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Systematic review of the cost-effectiveness of insulin in the treatment of type 2 diabetes

Vo Ngoc Yen Nhi[1], Pham Luong Son[1], Nguyen Tan Dung[2], Nguyen Thi Thu Thuy[1,*]

[1]*Hong Bang International University*

[2]*Health Technology Assessment & Application Institute*

ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) is a major chronic disease requiring lifelong treatment. Insulin therapies play a key role in glycemic control, but their cost-effectiveness varies widely across formulations and delivery methods. Objectives: Systematic review of the cost-effectiveness of insulin in the treatment of type 2 diabetes. Materials and methods: A systematic review (SR) following PRISMA guidelines searched PubMed, Cochrane, Embase, and Vietnamese journals up to December 4, 2024. Eligible studies met predefined criteria and were appraised using the CHEERS 2022 checklist. Cost data and ICERs were converted to 2024 USD for comparison. Results: From 7,873 records, 84 studies were included (3 on delivery forms, 5 on injection methods, and 76 on insulin molecules). Thirteen recent studies (2020 onward) were analyzed for comparisons between insulin molecules; most (12/13) used model-based analysis and were high-quality. Insulin degludec was cost-effective or dominant compared with other basal insulins; icodec saved 480 - 974 USD and gained 0.04 - 0.08 QALYs compared with degludec. Glargine 100 was cost-effective compared with NPH (ICER 424 - 21,590 USD) and dominant over detemir. Pen devices improved adherence and glycemic control despite higher costs; insulin pumps were more cost-effective than multiple daily injections (ICER 64,433 - 104,069 USD/QALY). Stepwise initiation saved 3,370 USD and added 0.08 QALYs. Conclusions: The SR confirmed the cost-effectiveness of new insulin therapies and provides valuable evidence for future pharmacoeconomic evaluations.

Keywords: *systematic review, insulin, cost-effectiveness*

1. INTRODUCTION

Type 2 diabetes mellitus (T2DM) is one of the most prevalent diseases worldwide, carrying a high risk of serious complications if blood glucose levels are not adequately controlled, thereby imposing a substantial disease burden on every nation. According to the International Diabetes Federation (IDF), in 2021, there were approximately 537 million people living with diabetes globally, and this number is projected to rise to 783 million by 2045. About 79% of individuals with diabetes live in low- and middle-income countries, and nearly half of them remain undiagnosed. [1]. In Vietnam, approximately 280,427 people are diagnosed with T2DM every year [2]. The direct medical cost for treating T2DM per patient in Vietnam was estimated at approximately 7,890,502 VND (95% CI: 7,826,270 - 7,954,734 VND) in 2023, with medication costs accounting for the largest proportion (51.80%) [3]. Therefore, the rational use of medications is crucial not only to achieve effective glycemic control but also to minimize adverse events, prevent complications, and optimize treatment costs. Insulin plays a vital role in preventing both acute and chronic complications and in improving patients' quality of life. In the context of limited healthcare resources, cost-effectiveness analysis (CEA) provides a scientific and objective assessment of the costs and therapeutic outcomes of different types of insulin, thereby supporting decision-making in selecting appropriate treatment options, optimizing expenditures, and enhancing the quality of diabetes care. Many pharmacoeconomic evaluations of insulin therapies have been conducted worldwide as well as in Vietnam; however, to date, no comprehensive review has been carried out to synthesize these studies, particularly one that integrates international findings with real-world data relevant to the Vietnamese context. Therefore, with the aim of providing data and evidence for pharmacoeconomic assessment based on real-world data in Vietnam, and offering an overview of previously published economic evaluations, the objective of this study is to identify, synthesize, and analyze published economic evaluations of insulin therapies for type 2 diabetes mellitus.

Corresponding author: Nguyen Thi Thu Thuy
Email: thuyntt1@hiu.vn

2. MATERIALS AND METHOD

2.1. Research subjects

All studies related to the cost-effectiveness evaluation of insulin therapies in the treatment of T2DM.

2.2. Research methods

2.2.1. Study design

The systematic review was conducted in accordance with the PRISMA 2020 guidelines for systematic reviews [4].

2.2.2 Methods

Research question

Research question: "What is the cost-effectiveness of insulin therapies in the treatment of T2DM?" The research question based on the PICOS framework is presented in Table 1.

Table1. PICOS

P (Populations)	Diabetes mellitus type 2
I (Intervention)	Insulin
C (Comparator)	Insulin
O (Outcome)	ICER, ICUR, CM, NMB
S (Study)	CEA, CUA, CBA, CMA

Idenfication

The literature search was conducted online using E-library data sources and the websites of Vietnamese medical journals.

Vietnamese-language sources included: Vietnam Medical Journal, Can Tho Journal of Medicine and Pharmacy, Hong Bang Science Journal, and the Journal of Pharmacy Research and Drug Information.

