

Original Research

Cost-effectiveness of pharmacist intervention in oral antidiabetic treated and insulin treated type 2 diabetes mellitus

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Abstract

Background: Type 2 diabetes mellitus (T2DM) is a significant global health issue and projected to affect around 643 million people by 2030. Objectives: This study analyzed the cost-effectiveness of pharmacist intervention in oral antidiabetic-treated and insulin-treated T2DM outpatients admitted to the University of Sumatera Utara (USU) Hospital, Medan, Indonesia. Methods: This pre and post quasi-experimental economic study analyzed the cost-effectiveness of pharmacist intervention in oral antidiabetic-treated and insulin-treated T2DM outpatients (n=106) admitted to USU Hospital based on payer perspective, period from April to July 2023. Baseline data for one-month treatment were assessed before pharmacist intervention. The pharmacist intervention was provided monthly for the following 3 months. The materials provided in the pharmacist intervention consisted of T2DM educational brochures and patient counseling. The clinical outcome measured pre and post pharmacist intervention was the proportion (%) of the patients with controlled glycated haemoglobin (HbA1c). Monthly direct medical costs before and after intervention were extracted from these patients' medical records. Cost-effectiveness ratios (CER) and incremental cost-effectiveness ratios (ICERs) for the oral antidiabetic and insulin therapies provided to these patients were analyzed. In this study, one-way sensitivity analysis and WHO threshold were also performed. Appropriate statistical analyses were also applied in this study. Results: Most (54.71%) of the T2DM patients were female. Their mean age was 58.61 ± 8.89 years. Of the 106 patients, 48 and 58 patients received oral antidiabetics and insulin therapies, respectively. CER (USD) for oral antidiabetic-treated patients: before pharmacist intervention, 39.67; after pharmacist intervention, 30.76. CER (USD) for insulin-treated patients: before pharmacist intervention, 1,326.78; after pharmacist intervention, 206.99. ICERs (USD) for: oral antidiabetic-treated patients, 2.7471; insulin-treated patients, -86.1376. Conclusion: Management of oral antidiabetic-treated and insulin-treated T2DM patients with pharmacist intervention was more cost-effective compared to that of standard treatment.

Keywords: type 2 diabetes mellitus; antidiabetics; pharmacist intervention; cost-effectiveness analysis

INTRODUCTION

Diabetes mellitus (DM) is a serious chronic metabolic disease associated with hyperglycemia and multiple complications such as cardiovascular disease and chronic kidney disease. The global incidence of DM reached up to 537 million people in 2021. It is predicted to increase to 643 million people in 2030 and 783 million people in 2045. Type 2 diabetes mellitus (T2DM) is the most common type of diabetes accounting for more than 90% of all diagnosed cases of DM in the world.¹ Indonesia was ranked as the 7th highest country with DM in the

world with 10.7 million people. In Southeast Asia, Indonesia was ranked as the country with the highest prevalence of DM patients.²

Over time, the continued increasing prevalence of T2DM leads to an increase in the number of its complications, including chronic and acute diseases with significantly increasing demand for health services and treatment costs and also a reduction in the quality of life (QOL) of the patients. Macrovascular complications of T2DM, such as coronary artery disease (CAD), stroke, and peripheral vascular disease, and microvascular complications, such as end-stage renal disease (ESRD), retinopathy, and neuropathy, account for the majority of the burden associated with diabetes.³ T2DM with its complications can have a significant negative impact on the quality of life and early mortality of the patients as well as health resources consumed by these patients, their families, and health systems.⁴

Various counseling, intervention, and economic studies to improve the management of T2DM have been conducted elsewhere. A pharmacist-physician collaborative care program for uncontrolled T2DM patients undertaken in Brazil indicated that this collaborative program was more effective than the standard care in the reduction and control of HbA1c levels.⁵ A systematic review conducted across databases (n=43 studies) proves that pharmacy-based diabetes education intervention improved the HbA1c of the patients in all studies.⁶ A more recent study conducted on T2DM patients admitted to a tertiary hospital in Indonesia demonstrated that pharmacist

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intervention significantly improved the QoL of the patients.⁷ A cost-effectiveness analysis of ideglira versus igarlix in the management of T2DM patients with uncontrolled basal insulin was undertaken in Czech Republic. This study indicated that ideglira was more cost-effective compared to igarlix in the management of T2DM patients.⁸

Even though programs to reduce the prevalence and optimize the management of T2DM have been undertaken in many countries (including patient counseling, pharmacist education, rational use of medicine, and economic analyses), however, facts indicate that its morbidity, mortality, complications, and treatment costs continue to rise.¹ With the scarce available resources and poor clinical outcomes, it is always important to conduct cost analysis. Cost-effectiveness analysis in the management of many diseases, including diabetes is limited in Indonesia. Therefore, the main objective of this present study was to analyze the cost-effectiveness of pharmacist intervention in oral antidiabetic-treated and insulin-treated (IT) T2DM outpatients admitted to USU Hospital, Medan, Indonesia.

