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Cost-utility of IDegLira versus alternative basal insulin intensification therapies in patients with type 2 diabetes mellitus uncontrolled on basal insulin in a Chinese setting

Junling Weng^{1,2}, Dunming Xiao^{1,2} and Yingyao Chen^{1,2*}

Abstract

Background In 2021, IDegLira was introduced in China as a treatment option for patients with type 2 diabetes mellitus (T2DM). We aimed to evaluate the long-term cost-utility of IDegLira compared to basal-bolus therapy and glucagon-like peptide-1 receptor agonist (GLP-1RA) added to basal insulin in patients with T2DM who remain uncontrolled on basal insulin in China.

Methods The Swedish Institute for Health Economics (IHE) T2DM Cohort Model was employed to project health and cost outcomes over a 30-year time horizon. Baseline cohort characteristics were derived from the DUAL II China study. Treatment effects were derived from DUAL VII study and a pooled analysis. Costs were considered from a health system perspective in China and expressed in 2023 Chinese yuan (CNY). Health outcomes were measured in quality-adjusted life years (QALYs). Health state utilities were obtained from several published sources. Future costs and clinical outcomes were discounted at an annual rate of 5%.

Results IDegLira was associated with an improvement of 0.810 QALYs and a cost reduction of CNY 91,217 compared to basal-bolus therapy. Similarly, compared to GLP-1RA added to basal insulin, IDegLira demonstrated a health gain of 0.011 QALYs and a cost reduction of CNY 23,815, establishing IDegLira as the dominant option. The sensitivity analyses indicated a 100% probability of IDegLira being cost-effective.

Conclusions For T2DM patients who remain uncontrolled on basal insulin, IDegLira was projected to be dominant and could offer better value compared to both basal-bolus therapy and GLP-1RA added to basal insulin in the Chinese setting.

Keywords Type 2 diabetes, IDegLira, Cost-utility, China

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Background

In 2021, China recorded the highest global number of diabetes cases, with a total of 140.9 million. Projections suggest this number will increase to 174.4 million by 2045. It is important to note that type 2 diabetes mellitus (T2DM) constitutes for over 90% of all diabetes cases globally. China's healthcare expenditure on adult diabetes patients reached \$165.3 billion, second only to the United States [1, 2]. This substantial economic burden presents significant challenges to the country's healthcare system.

According to China's treatment guidelines for T2DM, both basal insulin and glucagon-like peptide-1 receptor agonist (GLP-1RA) are recognized as effective injectable medications [3]. As the disease progresses, the patients' blood glucose levels tend to increase gradually, necessitating adjustments to the intensity of treatment for hyperglycemia control. For patients inadequately controlled on basal insulin, treatment options include basal-bolus therapy (basal insulin administered once daily in combination with prandial insulin administered three times daily) or GLP-1RA added to basal insulin. The combination of GLP-1RA and basal insulin leverages their complementary mechanisms of action, with GLP-1RA mitigating some adverse effects of basal insulin therapy, particularly hypoglycemia and weight gain. Additionally, the fixed-ratio combination reduces patient burden by consolidating multiple injections into a single daily dose [4, 5].

In 2021, IDegLira was introduced in China, providing a novel therapeutic option for these patients. IDegLira is a fixed-ratio combination of basal insulin (degludec) and GLP-1RA (liraglutide), administered as a once-daily subcutaneous injection [6]. The DUAL II China trial demonstrated that patients uncontrolled on basal insulin achieved superior HbA1c reductions and weight loss with IDegLira compared to insulin degludec, without an increased risk of hypoglycemia events [7].

Previous studies have conducted cost-effectiveness analyses of IDegLira compared to basal-bolus therapy or basal insulin combined with GLP-1RA in countries such as the United States, the United Kingdom, Czech Republic, Slovakia, Sweden, and the Netherlands, with results showing that IDegLira is cost-effective [8–13]. However, these findings may not be directly applicable to China due to differences in health system, population, and treatment practices. One study conducted within the Chinese context has established IDegLira as cost-effective when compared individually to insulin degludec and liraglutide [14]. Nonetheless, according to China's treatment guidelines for T2DM, IDegLira should also be evaluated against intensification therapies such as basal-bolus therapy and basal insulin combined with GLP-1RA [3].