E-library data sources included: PubMed, Cochrane, and Embase. To maximize the search yield, search strategies were developed on PubMed, Cochrane, and Embase by combining the following keywords: diabetes, type 2, insulin, cost-effectiveness, cost-benefit, and economic evaluation. On the websites of Vietnamese medical journals, the phrase "chi phí hiệu quả insulin" ("cost-effectiveness of insulin") was used to identify all relevant reports and evaluations. The search was updated up to 04/12/2025. Studies identified from the search were then screened for inclusion and exclusion according to the criteria presented in Table 2.

Table 2. Selection criteria and exclusion criteria

Selection criteria	Exclusion criteria
- By population: patients with type 2 diabetes mellitus (T2DM) - By intervention: treatment with insulin - By outcome indicators: ICER, ICUR, CM, NMB - By study design: CEA, CUA, CBA, CMA	- Studies without full-text availability - Studies comparing insulin in combination with oral antidiabetic drugs - Case reports, commentaries, letters, expert opinions, and systematic reviews - Full-text articles not written in English or Vietnamese

Two independent reviewers screened the titles, abstracts, and full texts of all retrieved records. The screening results were compared, and any disagreements were resolved through discussion and, if necessary, through consultation with a third reviewer.

Evaluation of research quality

The CHEERS 2022 checklist was used to assess the quality of the selected studies. The CHEERS 2022 checklist includes 28 criteria divided into seven main sections: Title, Abstract, Introduction, Methods, Results, Discussion, and Other relevant information [5]. Each reporting criterion was scored based on the completeness of the information provided. Specifically, a score of 1 point was assigned if the item was fully reported, 0.5 points if partially reported, and 0 points if not reported. No criterion was considered more important than the others. Items deemed not applicable to a given study were marked as "not applicable" and excluded from scoring.

Extract, synthesize, and present data

After collecting the relevant data, detailed information on the predefined study characteristics, methodologies, and outcomes was extracted. Cost indicators, incremental cost-effectiveness ratio (ICER), were standardized to a common currency (USD) using the CCEMG-EPPI-Centre cost converter tool to adjust all monetary values to 2024 USD [6]. Data extraction was performed independently by two reviewers to ensure accuracy and reduce extraction bias. Any inconsistencies between the two reviewers were resolved through discussion, and if needed, adjudicated by a third reviewer.

3. RESULTS

3.1. Identify studies related to the cost-effectiveness of insulin therapies in the treatment of type 2 diabetes

Using the keywords and search strategies described in the methodology section, a total of 7,873 records

were identified from three electronic databases - PubMed, Cochrane, and Embase - including both English and Vietnamese publications, along with additional sources from Vietnamese medical journals. After removing 1,281 duplicate records, 6,591 records remained for screening. Among these, 6,269 were excluded for not meeting the inclusion criteria, leaving 321 full-text articles for further assessment. Of these, 197 were excluded because they were conference abstracts, commentaries, or letters to the editor. Among the remaining 124 full-text studies, 9 were excluded due to being written in other languages, and 31 were excluded for evaluating insulin in combination with oral antidiabetic drugs. Consequently, 84 studies were included in the systematic review of cost-effectiveness. Of these 84 studies, 76 compared different insulin molecules, 3 compared formulations (vial vs. pen), and 5 compared administration methods of insulin. For studies assessing the cost-effectiveness of insulin molecules, to ensure up-to-date evidence, only those published from 2020 onward (13 studies) were analyzed in detail. Finally, 21 studies were selected for detailed data extraction and cost-effectiveness analysis.