METHODS

This pre and post quasi-experimental economic study analyzed the impact of pharmacist intervention on direct costs, clinical outcome (HbA1c), and cost-effectiveness of oral antidiabetic treated and insulin treated T2DM out-patients admitted to USU Hospital Medan, Province of Sumatera Utara, Indonesia period April to July 2023. The T2DM patients with complications, ages older than 18 years, and signed informed consent were included in this study. Using an electronic sample size calculator for the cohort study, the minimum sample size was 98 at a confidence level (1- α) of 95%, with 80% power (1- β as type II error), the proportion of the patients with controlled HbA1c before pharmacist intervention (π_1) and with pharmacist intervention (π_2) are 0.40 and 0.70 as guess values, respectively.⁹ During the study period, as many as 106 T2DM outpatients admitted to USU Hospital met the inclusion criteria. These patients then were used as the sample in this study. Ethical clearance of this study was obtained from the Ethic Committee of Health Research, Universitas Sumatera Utara No:341/KEPK/USU/2023. This study was conducted based on the payer (called *Badan Penyelenggara Jaminan Sosial* abbreviated as *BPJS*) perspective, then only direct costs were included in this study. These direct costs consisted of drug acquisition costs, physician service, laboratory examination, medical execution, administration, and pharmacist intervention. In the first month of treatment, the T2DM patients received standard management, followed by monthly pharmacist intervention in the next three months. Pharmacist intervention provided consisted of patient counseling about diabetes and its symptoms, the importance of adherence to the medications provided, and non-pharmacological approaches including diet, and exercise twice weekly for about 30 minutes. The brochure about counseling was also distributed to each of the T2DM patients recruited in this study at the beginning of the pharmacist intervention. Descriptive statistic was applied to

analyze the characteristics of the patients. The clinical outcome measured in this study was the proportion (%) of these T2DM patients with HbA1c levels of $\leq 7\%$ because this level has been considered as an indicator of controlled hyperglycemia.¹⁰ The significance of pharmacist intervention on the direct costs consumed and the proportion of controlled HbA1C levels of the T2DM patients was analyzed applying paired t-test ($p < 0.05$ was considered significant). Cost-effectiveness analysis (CEA) was conducted by calculating the cost-effectiveness ratio (CER) calculated by dividing costs to treat 100 T2DM patients with the proportion (%) of these patients with controlled HbA1c. The incremental cost-effectiveness ratio (ICER) was analyzed by calculating
$$\frac{\text{Cost}_{\text{after pharmacist intervention}} - \text{Cost}_{\text{before pharmacist intervention}}}{\text{Outcome}_{\text{after pharmacist intervention}} - \text{Outcome}_{\text{before pharmacist intervention}}}$$
¹¹ One-way sensitivity analysis was also performed to predict uncertainty by increasing drug costs to 5, 10, and 15%. CER and ICERS were recalculated to see how it changed the study result.

RESULTS

Characteristics of the patients are listed in Table 1. Most (54.71%) of the T2DM patients were female. Their mean age was 58.61 ± 8.89 (years). By age range, most of the T2DM patients were at the age range of 51- 60 (male 19.81% and female 24.52%) and 61-70 years (male 16.98% and female 21.69%). It was found that the incidence of T2DM increased as the patients' age increased. Three of the most common complications suffered by these T2DM patients were hypertension (57.5%), diabetic neuropathy (35.8%), and CHF (24.5%). Nearly one-fifth (18.9%) of them suffered from dyslipidemia and 34.9% of the patients experienced other diseases.