Given the substantial financial burden imposed by diabetes, this study conducted a long-term cost-utility

analysis of IDegLira in comparison with basal-bolus therapy, and GLP-1RA added to basal insulin from a Chinese health system perspective. The aim was to provide additional information across various stages of diabetes and furnish healthcare decision-makers with evidence to inform medical insurance policies and drug pricing decisions.

Methods

We designed and reported this study following the Consolidated Health Economic Evaluation Reporting Standards (CHEERS) 2022 checklist [15].

Model structure

The Swedish Institute for Health Economics (IHE) T2DM Cohort Model was used for the cost-utility analysis. The IHE Cohort Model was designed in Microsoft Excel 2013 using Visual Basic for Applications and has been externally validated [16]. This model employs two parallel Markov chains, covering microvascular (eye disease, lower extremity disease and kidney disease) and macrovascular (ischemic heart disease, myocardial infarction, heart disease and stroke) health states. It incorporates multiple variables such as cohort baseline characteristics, costs, utility weights, and treatment effects. Its outcomes include cumulative incidences of complications and adverse events, life years, quality-adjusted life years (QALYs), costs and incremental cost-effectiveness ratio (ICER). The model has a cycle length of 1 year and a maximum time horizon of 40 years. A schematic diagram of the model can be seen in Fig. 1. Further details regarding the model structure can be found in the relevant publications [9, 17].

Model inputs

Baseline cohort characteristics

Baseline cohort characteristics were sourced from DUAL II China (Table 1) [7]. This study was a 26-week, randomized, double-blinded, multicenter, phase 3 trial (NCT03175120). Additional required information for the model was supplemented from published literatures [14, 18].

Treatment outcomes

We compared IDegLira to basal-bolus therapy (group one) and GLP-1RA added to basal insulin (group two). Due to the lack of clinical studies conducted within the Chinese population, the treatment effects were derived from published literature (Table 2) [19, 20]. Basal-bolus therapy specifically consisted of insulin glargine combined with thrice-daily insulin aspart, while GLP-1RA added to basal insulin involved insulin glargine and liraglutide. According to Chinese clinical guidelines, intensification therapy (basal-bolus therapy) should be initiated