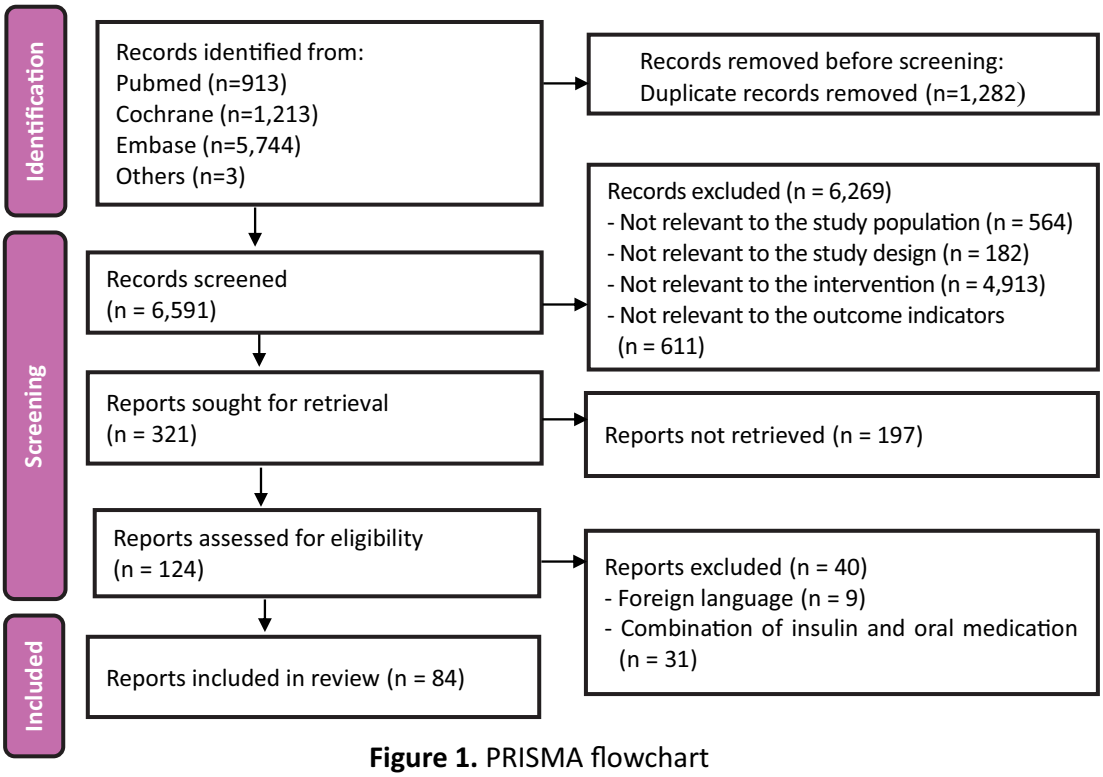

Figure 1. PRISMA flowchart

3.2. Synthesize and analyze the results from selected studies related to the cost-effectiveness of insulin therapies in the treatment of type 2 diabetes mellitus

3.2.1. Evaluation of research quality

The quality assessment results based on the CHEERS 2022 checklist indicated that the studies were of good quality or higher. All studies provided complete reporting of the criteria in the title, abstract, introduction, results, discussion, and other relevant information sections. Regarding the methods section, since most studies were published after 2022, the criteria related to distributional characteristics, patient-related factors, and the involvement of health economists were not fully reported.

3.2.2. Characteristics of the studies

Between active ingredients

Table 3. The characteristics of studies evaluating comparisons between active insulin ingredients

No.	Authors (Year)	Country	Comparators	Perspective	Discount Rate
1.	Evans et al. (2020)	Netherlands	Degludec vs. Glargine U300	Societal	NA
2.	Jendle et al. (2020)	Sweden	Degludec vs. basal insulin	Societal	NA

No.	Authors (Year)	Country	Comparators	Perspective	Discount Rate
3.	Haldrup et al. (2020)	Italy	Degludec vs. basal insulin	Healthcare system	3%
4.	Shafie et al. (2020)	Malaysia	Glargine vs. NPH; Detemir vs. NPH	Third-party payer	3%
5.	Nguyen Minh Van et al. (2021)	Vietnam	Glargine U100 vs. Detemir	Third-party payer	3%
6.	Nguyen Minh Van et al. (2021)	Vietnam	Glargine U100 vs. Detemir	Third-party payer	3%
7.	Luo et al. (2022)	China	Degludec/aspart vs. biphasic insulin aspart 30	Healthcare system	5%
8.	Shao et al. (2023)	USA	Glargine U300 vs. Degludec U100	Healthcare system	3%
9.	Nosrati et al. (2023)	Iran	Glargine U100 vs. NPH	Healthcare system	NA
10.	Hu et al. (2024)	China	Icodec vs. Degludec	Healthcare system	5%
11.	Shao et al. (2024)	USA	Glargine U300 vs. Glargine U100	Healthcare system	3%
12.	Hussin et al. (2024)	Malaysia	Insulin analogues vs. Human insulin	Healthcare system	NA
13.	Dai et al. (2024)	China	Icodec vs. Degludec	Healthcare system	5%

Note: NA: not available

The review indicated that the included studies were conducted in various regions, including European countries such as the Netherlands, Sweden, and Italy; Asian countries such as Malaysia, Vietnam, China, and Iran; and in the United States of America. Among these, eight studies were performed from the healthcare system perspective, three from the third-party payer perspective, and two from the societal perspective. The studies demonstrated a wide diversity of insulin types evaluated, including rapid-acting insulins (Biphasic Insulin Aspart 30, Degludec/Aspart), basal or long-acting insulins (Degludec, Glargine U100, Glargine U300, Detemir, Icodec), intermediate-acting insulin (NPH), and human insulin. Regarding discount rates, six studies applied a 3% rate, three studies applied a 5% rate, while four studies did not specify the discount rate used.