The treatment models for the oral antidiabetic-treated and insulin-treated T2DM outpatients before and after intervention are shown in Table 2. Of the 106 T2DM patients involved in this study, as many as 48 patients received oral antidiabetic drugs and 58 patients received insulin therapy. Variety of oral antidiabetic monotherapy or combinations were provided to these patients. The most frequently prescribed oral antidiabetic

Table 1. Characteristics of the T2DM outpatients (n= 106)

Characteristics		Male (%)	Female (%)
Age of the patients (years)	18-30	1 (0.94)	2 (1.88)
	31-40	3 (2.83)	0 (0.00)
	41-50	3 (2.83)	3 (2.83)
	51-60	21 (19.81)	26 (24.52)
	61-70	18 (16.98)	23 (21.69)
	>70	2 (1.88)	4 (3.77)
Mean age of the patients (years)	58.61 (SD = 8.89)		
Complications (%)	Hypertension	57.5	
	Diabetic neuropathy	35.8	
	CHF	24.5	
	Dyslipidemia	18.9	
	Others	34.9	

Table 2. Treatment model for oral antidiabetic-treated and insulin-treated T2DM outpatients before and after intervention

Oral antidiabetic treatment model	Number of Patients (n=48)		Insulin therapy model	Number of Patients (n=58)	
	Before intervention	After intervention		Before intervention	After intervention
Metformin + Glimepiride	26	24	Insulin aspart + Lantus	33	30
Metformin	6	9	Novomix	6	11
Metformin + Diamicon		4	Novorapid + Levemir		6
			Apidra + Lantus		5
Metformin + Gliclazide	5		Insulin aspart + Insulin detemir	6	
Glimepiride	3	6	Insulin glulisine + Insulin glargine	4	
Metformin + Diamicon + Pioglitazone		1			
Metformin + Gliclazide + Pioglitazone	2		Ryzodeg	3	2
Metformin + Glimepiride + Pioglitazone	2	1	Insulin glulisine + Levemir	2	
Metformin + Glimepiride + Acarbose	2	1	Ryzodeg + Metformin	2	2
Gliquidone	1	1	Novomix + Acarbose	1	1
Metformin + Gliquidone	1	1	Novomix + Glimepiride	1	1
Treatment for T2DM Complications					
Medications	Number of patients				
	Before intervention		After intervention		
Gabapentin	58		55		
Amlodipine	42		42		
Candesartan	39		35		
Vitamin B complex	31		15		
Simvastatin	27		20		
Natrium Diclofenac	10		6		
Omeprazole	8		7		
Paracetamol	8		4		
Ranitidine	7		2		
Bisoprolol	6		5		

drugs were combinations of metformin and glimepiride, followed by metformin and its combination with gliclazide. In the insulin-treated T2DM patients, as also shown in Table 2, insulin monotherapy or combinations of insulin were provided to these patients.

To treat complications, other drugs were also provided to these T2DM patients. Five of the most widely prescribed drugs in the management of these T2DM patients before and after intervention in decreasing order were gabapentin, amlodipine, candesartan, vitamin B complex, and simvastatin.

Cost-effectiveness analysis

Direct costs consumed by the oral antidiabetic-treated and insulin-treated patients before and after pharmacist intervention are listed in Table 3. Components of the direct costs accounted in this study consisted of drug acquisition costs, physician service, laboratory examination, medical execution, administration, and pharmacist intervention. Direct medical costs were analyzed by multiplying the number of doses/physician visits/laboratory examinations/

medical executions/administrations with the cost per dose/physician visit/laboratory examination/medical execution/administration. Monthly number of pharmacist intervention for each intervention group was assumed 20. The cost consumed/intervention was assumed IDR 37,500. Thus, one-month costs consumed for pharmacist intervention was IDR 750,000 or USD 48.62 (USD to IDR July 2023 was 15,427).

These T2DM patients visit the hospital monthly to check their clinical conditions and to get one-month medications. Table 3 indicates that one-month direct medical costs consumed by the oral antidiabetic-treated T2DM patients (n=48) before and after intervention were USD 837.99 and USD 856.45, respectively. There was no statistically significant difference between the monthly direct costs consumed by oral antidiabetic-treated T2DM patients before and after intervention, $p = 0.395$. Monthly direct medical costs consumed by the insulin-treated T2DM patients (n=58) was significantly lower after intervention (USD 1,920.86) compared to those before intervention (USD 2,308.59), $p = 0.001$.

Table 3. Components of direct costs consumed by the oral antidiabetic-treated and insulin-treated patients before and after intervention				
Components of direct costs	Monthly Costs/48 oral antidiabetic-treated patients (USD)		Monthly Costs/58 insulin-treated patients (USD)	
	Before intervention	After intervention	Before intervention	After intervention
Drug acquisition costs	162.09	164.34	1,481.60	1,209.19
Physician service	476.44	486.16	584.37	554.22
Laboratory examination	103.52	69.49	138.91	16.46
Medical execution	19.77	11.67	9.72	1.62
Administration	76.17	76.17	93.99	90.75
Pharmacy intervention		48.62		48.62
Total	837.99	856.45	2,308.59	1,920.86