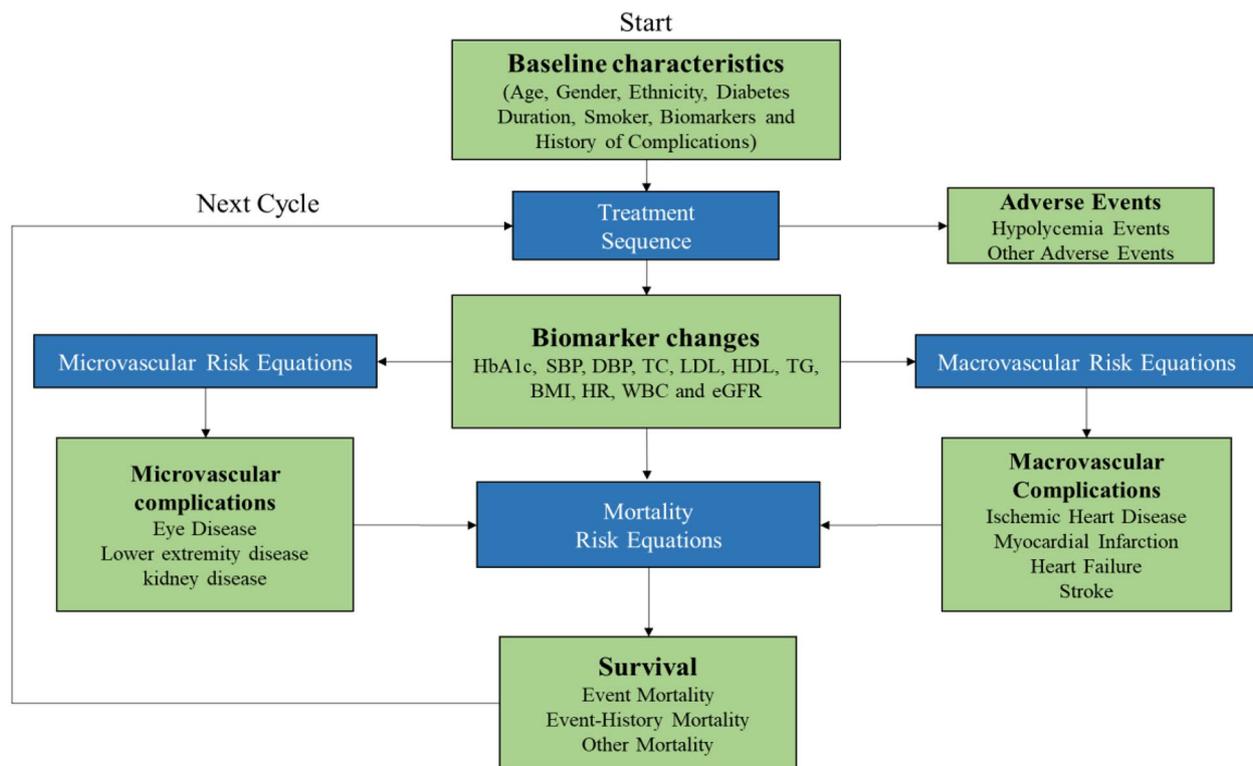


Fig. 1 Model structure. Abbreviations: SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglycerides; BMI, body mass index; HR, heart rate; WBC, white blood cell count; eGFR, glomerular filtration rate

Table 1 Baseline characteristics from DUAL II China

Characteristic	Mean	Standard deviation
Demographics		
Male (%)	60.5	Not applicable
Age (y)	54.7	9.9
Duration of diabetes (y)	11	6
Baseline risk factors		
HbA1c (%)	8.94	1.19
Fasting plasma glucose (mmol/L)	9.75	2.8
Total cholesterol (TC, mmol/L)	4.53	Not report
Low-density lipoprotein cholesterol (LDL, mmol/L)	2.39	Not report
High-density lipoprotein cholesterol (HDL, mmol/L)	1.11	Not report
Triglycerides (TG, mmol/L)	1.85	Not report
Body mass index (BMI, kg/m ²)	27.4	3.1

when HbA1c levels reached 9% [3]. The risk equation for complications was derived from the United Kingdom Prospective Diabetes Study (UKPDS) 82 [21].

Costs and utilities

This study considered direct medical costs, including medication, needles, self-monitoring of blood glucose (SMBG), and costs associated with complications.

Monetary values were expressed in Chinese Yuan (CNY) for the year 2023. The costs of complications were sourced from the literature and adjusted to 2023 using the consumer price index (CPI) (Supplement). The costs per package of IDegLira, insulin degludec, glargine, aspart and liraglutide were determined based on the average bidding price obtained from the price database [22]. Drawing from the DUAL VII trial for basal-bolus therapy, the average daily dosage was standardized: 52 units for insulin glargine, 32 units for insulin aspart, and 40 units for IDegLira [19]. Correspondingly, based on data extracted from the published literature of GLP-1RA added to basal insulin, the set dosages were determined as 35.8 units per day for insulin glargine and 1.8 mg per day for liraglutide [23]. Consequently, the annual treatment costs were as follows: IDegLira was CNY 14,555.58, basal-bolus was CNY 21,835.03, and GLP-1RA added to basal insulin was CNY 18,264.22. Utility value parameters were sourced from the pertinent literatures (Supplement).

Statistical approach and sensitivity analysis

In the base-case analysis, the baseline age of the population was 54.7 years. Recognizing the prolonged life expectancy within the Chinese population, our analysis was projected over a 30-year horizon [24]. Following the