Between insulin pens and vials

Table 4. The characteristics of studies evaluating comparisons between insulin pens and vials

No.	Authors (Year)	Country	Comparators	Perspective	Discount Rate
1	Lee et al. (2006) [7]	United States	Before-and-after comparison	Third-party payer	NA
2	Cobden et al. (2007) [8]	United States	Before-and-after comparison	Third-party payer	NA
3	Kamrul-Hasan et al. (2023) [9]	Bangladesh	Cross-sectional comparison	Healthcare system	NA

The cost-effectiveness studies comparing insulin vials and insulin pens were conducted in Asia (Bangladesh) and America (the United States). Among these, two studies were performed from the third-party payer perspective, and one study was conducted from the healthcare system perspective. Two studies employed a before-and-after comparison design (comparing outcomes before and after switching from vial to pen use), while the study by Kamrul-Hasan et al. adopted a cross-sectional comparison between the two delivery methods [10]. All three studies did not specify any discount rate.

Between insulin injection methods

Table 5. The characteristics of studies evaluating comparisons between insulin injection methods

No.	Authors (Year)	Country	Comparators	Perspective	Discount Rate
1	Wake et al. (2000) [11]	Japan	Conventional (1 - 2 injections/day) vs. multiple injections (≥3/day)	Payer	3%
2	Saunders et al. (2014) [12]	Multinational	SWA (stepwise addition) vs. FBB (full basal-bolus initiation)	Healthcare system	3.50%
3	Valentine et al. (2015) [13]	United Kingdom	Conventional vs. intensified insulin regimen	Healthcare system	3.50%

No.	Authors (Year)	Country	Comparators	Perspective	Discount Rate
4	Roze et al. (2016) [14]	Netherlands	Multiple daily injections vs. continuous subcutaneous insulin infusion (CSII)	Third-party payer	Cost: 4%; Effectiveness: 1.5%
5	Roze et al. (2019) [15]	Finland	Multiple daily injections vs. continuous subcutaneous insulin infusion (CSII)	Societal	3%

The cost-effectiveness studies comparing different insulin injection methods were conducted in European countries (the Netherlands, Finland, and the United Kingdom), an Asian country (Japan), and in multinational settings. The review identified two studies conducted from the healthcare system perspective, one from the third-party payer perspective, one from the societal perspective, and one from the payer perspective. Among these, two studies compared multiple daily injections with continuous subcutaneous insulin infusion, one compared multiple daily injections with conventional (once or twice daily) injections, one compared intensified versus conventional regimens, and one compared the stepwise addition (SWA) method with full basal-bolus initiation (FBB). Regarding discount rates, two studies applied a 3% rate, two applied a 3.5% rate, and one applied 4% for costs and 1.5% for effectiveness.

3.2.3. Methods of studies

Between insulin ingredients

Table 6. The methods of studies evaluating comparisons between active insulin ingredients

No.	Authors (Year)	Study Design	Time Horizon	Cycle Length	Type of Cost	Type of Outcome	Sensitivity Analysis
1	Evans et al. (2020)	Modeling	1 year	NA	Direct medical, societal	QALY	DSA, PSA
2	Jendle et al. (2020)	Modeling	1 year; Lifetime	NA; 1 year	Direct medical, societal	QALY	DSA
3	Haldrup et al. (2020)	Modeling	Lifetime	1 year	Direct medical	QALY	DSA
4	Shafie et al. (2020)	Modeling	Lifetime	1 year	Direct medical	QALY	DSA
5	Nguyen Minh Van et al. (2021)	Modeling	1 year	NA	Direct medical	QALY	DSA
6	Nguyen Minh Van et al. (2021)	Modeling	40 years	1 year	Direct medical	QALY	DSA
7	Luo et al. (2022)	Modeling	30 years	1 year	Direct medical	QALY	DSA, PSA
8	Shao et al. (2023)	Modeling	Lifetime	1 year	Direct medical	QALY	DSA, PSA
9	Nosrati et al. (2023)	Modeling	1 year	NA	Direct medical	QALY	NA
10	Hu et al. (2024)	Modeling	40 years	1 year	Direct medical	QALY	DSA, PSA
11	Shao et al. (2024)	Modeling	Lifetime	1 year	Direct medical	QALY	DSA, PSA
12	Hussin et al. (2024)	Cross-sectional	3 months	NA	Direct medical	HbA1c and FBS	NA
13	Dai et al. (2024)	Modeling	40 years	1 year	Direct medical	QALY	DSA, PSA

Notes: HbA1c (Hemoglobin A1c); FBS (Fasting Blood Sugar); NA (Not Answered); DSA (Deterministic Sensitivity Analysis); PSA (Probabilistic Sensitivity Analysis); QALY (Quality-Adjusted Life Year)