Table 4 shows cost-effectiveness analysis in oral antidiabetic-treated and insulin-treated T2DM patients. The monthly direct costs consumed to treat 100 oral antidiabetic-treated patients before and after intervention, as shown in Table 4, were USD 1,745.81 and USD 1,784.27, respectively. Proportions of the oral antidiabetic-treated T2DM patients with controlled HbA1c levels before and after pharmacist intervention were 44% and 58%, respectively. Therefore, cost-effectiveness ratios in the management of oral antidiabetic-treated T2DM patients before and after pharmacist intervention were USD 39.67 and USD 30.76, respectively. Analysis of ICER indicated that USD 2.7471 extra cost per patient is required to increase the outcome or proportion of patients with controlled HbA1c from 44% to 58%. In this present study, similar results were also found for the management of insulin-treated T2DM patients before and after pharmacist intervention. Monthly direct costs consumed to treat 100 insulin-treated patients before and after pharmacist intervention were USD 3,980.33 and USD 3,311.83, respectively. Proportions of the insulin-treated T2DM patients with controlled HbA1c levels before and after pharmacist intervention were 3% and 16%, respectively. Hence, cost-effectiveness ratios in the management of insulin-treated T2DM patients before and after pharmacist intervention were USD 1,326.78 and USD 206.99, respectively. Based on the analysis of ICER, however, indicated that USD 86.1376 of extra cost per patient was saved to increase T2DM patients with controlled HbA1c from 3% to 16%.

Sensitivity Analysis

Results of the one-way sensitivity analysis conducted in this

study are shown in Table 5. This sensitivity analysis indicated that although drug acquisition costs were increased by 15%, the overall conclusions did not change. This means that the results of CEA are not affected by uncertainty.

DISCUSSION

This present study aimed to analyze the cost-effectiveness of pharmacist intervention in the management of oral antidiabetic-treated and insulin-treated T2DM patients. The mean age of the patients was 58.61 years (SD=8.89). It was found that the incidence of T2DM increased with age. A previous study has also indicated that the incidence of T2DM was higher at late age (51 years old or older). [12] With regards to antidiabetic utilization, this study found that a combination of metformin and glimepiride was the most frequently provided to these patients. Many studies on antidiabetic utilization have been conducted by researchers in many parts of the world. A retrospective observational study conducted in a tertiary care hospital found that the most frequently prescribed antidiabetic drug was also metformin.¹³ Another study focused on antidiabetic drug utilization patterns in T2DM patients in a tertiary care hospital also argued that the most often antidiabetic provided to these patients was metformin.¹⁴ The choice of antidiabetic drugs for T2DM patients is determined by the clinical condition of these patients and the complications that they also suffered. In terms of cost-effectiveness analysis, this study proved that pharmacist intervention exhibited greater effectiveness (proportion of the T2DM patients with controlled level of HbA1c) in both groups, oral antidiabetic-treated and insulin-

Table 4. Cost-effectiveness analysis in oral antidiabetic-treated and insulin-treated T2DM patients					
Patient group	Monthly Costs (USD) to treat 100 patients	Patients with controlled HbA1C (%)	CER	ICER	Management of T2DM with pharmacist intervention
Oral antidiabetic-treated T2DM patients before intervention	1,745.81	44	39.67	2.7471	More effective and more costly
Oral antidiabetic-treated T2DM patients after intervention	1,784.27	58	30.76		
Insulin-treated T2DM patients before intervention	3,980.33	3	1,326.78	-86.1376	Dominant (more effective and less costly)
Insulin-treated T2DM patients after intervention	3,311.83	16	206.99		



Table 5. Results of one-way sensitivity analysis				
Description	Oral antidiabetic-treated patients		Insulin-treated patients	
	Before pharmacist intervention	After pharmacist intervention	Before pharmacist intervention	After pharmacist intervention
Monthly direct cost (USD) to treat 100 patients (x) at increased:				
5% of acquisition cost	1,762.68	1,801.37	4,108.05	3,419.51
10% of acquisition cost	1,779.58	1,818.50	4,235.78	3,519.38
15% of acquisition cost	1,796.46	1,835.65	4,363.50	3,624.55
Patients with controlled HbA1C (%)	44	58	3	16
CER at increased:				
5% of acquisition cost	40.06	31.06	1,369.35	213.72
10% of acquisition cost	40.45	31.35	1,411.93	219.96
15% of acquisition cost	40.83	31.65	1,454.50	226.53
ICER at increased:	Oral antidiabetic therapy after intervention:		Insulin therapy after intervention:	
5% of acquisition cost	More effective and more costly		Dominant	
10% of acquisition cost	More effective and more costly		Dominant	
15% of acquisition cost	More effective and more costly		Dominant	
ICER, incremental cost-effectiveness ratio				