Table 2 Treatment effects

Variable	Group one (Vs. basal-bolus)		Group two (Vs. Basal insulin + GLP-1RA)		
	IDegLira	Basal-bolus	IDegLira	Basal + GLP-1RA	Basal-bolus
HbA1c (%)	-1.5 ^[18]	-1.5 ^[18]	-1.68 ^[19]	-1.33* ^[19]	-1.39* ^[19]
SBP (mmHg)	-4.5 ^[18]	-1.2 ^[18]	-6.84 ^[19]	-4.68 ^[19]	1.83* ^[19]
TC (mmol/L)	-0.18 ^[18]	0.06 ^[18]	-0.27 ^[19]	-0.34 ^[19]	-5.80 ^[19]
LDL (mmol/L)	-0.05 ^[18]	0.06 ^[18]	-0.20 ^[19]	-0.25 ^[19]	-0.08 ^[19]
HDL (mmol/L)	0 ^[18]	0.05 ^[18]	0.01 ^[19]	-0.02 ^[19]	0.01 ^[19]
TG (mmol/L)	-0.21 ^[18]	-0.12 ^[18]	-0.21 ^[19]	-0.19 ^[19]	-0.18 ^[19]
BMI (kg/m ²)	-1.02 ^[19]	1.42* ^[19]	-1.02 ^[19]	-1.27 ^[19]	1.42* ^[19]
Mild hypoglycemia (PYE)	0.9016 ^[18]	7.8443 ^[18]	1.219 ^[19]	1.241 ^[19]	10.563* ^[19]
Severe hypoglycemia (PYE)	0.03 ^[18]	0.08 ^[18]	0.004 ^[9]	0 ^[9]	0.024 ^[19]

Notes: For values measured in mg/dl, TC, HDL, and LDL were divided by 38.67, and TG was divided by 88.57 to convert to mmol/L

Abbreviations: SBP, systolic blood pressure; TC, total cholesterol; LDL, low-density lipoprotein; HDL, high-density lipoprotein; TG, triglycerides; BMI, body mass index; PYE, events/patient-year

*Statistically significant

Table 3 Base case results

Treatment	Cost (CNY)	Incremental cost	Life expectancy (years)	Incremental Life expectancy	QALY	Incremental QALY	ICER (CNY/QALY)
Group one (Vs. basal-bolus therapy)							
IDegLira	518,503	-	12.406	-	7.499	-	-
Basal-bolus therapy	609,721	-91,217	12.333	0.073	6.689	0.810	Dominant
Group two (Vs. basal insulin + GLP-1RA)							
IDegLira	528,149	-	12.433	-	7.267	-	-
Basal insulin + GLP-1RA	551,964	-23,815	12.415	0.017	7.255	0.011	Dominant

China guidelines for pharmacoeconomic evaluations, the discount rate for future costs and clinical outcomes was set at 5% [25]. According to the current research for chronic diseases treatment in China, the threshold was set as 1.5 times per capita gross domestic product (GDP) of China (CNY 134,037/QALY) in this study [26].

Furthermore, to ascertain the robustness of the base case analysis results, we conducted one-way sensitivity analysis (OWSA) and probabilistic sensitivity analysis (PSA). In OWSA, we varied the horizon, discount rate, cost of complications and drugs, treatment effects and threshold for initiating an intensified treatment. PSA was conducted over 1000 iterations, with treatment effects standard errors referenced from the publication [9]. For parameters without standard errors, we made assumptions based on published literature [9]. Convergence graphs were examined to confirm whether stable results were simulated in PSA. Since semaglutide has entered the Chinese market, we considered replacing liraglutide with semaglutide in group two for the scenario analysis. We obtained the parameters (HbA1c, systolic blood pressure and diastolic blood pressure) for the comparison in the scenario analysis using an indirect comparison method.^[27] The estimated treatment difference in terms of HbA1c reduction between IDegLira and semaglutide added to

basal insulin was 0.9% and 1.7%, respectively.^[7, 28] The annual treatment costs for semaglutide added to basal insulin was CNY 22,555.75. For details, please refer to the supplementary materials.

Results

Base case analysis

The base case results are summarized in Table 3. When compared to basal-bolus therapy (group one), IDegLira demonstrated a health gain of 0.810 QALYs coupled with a cost reduction of CNY 91,217, establishing IDegLira as the dominant therapeutic option. Similarly, in the analysis comparing GLP-1RA added to basal insulin (group two), the IDegLira group exhibited a gain of 0.011 QALYs accompanied by a cost saving of CNY 23,815.