The modeling method was applied in all studies except for the study by Hussin et al. (2024), which employed a cross-sectional design combined with retrospective data collection. Among the twelve studies using modeling approaches, four conducted cost-effectiveness analyses over a short-term horizon (1 year), while the remaining studies applied long-term horizons (30 years, 40 years, or lifetime). The cross-sectional study by Hussin et al. (2024) was conducted over a 3-month period. Consistent with the societal perspective, relevant studies evaluated both direct and indirect medical costs, whereas those conducted from the healthcare system or third-party payer per-

spectives considered only direct medical costs. All modeling studies reported QALY as the primary outcome measure, while the study by Hussin et al. (2024) assessed HbA1c and fasting blood sugar (FBS) levels as effectiveness outcomes. Overall, the review found that 6 out of 13 studies performed both deterministic (DSA) and probabilistic sensitivity analyses (PSA), 5 studies conducted only deterministic sensitivity analyses, and 2 studies did not perform any sensitivity analysis.

Between insulin pens and vials

Table 7. The methods of studies evaluating comparisons between insulin pens and vials

No.	Authors (Year)	Study design	Study duration	Type of cost	Type of outcome	Sensitivity analysis
1	Lee et al. (2006) [7]	Cross-sectional	6 months before switching to an insulin pen and 2 years after switching	Direct medical cost	Medication adherence rate, incidence of hypoglycemia	Not performed
2	Cobden et al. (2007) [8]	Cross-sectional	6 months before switching to an insulin pen and 2 years after switching	Direct medical cost	Medication adherence rate, incidence of hypoglycemia	Not performed
3	Kamrul-Hasan et al. (2023) [9]	Cross-sectional	6 months	Direct medical cost	Medication adherence rate, HbA1c	Not performed

All studies comparing insulin pens and vials employed a cross-sectional design, with two studies conducting before-and-after comparisons of outcomes prior to and following the use of insulin pens, over periods of 6 months and 2 years, respectively. For the study that performed a concurrent comparison between insulin pens and vials, the review recorded a study duration of 6 months. Consistent with the healthcare system or third-party payer perspective, only direct medical costs were evaluated. The studies assessed HbA1c levels and treatment adherence rates as effectiveness outcomes, and no sensitivity analysis was performed in any of the studies.

Between insulin injection methods

Table 8. The methods of studies evaluating comparisons between insulin injection methods

No.	Authors (Year)	Study design	Study duration	Type of cost	Type of outcome	Sensitivity analysis
1	Wake et al. (2000) [11]	Cross-sectional	10 years	Direct medical cost	% of macrovascular and microvascular events, % mortality	Not performed
2	Saunders et al. (2014) [12]	Modeling	5 years	Direct medical cost	QALY	DSA, PSA
3	Valentine et al. (2015) [13]	Modeling	Lifetime	Direct medical cost	QALY	DSA
4	Roze et al. (2016) [14]	Modeling	Lifetime	Direct medical cost	QALY	DSA, PSA
5	Roze et al. (2019) [15]	Modeling	Lifetime	Direct medical and indirect costs	QALY	DSA

Notes: DSA (Deterministic Sensitivity Analysis); PSA (Probabilistic Sensitivity Analysis); QALY (Quality-Adjusted Life Year).

Most of the studies adopted a modeling design, except for the study by Wake et al. (2000) [11] which employed a cross-sectional approach. Among the four modeling studies, three out of four conducted cost-effectiveness analyses over a lifetime horizon, while the study by Saunders et al. (2014) [12] used a 5-year

horizon. The cross-sectional study was carried out in a population of patients with type 2 diabetes over a 10-year period. All studies assessed direct medical costs, except for Roze et al. (2019) [15], which also included indirect costs. Modeling studies reported QALY as the primary outcome, whereas the cross-sectional study measured the incidence of vascular events and mortality rates as effectiveness outcomes.