treated T2DM patients compared to those before pharmacist intervention. The proportion of the oral antidiabetic-treated T2DM patients with controlled level of HbA1c before intervention was only 44% and increased to 58% after intervention. Similar result was also found in the insulin-treated T2DM patients, in which before intervention, only 3% of the patients achieved the controlled HbA1c level, however, after intervention, this value improved to 16%. These results proved that the implementation of pharmacist intervention is extremely important in the management of T2DM patients. This study indicated a slight increase in costs consumed in the management of oral antidiabetic-treated patients with pharmacist intervention compared to those before pharmacist intervention. This result was due to higher drug acquisition costs in the management of oral antidiabetic-treated patients with pharmacist intervention and costs consumed by pharmacists to provide intervention compared to those before pharmacist intervention as shown in Table 3. However, CER in the management of the oral antidiabetic-treated patients with pharmacist intervention was lower (30.76), as shown in Table 4, compared to those without pharmacist intervention (39.67). Overall, this study proved that pharmacist intervention has a positive impact on the management of T2DM patients. As proved by analysis of ICER, extra costs of USD 2.7471 per patient were required in the management of oral antidiabetic-treated T2DM patients with pharmacist intervention. This analysis is essential to undertake since it can be used as a consideration to decide whether such an amount of money is a reasonable amount to pay by the policymaker.¹⁵ In this instance, to decide whether to include pharmacist intervention in the management of T2DM depends on budget limitations provided by the payer or BPJS. However, the ICER of USD 2.7471 for the management of oral antidiabetic-treated T2DM patients is less than the estimated Indonesian gross domestic product per capita for the year 2022, USD 4788.^{16,17}

Therefore, based on the World Health Organization choice threshold, the ICER is cost-effective. In the case of insulin-treated T2DM patients, this study proved that pharmacy intervention was dominant in that it reduced both costs consumed by the T2DM patients and their HbA1c level as well. Thus, pharmacist intervention in the management of T2DM patients is required to optimize resources and clinical outcomes. This present study supported many types of economic intervention studies in the management of T2DM patients performed in a few countries. One of which is the cost-effectiveness analysis of a mobile-based intervention for patients with T2DM conducted in a tertiary hospital in China. This study found that the mobile-based intervention improved the HbA1c and treatment costs of the patients compared to usual care.¹⁸ A systematic review and meta-analysis regarding the impact of clinical pharmacist interventions on health and economic outcomes in T2DM proved that clinical pharmacist interventions significantly reduced HbA1c levels compared to usual care (standardized mean difference: -0.52, $p < 0.001$). This study also found that the intervention on T2DM patients reduced costs significantly compared to usual care.¹⁹ In addition, a cost-effectiveness of a six-month home medication review (HMR) was conducted by clinical pharmacists in the management of patients with T2DM applying a Markov model. This HMR also indicated a reduction of HbA1c level and an improvement of the QoL of these patients. This study also proved a reduction of costs in the management of the patients.²⁰ All these studies prove the important active roles of pharmacists as a component of healthcare providers in optimizing health resources consumed and improving the clinical outcomes to avoid from further complications in the management of patients with T2DM. Therefore, collaboration among healthcare providers in the management of T2DM patients should always be practiced to improve the patients' outcomes.

CONCLUSIONS

Pharmacist intervention plays an important role in providing a cost-effective management of oral antidiabetic-treated and insulin-treated T2DM patients. Therefore, the study results could be considered by policy makers to improve the management of T2DM patients and healthcare.

AUTHOR CONTRIBUTIONS

AN: Conceptualization, data acquisition, data analysis and interpretation, project administration, writing article draft, review, editing, and approval of the final version to be submitted. BI: Conceptualization, data acquisition, data analysis and interpretation, project administration, writing article draft, review, editing, and approval of the final version to be submitted. DL: Conceptualization, data acquisition, data analysis and interpretation, project administration, writing article draft, review, editing, and approval of the final version to be submitted. KK: Conceptualization, data acquisition, data analysis and interpretation, project administration, writing article draft, review, editing, and approval of the final version

to be submitted. WW: data acquisition, data analysis and interpretation, writing article draft, review, and editing.

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CONFLICTS OF INTEREST

None

ETHICS STATEMENT

Ethical clearance was obtained from the Ethic Committee of Health Research, Universitas Sumatera Utara No:341/KEPK/USU/2023.

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