Sensitivity analysis

In one-way sensitivity analysis, variations in parameters such as time horizon, discount rates, treatment intensification threshold, and complication costs did not alter the dominant outcome of IDegLira (Table 4). The convergence graphs confirmed the stability of the results in PSA (Supplement). Notably, a significant portion of data points in the cost-effectiveness scatter plot were positioned in the fourth quadrant. Moreover, the

Table 4 One-way sensitivity analysis results

	Group one (Vs. basal-bolus therapy)			Group two (Vs. basal insulin + GLP-1RA)		
	Δ Cost (CNY)	Δ QALY	ICER	Δ Cost (CNY)	Δ QALY	ICER
Base case	-91,217	0.810	Dominant	-23,815	0.011	Dominant
10-y time horizon	-84,490	0.721	Dominant	-22,689	0.007	Dominant
20-y time horizon	-90,442	0.780	Dominant	-23,708	0.009	Dominant
40-y time horizon	-90,693	0.817	Dominant	-23,736	0.012	Dominant
0% discount rates	-112,915	1.067	Dominant	-28,791	0.021	Dominant
8% discount rates	-81,469	0.710	Dominant	-21,465	0.009	Dominant
Treatment intensification at HbA1c 8.5%	-60,959	0.567	Dominant	-15,506	0.005	Dominant
Treatment intensification at HbA1c 9.5%	-146,577	1.269	Dominant	-39,883	0.022	Dominant
Upper 95% CI of HbA1c change in IDegLira arm	-90,441	0.805	Dominant	-22,525	0.003	Dominant
Lower 95% CI of HbA1c change in IDegLira arm	-92,199	0.816	Dominant	-34,751	0.109	Dominant
Upper 95% CI of BMI change in IDegLira arm	-91,146	0.781	Dominant	-23,596	-0.079	Reversed ICER
Lower 95% CI of BMI change in IDegLira arm	-91,285	0.838	Dominant	-23,862	0.032	Dominant
Upper 95% CI of hypoglycemic episodes in IDegLira arm	-87,762	0.756	Dominant	-20,229	-0.045	Reversed ICER
Lower 95% CI of hypoglycemic episodes in IDegLira arm	-93,043	0.839	Dominant	-26,080	0.047	Dominant
Complication costs + 20%	-101,303	0.810	Dominant	-24,332	0.011	Dominant
Complication costs - 20%	-81,132	0.810	Dominant	-23,299	0.011	Dominant

cost-effectiveness acceptability curve indicated a 100% probability of IDegLira being cost-effective (Fig. 2). However, in the one-way sensitivity analysis, when the body mass index (BMI) and hypoglycemia parameters in the IDegLira arm were altered, IDegLira showed a lower QALY compared to GLP-1RA added to basal insulin. In the scenario analysis, we compared the cost-effectiveness of IDegLira with the combination of insulin glargine and semaglutide. The results showed that the total cost for the IDegLira group decreased by CNY 36,972, but the QALY decreased by 0.044.

Discussion

This study employed the IHE cohort model to evaluate the cost-effectiveness of IDegLira compared to basal insulin intensification therapies in the Chinese setting. The results indicated that, following price negotiations for healthcare coverage, IDegLira emerged as the dominant option when compared to both basal-bolus therapy and GLP-1RA added to basal insulin for T2DM patients uncontrolled on basal insulin. Sensitivity analyses further reinforced the robustness of these findings.

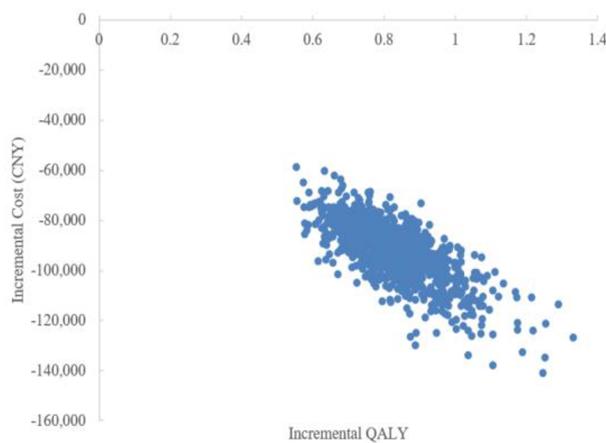
In the comparative analysis with basal-bolus therapy, simulation of the IDegLira group revealed an incremental gain in QALYs of 0.81 and a reduction in total costs by CNY 91,217. Specifically, the substantial costs associated with daily four times self-monitoring of blood glucose in the basal-bolus therapy result in higher annual expenditures compared to IDegLira. The DUAL VII trial demonstrated similar efficacy in HbA1c reduction between both approaches, yet IDegLira notably exhibited benefits in terms of body weight loss and lower hypoglycemia rates [19]. Although current clinical guidelines have not explicitly recommended IDegLira as a replacement for

basal-bolus therapy [29, 30], the cost-effectiveness and clinical evidence suggest that patients requiring basal-bolus therapy may find IDegLira a worthy consideration.

