studies present cost estimation from a healthcare system perspective[17–21] And four studies present from a payer perspective[15,16,22,23]

In analyzing the study of health economics there are several perspectives used among the patients' perspectives, the health-care system perspectives, the employer's perspectives, the government's and the community's. The patient's perspective covers the enormous cost the patient must spend. A health-care system perspective covers costs by hospitals and clinic services. The employer's perspective involves the loss of work productivity. The perspective of governments includes programs that are held to promote health or support health programs. Society's perspective includes the loss of one's income as a result of caring for the sick. In the review, there are 5 studies in which his research has used a health-care system perspective to report the cost of treatment for type 2 diabetes mellitus[17–21]. And there were four studies that used payer perspective to report the cost of treatment for type 2 diabetes mellitus[15,16,22,23].

Components of Medical Costs Associated with Diabetes

The components of medical costs are categorized into: average annual direct medical costs per person, average annual antidiabetic drug costs per person, components included in direct medical cost estimates, and components included in antidiabetic drug cost estimates (Table III). In this review, currency values have been converted to US dollars using the exchange rate on August 4, 2024, for all included studies.

The method of calculating costs is as follows:
If the reported currency is already in US dollars, the way to calculate the future value is:
$C= (1+r)^n$
C= future value
r= discount rate (3%)
n= time period

If the reported currency is not in US dollars, the way to calculate the future value is by using the formula above and then the calculation results are converted to US dollars. The exchange rates adopted in this study are 1 USD = 0,95 EUR, 1 USD = 1,36 S$, and 1 USD = 133,11 KES.

Each study had different components of direct medical cost estimation. Components included hospital services, physician services, and laboratory tests (Table III). The drug component in the reviewed studies also considered varying drug cost calculations (Table IV).

Table III shows that expenditure on average annual direct medical costs per person in Singapore (2.370,71)[16] and China (2.596,76)[18] were quite similar, but varied in the average reported medication costs of 188,88 and 1.178,93, respectively. Quite similar expenditures were also seen in studies in Lithuania and Indonesia at 1.564,30[15] and 1.711,56[23]. There was an almost two-fold difference in direct medical costs of diabetes mellitus treatment in two studies conducted in Pakistan and Kenya of 678,39[19] and 343,93[21], respectively. Nearly double the difference was also found in studies in Bangladesh (961,39)[20] and Vietnam (489,61)[22]. The lowest average direct medical cost expenditure was reported in Kenya 276,02[21] and the highest expenditure was reported in Spain 5.090,48[17]. Treatment costs varied from 34,23[23] to 645,52[20] of the average annual direct medical costs per person.

Table 1. Cost of mean annual direct cost per person and mean annual medicine cost per person in the included studies

Country	Income group classification	Direct cost estimated on basis of following components	Mean annual direct medical cost per person (USD)	Mean annual antidiabetic medicine cost per person (USD) (% of total direct cost)
Lithuania[15]	High income	Hospital services, physician services inpatient care, outpatient care, drugs, physician services, lab tests, medications	1.564,30	733,82 (46,91%)
Singapore[16]	High income	Inpatient hospitalization, accident and emergency (A&E) and ambulatory outpatient care (physician visits, allied health visits, laboratory tests and medications)	2.370,71	188,88 (8 %)

Country	Income group classification	Direct cost estimated on basis of following components	Mean annual direct medical cost per person (USD)	Mean annual antidiabetic medicine cost per person (USD) (% of total direct cost)
Spain[17]	High income	Primary care visits (differentiating between doctor's or nurse's visits, and between place of visit, i.e., in the office or at home), hospitalizations, referrals to specialist care, diagnostic tests, outpatient visits, medication, dialysis treatment, and use of self-monitoring test strips.	5.090,48	1.522,19 (29.74 %)
China[18]	High income	Medications, laboratory tests, outpatient, inpatient, examinations, medical devices, such as glucose meters and test strips, and other medical supplies.	2.596,76	1.178,93 (45,4%)
Pakistan[19]	Under middle income	Costs of hospitalization, out-patient visits, medicine, and laboratory tests	678,39	291,22 (42,4%)
Bangladesh[20]	Under middle income	Costs of hospitalisation, outpatient visits, medicine, laboratory tests, and other service utilisation (including the use of self-monitoring blood glucose and consumables)	961,39	645,52 (60,7%)
Kenya[21]	High income	Registration, outpatient, inpatient, consultation, medicines and laboratory services	343,93	273,62 (52,4%)
Vietnam[22]	Under middle income	Costs of hospitalization, outpatient care, emergency care, non-diabetes-related medications, and antihyperglycemic medications	489,61	35,42 (14%)
Indonesia[23]	Under middle income	Hospitalization, specialist visits, unbundled non-diabetes-related medication, and unbundled anti-hyperglycemic medications	1.711,41	34,23 (2%)