3.2.4. Results of studies

Between insulin ingredients

Table 9. The main results of studies comparing insulin ingredients

No.	Authors (Year)	Com-parators	Currency (Study Year)	D_{cost}		D_{Effect}	ICER		WTP (Study year)	Con-clusion
				Study year	USD 2024		Study year	USD 2024		
						QALY				
1	Evans et al. (2020)	Degludec vs. Glargine 300	EUR (2018)	-24.71	-38.84	0.0045	Dominant		20,000	Dominant
2	Jendle et al. (2020)	Degludec vs. Basal insulin (one-year)	SEK (2018)	1,181	168.34	0.02	64,298	9.164,86	500,000	Cost-effective
		Degludec vs. Basal insulin (lifetime)	SEK (2018)	-2,114	-301.32	0.08	Dominant			Dominant
3	Haldrup et al. (2020)	Degludec vs. Basal insulin	EUR (2017)	-2,682	6,356.2	0.628	Dominant		30,000	Dominant
4	Shafie et al. (2020)	Glargine 100 vs. NPH	MYR (2015)	492	423.85	0.1317	3,732	3.215	29,080	Cost-effective
		Detemir vs. NPH		-6,727	5,795.17	0.8567	Dominant			Dominant
5	Nguyen Minh Van et al. (2021)	Glargine 100 vs. detemir	VND (2021)	-1,853,848	-247.65	0.0008	Dominant		193,191,255	Dominant
6	Nguyen Minh Van et al. (2021)	Glargine 100 vs. detemir	VND (2021)	-26,288,432	-3,510.59	0.21	Dominant		193,191,255	Dominant
7	Luo et al. (2022)	Degludec/ aspart vs. biphasic insulin aspart 30	CNY (2021)	3,888	1,132.62	0.28	13,886	4.045,17	80,976	Cost-effective
8	Shao et al. (2023)	Glargine 300 vs. Degludec 100	USD (2018)	2,250	2,750.38	0.027	Dominant		5,000	Dominant
9	Nosrati et al. (2023)	Glargine 100 vs. NPH	USD (2022)	2.3	25.14	0.001	1,975	21.589,82	2,756	Cost-effective

No.	Authors (Year)	Com-parators	Currency (Study Year)	D_{cost}		D_{Effect}	ICER		WTP (Study year)	Con-clusion
				Study year	USD 2024		Study year	USD 2024		
						QALY				
10	Hu et al. (2024)	Icodec vs. Degludec	USD (2023)	-233.81	-479.96	0.04	Dominant		12,680.83 To 38,042.29	Dominant
11	Shao et al. (2024)	Glargine 300 vs. Glargine 100	USD (2019)	583	699.74	0.077	7,522	9,033.66	50,000	Cost-effective
12	Dai et al. (2024)	Icodec vs. Degludec	USD (2023)	-474.48	-974.01	0.08	Dominant		12,680.83 To 38,042.29	Dominant
						Clinical rate				
13	Hussin et al. (2024)	Analog vs. Human insulin	MYR (2020)	292.85	239.44	HbA1c : −0.45 FBS: −0.96	There was no significant clinical improvement in patients' HbA1c and fasting blood sugar (FBS) levels after insulin intensification, despite the higher treatment costs.			

Notes: HbA1c (Hemoglobin A1c); FBS (Fasting Blood Sugar); NA (Not Answered); DSA (Deterministic Sensitivity Analysis); PSA (Probabilistic Sensitivity Analysis); QALY (Quality-Adjusted Life Year)

Among the studies evaluating cost-effectiveness using the ICER/QALY indicator, all three studies reported that insulin degludec regimens were either dominant or cost-effective compared with other basal insulins. However, when comparing degludec with glargine U300, the findings were inconsistent: the study by Evans et al. (2020) conducted in the Netherlands with a 1-year time horizon showed that degludec was dominant, whereas Shao et al. (2023) in China, with a 40-year time horizon, reported the opposite result. Two studies that analyzed the cost-effectiveness between icodec and degludec found that icodec was both cost-saving (saving USD 479.96 and 974.01) and more effective, with an incremental gain of 0.04 - 0.08 QALY. Insulin glargine U100 was found to be cost-effective compared with NPH insulin (n = 2 studies), dominant over detemir (n = 2 studies), but dominated by glargine U300 (n = 1 study). The study by Hussin et al. (2024), which assessed incremental cost and clinical benefit ratios, showed that the use of insulin analogs resulted in higher costs without significant clinical improvement in HbA1c or fasting blood sugar (FBS) levels.

Between insulin pens and vials

The study by Kamrul-Hasan et al. (2023) analyzed the cost-effectiveness of insulin pens compared with disposable plastic syringes among patients with type 2 diabetes at a medical college in Bangladesh. The results showed that the mean HbA1c level in patients using insulin pens was lower (7.8%) than in those using plastic syringes (8.5%), indicating better glycemic control in the pen group. However, the monthly treatment cost was significantly higher for insulin pens, with 65% of patients spending more than 1,000 BDT, whereas 90% of syringe users paid less than 500 BDT. These findings highlight a trade-off between improved glycemic control and higher treatment costs when using insulin pens compared with conventional syringes [10]. The study by Cobden et al. (2007) conducted a retrospective data analysis and revealed a significant increase in medication adherence (from 59% to 68%) and a reduction in hypoglycemic events after switching to insulin pens (OR = 0.4, $p < 0.05$). In addition, the study reported a substantial annual cost reduction of USD 1,748. These findings suggest that switching to biphasic insulin analog pens can improve clinical outcomes and reduce treatment costs for patients with T2DM [8]. The study by Lee et al. (2006) evaluated the impact of switching from insulin vials to insulin pens among patients with type 2 diabetes, focusing on medication adherence and pharmacoeconomic outcomes. The results

indicated a significant increase in treatment adherence (from 62% to 69%) and a reduction in hypoglycemic events (OR = 0.50) after the switch. Moreover, the healthcare costs associated with diabetes care decreased, particularly those related to emergency visits, demonstrating both economic benefits and improved clinical outcomes with the use of insulin pens[7].