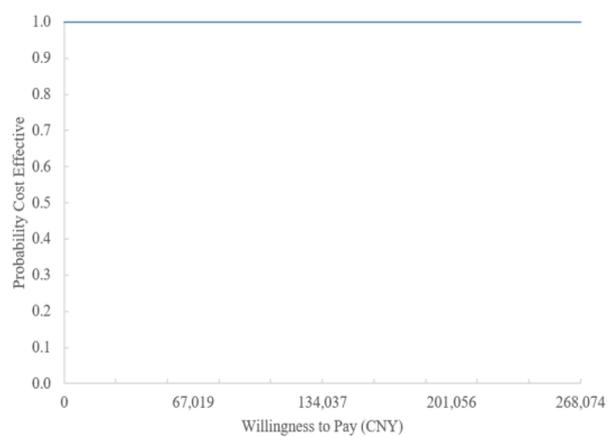
In the comparative analysis between IDegLira and GLP-1RA added to basal insulin, IDegLira demonstrated a marginal increase in QALYs by 0.011. Consequently, the cost-effectiveness of IDegLira may predominantly depend on its pricing. Previous studies evaluating the cost-effectiveness of IDegLira compared to its individual components in the Chinese setting have indicated that prior to price reduction, the ICER of IDegLira versus insulin degludec was United States dollar (USD) 99,464.12/QALYs, and versus liraglutide was USD 143,348.26/QALYs, both substantially exceeding the cost-effectiveness threshold in China [31]. However, post-price reduction, IDegLira emerged as dominant over both insulin degludec and Liraglutide. Negotiations with the Chinese National Healthcare Insurance have resulted in a notable enhancement in the cost-effectiveness of IDegLira [14, 32].

In accordance with the American Diabetes Association (ADA) guideline, it has been clearly stated that IDegLira can serve as an alternative to basal insulin combined with GLP-1RA [29]. One significant advantage lies in IDegLira's ability to reduce the frequency of injections thereby enhancing medication adherence [6]. Moreover, findings from a study spanning the UK, Canada and China revealed that injection disutilities were substantially greater in China compared to the UK and Canada [33]. Hence, utilization of IDegLira among Chinese patients requiring basal insulin combined with GLP-1RA therapy may offer a greater clinical advantage. Nevertheless, when the upper 95% confidence interval (CI) of BMI change and hypoglycemic episodes for the IDegLira arm