**N/A: Not Available*

The highest direct medical cost expenditure of the nine included studies was six studies with research results stating that hospitalization costs were the highest cost of all direct medical costs[15–19,22,23]. This is similar to previous research conducted in Singapore in which inpatient care while in the hospital is the largest component of medical expenditure[25]. Two studies stated that the highest direct cost was the cost of medicines[20,21]. This is in accordance with research conducted by Kansra and Oberoi (2023) that the highest component of diabetes costs is the cost of drugs[27].

In Table III, all studies accounted for outpatient and inpatient hospital visits, medication costs, and laboratory examination costs. Four studies accounted for physician visits[15–17,23]. In Table III, there are two trends in the drug cost component: countries reporting low drug expenditure such as Singapore (8%)[16], Spain (29,74%)[17], Vietnam (14%)[22] and Indonesia (2%)[23]. A study conducted in Mali[28] also reported low costs for medicines (5%). Then some countries report high costs for medicines such as Lithuania (46,91%)[15], China (45,5%)[18], Pakistan (42,4%)[19], Bangladesh (60,7%)[20], and Kenya (52,4%)[21]. This is similar to a study conducted in China which also reported high costs for medicines (79,7%)[29].

The use of antidiabetic drugs is increasing, resulting in increased drug costs[30]. Table IV presents the types of drugs used in each article, the average annual drug cost per person of each drug, and the percentage of users. The drugs included can be categorized as oral hypoglycemic medication, insulin, a combination of oral and insulin, and oral and non-insulin injectable hypoglycemic medication. From these data, 6 studies showed that the most widely used drugs were oral hypoglycemic drugs[15–18,22,23] and 3 studies showed that the most widely used drug was a combination of oral and insulin[19–21]. The cost of the most expensive drug is different in each country, some mention that the most expensive drug is oral and non-insulin injectable hypoglycemic medication[15], in China the most expensive drug is insulin[18], while the average article mentions the most expensive drug is combination of oral and insulin[19–21].

Table 2. Characteristics of antidiabetic drugs and mean annual medications cost per person

Country	Type of DM Medication	Mean annual medications cost per person (USD)	% Number of patients
Lithuania[15]	Oral	122,31	63,4
	Oral + non-insulin injectable hypoglycemic medication	959,70	0,9
	Oral + insulin	833,01	9,4
	Insulin	669,03	13,4
Singapore[16]	Oral	N/A	57,2
	Insulin	N/A	3
	Oral + insulin	N/A	9
Spain[17]	Non-insulin antidiabetic drugs	N/A	56,2
	Insulin (alone or with other antidiabetic drugs)	N/A	16,8
China[18]	Oral	1.076,05	52,4
	Insulin	1.150,16	9,5
	Oral + insulin	962,01	30,9
	Glp-1 ra	1.342,35	1,3
Pakistan[19]	Oral	505,20	37,7
	Insulin	745,39	12,0
	Oral + insulin	1.030,03	44,8
	GLP-1 and NGI	N/A	3,4
Bangladesh[20]	Oral	585,67	34,5
	Insulin	864,11	6,9
	Oral + insulin	1.194,08	58,6
Kenya[21]	Metformin	81,22	N/A
	Metformin + insulin	151,46	N/A
	Metformin + glibenclamide	122,81	N/A
Vietnam[22]	Oral	N/A	9
	Insulin	N/A	5
Indonesia[23]	Oral	N/A	56
	Insulin	N/A	28
	Oral + insulin	N/A	16

In research conducted by Domeikine (2014)[15] of 762 patients included in the study, 65,1% of participants had diabetes complications either one or more complications. The average annual cost per person for patients who did not experience complications and patients who experienced complications was different. Study participants with no complications spent USD 1047,17, while participants with 3 or more complications spent USD 173.683. Complications related to diabetes account for 70% of the total direct medical costs[22]. Diabetes patients who experience complications incur costs twice as large compared to diabetes patients without complications or three times greater than patients who do not undergo hospitalization[19,23].

Factors associated with direct medical costs

Factors that affect the cost of diabetes therapy are age[17,20,22], gender[17,19,22], duration of diabetes[18–20], antidiabetic drugs[15–17], complications[15–18,20], and comorbidities[20]. These factors have statistically significant differences in the cost of diabetes therapy. Knowing the factors that affect costs can help identify areas that can be intervened to reduce costs, but still optimize treatment.