Between insulin injection methods

Two cost-effectiveness studies comparing continuous subcutaneous insulin infusion (CSII) with multiple daily injections (MDI) conducted in Europe both reported that CSII was cost-effective, with ICER values ranging from 64,432.51 to 104,069.15 USD per QALY (2024 USD). Two studies comparing intensified insulin regimens versus conventional injections yielded contradictory results. The study by Valentine et al. (2015) [13] conducted in the United Kingdom reported an ICER of 111,299.57 USD per QALY, exceeding the country's willingness-to-pay threshold; thus, the intensified regimen was not cost-effective compared with the conventional regimen. In contrast, Wake et al. (2000) [11] in Japan found that the intensified injection regimen was cost-saving (saving 1,541.39 USD) and reduced complication rates, resulting in more event-free life-years among patients with type 2 diabetes. The study by Saunders et al. (2014) [12], which compared stepwise insulin initiation with full-dose initiation, demonstrated that the stepwise approach was dominant, leading to the cost savings of 3,369.90 USD and an incremental gain of 0.08 QALY. Therefore, stepwise insulin initiation was superior to full-dose initiation at baseline.

Table 10. The main results of studies comparing insulin injection methods

No.	Authors (Year)	Com-parators	Currency (Study Year)	D_{cost}		D_{Effect}	ICER		WTP (Study year)	Con-clusion
				Study year	USD 2024		Study year	USD 2024		
						QALY				
1	Saunders et al. (2014) [12]	SWA vs. FBB	USD (2013)	-2,542	-3,369.90	0.08	Dominant		NA	Dominant
2	Valentine et al. (2015) [13]	Intensified regimen vs. conventional regimen	GBP (2011)	5,771	11,587.56	0.15	55,431	111,299.57	20,000	Not cost-effective
3	Roze et al. (2016) [14]	Continuous subcutaneous insulin infusion (CSII) vs. multiple daily injections (MDI)	EUR (2013)	27,051	44,759.91	0.43	62,895	104,069.15	80,000	Cost-effective
4	Roze et al. (2019) [15]	Continuous subcutaneous insulin infusion (CSII) vs. multiple daily injections (MDI)	EUR (2017)	15,206	20,482.52	0.32	47,834	64,432.51	50,000	Cost-effective

No.	Authors (Year)	Com-parators	Currency (Study Year)	D_{cost}		D_{Effect}	ICER		WTP (Study year)	Con-clusion
				Study year	USD 2024		Study year	USD 2024		
						Clinical rate				
5	Wake et al. (2000) [11]	Intensified regimen vs. conventional regimen	USD (1998)	-1,215	-1,541.39	Reduce the rate of clinical events, increase event-free life years	Dominant		NA	Dominant

Notes: ICER (Incremental Cost-Effectiveness Ratio); WTP (Willingness to Pay); QALY (Quality-Adjusted Life Year); FBS (Fasting Blood Sugar); NA: not available

4. DISCUSSIONS

From three online databases - PubMed, Cochrane, and Embase - as well as domestic medical journals, a total of 7,873 records were identified. After removing duplicates and screening based on inclusion and exclusion criteria, 84 studies met the eligibility requirements. To ensure the inclusion of the most up-to-date evidence, 21 studies were selected for data extraction, characteristic analysis, and result synthesis. Among these, 3 studies compared formulations (insulin vials vs. pens), 5 studies compared injection methods, and 13 studies evaluated the cost-effectiveness of different insulin molecules published from 2020 onward.