IDegLira versus basal-bolus therapy

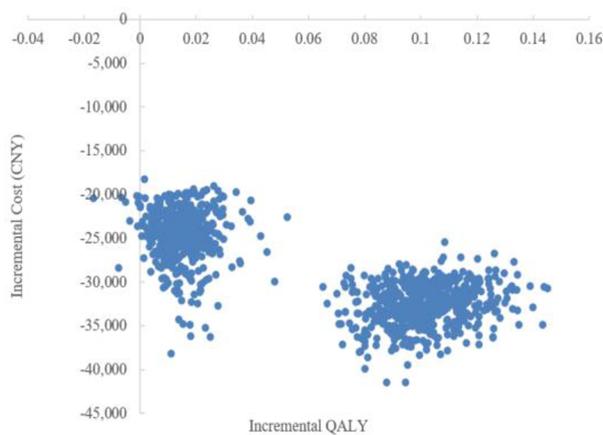


(A) Cost-effectiveness scatter plot

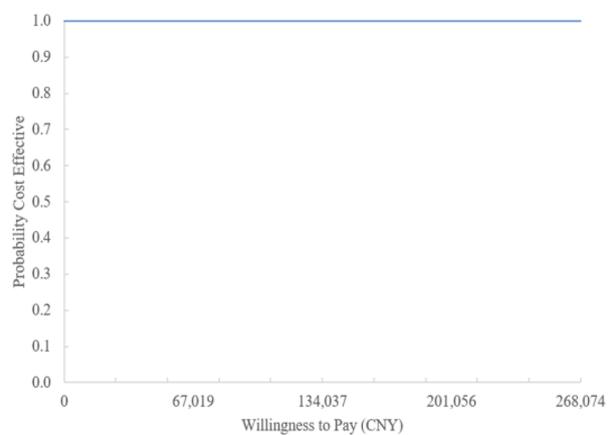


(B) Cost-effectiveness acceptability curve

IDegLira versus GLP-1RA added to basal insulin



(A) Cost-effectiveness scatter plot



(B) Cost-effectiveness acceptability curve

Fig. 2 Probabilistic sensitivity analysis results

were taken (reducing the BMI control capability of IDegLira and increasing the occurrence of hypoglycemic events), reversed ICERs were observed, resulting in a reduction in QALY gain in the OWSA. It was also found that IDegLira may have a lower QALY gain compared to basal insulin combined with semaglutide in the scenario analysis. Recent reviews have indeed shown that newer

GLP-1RAs, such as semaglutide and tirzepatide, demonstrate more favorable outcomes in terms of HbA1c control, weight control and blood pressure management [34–36]. As a result, the combination of basal insulin with GLP-1RA remains a promising avenue for further advancement. More research is needed to explore the implications of these newer GLP-1RAs on health system.

Some limitations should be considered in interpreting the results. Firstly, the study relied on relatively short-term clinical trial data to make long-term projections, a limitation common to related health economic analyses. Secondly, the treatment effects were not derived from studies based on the Chinese population. Therefore, future clinical trials, particularly real-world studies involving related patients, are imperative to validate the findings in our study. Thirdly, the risk equation derived from the UKPDS 82 primarily encompasses White Caucasian, Afro-Caribbean and Asian-indian populations. Consequently, caution should be exercised when extrapolating model outcomes to the Chinese population. Fourthly, the IHE model, as a cohort-based model, simulates outcomes based on the average baseline characteristics of the cohort. Compared to microsimulation, it has limitations in capturing patient heterogeneity [16]. Last but not least, our study specifically targeted patients with inadequate glycemic control on basal insulin, thus limiting the generalizability of our conclusions to individuals with inadequate control on GLP-1RAs. Notably, the ADA guideline advocates for GLP-1RA as an initial injectable option, suggesting a need for further exploration within this specific patients [29].

Conclusion

In conclusion, for T2DM patients uncontrolled on basal insulin, IDegLira was projected to be dominant both compared to basal-bolus therapy and GLP-1RA added to basal insulin in the Chinese setting.

Abbreviations

T2DM	Type 2 diabetes mellitus
GLP-1RA	Glucagon-like peptide-1 receptor agonist
CHEERS	Consolidated Health Economic Evaluation Reporting Standards
IHE	Swedish Institute for Health Economics
QALYs	Quality-adjusted life years
ICER	Incremental cost-effectiveness ratio
UKPDS	United Kingdom Prospective Diabetes Study
SBP	Systolic blood pressure
DBP	Diastolic blood pressure
TC	Total cholesterol
LDL	Low-density lipoprotein
HDL	High-density lipoprotein
TG	Triglycerides
BMI	Body mass index
HR	Heart rate
WBC	White blood cell count
eGFR	Glomerular filtration rate
SMBG	Self-monitoring of blood glucose
CNY	Chinese Yuan
CPI	Consumer price index
GDP	Gross domestic product
OWSA	One-way sensitivity analysis
PSA	Probabilistic sensitivity analysis
USD	United States dollar
ADA	American Diabetes Association

Supplementary Information

The online version contains supplementary material available at <https://doi.org/10.1186/s13098-025-01722-8>.

Supplementary Material 1

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Author contributions

The study was conceived and designed by all authors. Junling Weng and Dunming Xiao contributed to data collection. Junling Weng conducted the analyses presented. All authors were involved in writing the present manuscript.

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Data availability

All data generated or analysed during this study are included in this published article [and its supplementary information files].

Declarations

Ethics approval and consent to participate

Not applicable.

Consent for publication

Not applicable.

Competing interests

The authors declare no competing interests.

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