Discussion

Nine articles were identified in this systematic review, addressing diabetes care costs and diabetes drug costs. Six articles were based on data from Asia, two articles from Europe, and one article from Africa. The main focus of most articles was type 2 diabetes. This gap provides an opportunity to address the future costs of treating type 1 diabetes mellitus.

There are growing concerns about increased prevalence and the burden of non-communicable diseases. The enormity of direct medical costs can impose a heavy financial burden on both society and health services systems. Hence, efforts should be made to identify curse-free medical costs and increase preventive investments so that the severity and severity of further complications may decrease. In addition, the concept of affordability needs to be further examined within the framework of the health system structure, and the potential role of government and other system stakeholders in managing medical costs should be scrutinized. Governments should also be encouraged to

provide information on the costs (to patients and insurers) and procurement prices of diabetes care.

The IAF Diabetes Model predicts an increase in the number of people with diabetes, both type 1 and type 2 diabetes from 19 million to 54 million. The economic cost burden because of diabetes also increases as the number of people suffer by 53%. Despite preventive efforts and medical progress, diabetes still presents a health crisis in terms of significant spread, disease rates, and financial burdens. In the next 15 years, it will be expected that the crisis will only worsen. Therefore, incentives must be made in the government backed diabetes screening and prediabetes to help communities prevent or delay the development of diabetes. Another major obstacle to the prevention or delay in developing diabetes is society's behavior to promote a healthy lifestyle[31].

Type 2 diabetes is increasing in prevalence, along with an aging population, urbanization and rapid economic growth. These have resulted in a large population using healthcare products and services. Chronic complications related to diabetes mellitus also negatively impact patients' quality of life[10,17,19]. With the estimated prevalence of diabetes as well as the increasing demand for medical care, diabetes is placing an increasing burden on health budgets[16]. This is following previous research which states that people suffering from diabetes are associated with a very high lifetime expenditure on diabetes treatment although it is also associated with a decreased life expectancy of patients[32].

The presence of complications will increase the cost of therapy which will have an impact on the government as an insurance provider and will also have an impact on individuals. Individuals with diabetes will incur direct non-medical costs such as transportation and food. This greatly impacts the economy of people with diabetes because there is a significant increase in expenditure caused by many trips to health facilities to treat more complex medical conditions, which adds to the burden on individuals. In addition to the economic impact, diabetes and its complications can impact an individual's employability. Diabetes prevention efforts can prevent the onset of more severe diabetes and prevent complications from occurring, thereby significantly reducing medical costs[32]. To control diabetes and its complications, it is possible to use insulin therapy earlier to achieve and maintain better glycemic control with fewer side effects and better compliance[33]. Good glycemic control is expected to result in long-term cost savings due to fewer complications and reduced hospitalizations.

This review reveals the antidiabetic drug costs and direct medical costs attributable to T2DM from 2014 to 2023. Limitations of this review include variations in the methodology used and different healthcare systems in different countries. Differences in methodology include the inclusion criteria as well as the various elements included in the calculation of total direct medical costs and drug costs. This study did not rule out differences in the sample size of the study. This decision can be influential as it may include studies that are of low quality and have less reliable cost estimation results.

Conclusion

This review has illustrated the economic impact caused by type 2 diabetes globally. The increasing incidence of diabetes has resulted in a significant financial burden to society and healthcare systems. Efforts should be made to prevent diabetes and its complications so that the economic burden can be reduced. As such, it is important to provide evidence on the economic burden of managing diabetes and its complications as part of health system reforms aimed at minimizing the long-term economic burden of this rising epidemic.

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Author Contribution

Data curation and original draft.	:	RNI
Supervision, review, and editing	:	DE, TMA

Competing Interests

The authors declare no conflict of interest.

Abbreviation

T2DM	:	Type 2 Diabetes Mellitus
DM	:	Diabetes Mellitus
CHEERS	:	Consolidated Health Economic Evaluation Reporting Standards
LMICs	:	Low- and Middle-Income Countries
HICs	:	High-Income Countries
USD	:	United States Dollar
ICD-10	:	International Classification of Diseases, 10th Revision
GLP-1 RA	:	Glucagon-Like Peptide-1 Receptor Agonist
NGI	:	Non-Insulin Injectable
A&E	:	Accident and Emergency
EPI	:	Expanded Program on Immunization

IAF : International Diabetes Federation (note: often written as IDF)

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