Studies comparing insulin molecules were conducted across various countries worldwide, with model-based methods applied in most cases. The review found that insulin degludec was dominant or cost-effective compared with basal insulins, insulin icodec was superior to degludec, and insulin glargine U100 was cost-effective compared with NPH insulin (n = 2 studies) and dominant over detemir. The systematic review by Gkrinia et al. (2023), which reviewed 21 economic evaluations of insulin use in type 2 diabetes across multiple countries between 2016 and July 2023, indicated that newer insulin products (e.g., degludec or degludec/liraglutide combination) were more expensive but potentially cost-effective due to reduced hypoglycemia and increased QALY. In scenarios with higher treatment adherence, QALY gains ranged from 0.456 to 0.653, and ICER values ranged between USD 1,450 and 12,360 per QALY [16]. Narrative health-economic reviews have emphasized that ultra-long-acting basal insulin, particularly insulin degludec, tends to be cost-effective primarily due to reductions in hypoglycaemia and improved real-world adherence, despite their higher acquisition costs. This review also highlighted structural challenges in insulin evaluation, including the limitations of treat-to-target clinical trials, which often equalize HbA1c outcomes between comparators and thereby mask potential incremental benefits observable in real-world settings. These considerations reinforce the need for comprehensive economic evaluations that integrate both clinical trial and real-world evidence [17]. All studies comparing insulin pens and vials employed a cross-sectional design, showing that although insulin pens increased costs, they improved treatment adherence and glycemic control. A meta-analysis of insulin pen versus vial therapy similarly demonstrated that switching to pens enhanced adherence and treatment persistence, despite higher drug costs [18]. Cranston et al. (2023) conducted a systematic literature review of connected insulin-pen systems and found preliminary evidence that these platforms can improve insulin-use behaviour, patient satisfaction, and potentially reduce diabetes-related costs, albeit based on a limited number of observational studies and only two RCTs [19]. Cost-effectiveness analyses comparing injection methods revealed that continuous subcutaneous insulin infusion (CSII) was more cost-effective than multiple daily injections (MDI), and that the stepwise addition approach was superior to full-dose initiation, as shown in model-based evaluations. These findings collectively suggest that, despite higher acquisition costs, insulin pen devices, especially newer connected pen platforms, offer meaningful advantages in adherence, usability, and real-world

treatment effectiveness, which may translate into improved long-term clinical and economic outcomes.

This systematic review followed the PRISMA guidelines to ensure transparency and rigor in study identification and selection. Additionally, study quality was appraised using the CHEERS checklist, ensuring adherence to reporting standards for economic evaluations. Cost and ICER parameters were standardized to 2024 USD values, facilitating comparability across studies. Overall, this review provides a valuable foundation for future pharmacoeconomic research evaluating the cost-effectiveness of insulin therapies in Vietnam. However, due to limitations in database coverage and language scope (English and Vietnamese), relevant studies in other databases or languages may have been missed.

5. CONCLUSIONS

The systematic review demonstrated the cost-effectiveness of newer insulin therapies and provided valuable evidence for future pharmacoeconomic studies. At present, cost-effectiveness research on insulin in Southeast Asia remains limited; therefore, the implementation of additional studies in this area is essential to strengthen the regional evidence base and support healthcare decision-making.

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Tổng quan hệ thống chi phí - hiệu quả của insulin trong điều trị đái tháo đường tuýp 2

Võ Ngọc Yến Nhi, Phạm Lương Sơn, Nguyễn Tấn Dũng, Nguyễn Thị Thu Thủy

TÓM TẮT

Đặt vấn đề: Đái tháo đường tuýp 2 (ĐTĐ tuýp 2) là bệnh mạn tính phổ biến cần điều trị suốt đời. Liệu pháp insulin đóng vai trò quan trọng trong kiểm soát đường huyết, nhưng hiệu quả chi phí thay đổi đáng kể giữa các dạng và phương pháp sử dụng. Mục tiêu: Tổng quan hệ thống chi phí - hiệu quả của insulin trong điều trị đái tháo đường tuýp 2. Đối tượng và phương pháp nghiên cứu: Tổng quan hệ thống (SR) theo hướng dẫn PRISMA được thực hiện trên PubMed, Cochrane, Embase và các tạp chí Việt Nam đến 4/12/2024. Các nghiên cứu đủ điều kiện được đánh giá bằng danh mục CHEERS 2022. Dữ liệu chi phí và ICER được quy đổi sang USD năm 2024. Kết quả: Trong 7,873 bài, có 84 nghiên cứu được chọn (3 về dạng sử dụng, 5 về cách tiêm, 76 về phân tử insulin). Mười ba nghiên cứu gần đây (từ 2020) được phân tích, đa số (12/13) dùng mô hình mô phỏng và đạt chất lượng tốt. Insulin degludec có chi phí - hiệu quả hoặc vượt trội so với các insulin nền khác; icodec tiết kiệm 480 - 974 USD và tăng 0.04 - 0.08 QALY so với degludec. Glargine 100 hiệu quả hơn NPH (ICER 424 - 21,590 USD) và vượt trội detemir. Bút tiêm cải thiện tuân thủ và kiểm soát đường huyết dù chi phí cao hơn; bơm insulin hiệu quả hơn tiêm nhiều lần (ICER 64,433 - 104,069 USD/QALY). Kết luận: SR khẳng định tính chi phí - hiệu quả của các liệu pháp insulin mới và cung cấp bằng chứng hữu ích cho các nghiên cứu kinh tế dược trong tương lai.

Từ khóa: *tổng quan hệ thống, insulin, chi phí - hiệu quả*

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