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Real-world cost-effectiveness of insulin degludec in type 1 and type 2 diabetes mellitus from a Swedish 1-year and long-term perspective

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ABSTRACT

Background and aims: The ReFLeCT study demonstrated that switching to insulin degludec from other basal insulins was associated with reductions in glycated hemoglobin and hypoglycemic events in type 1 (T1D) and type 2 diabetes (T2D), and reductions in insulin doses in T1D. The aim of the present analysis was to assess the short- and long-term cost-effectiveness of switching to insulin degludec in Sweden.

Methods: Short-term outcomes were evaluated over 1 year in a Microsoft Excel model, while long-term outcomes were projected over patient lifetimes using the IQVIA CORE Diabetes Model. Cohort characteristics and treatment effects were sourced from the ReFLeCT study. Costs (in 2018 Swedish krona [SEK]) encompassed direct medical expenditure and indirect costs from loss of workplace productivity. In the long-term analyses, patients were assumed to receive insulin degludec or continue prior insulin therapy (primarily insulin glargine U100) for 5 years, before all patients intensified to once-daily degludec and mealtime aspart.

Results: Switching to insulin degludec was associated with improved quality-adjusted life expectancy of 0.04 and 0.02 quality-adjusted life years (QALYs) over 1 year, and 0.16 and 0.08 QALYs over patient lifetimes, in T1D and T2D. Combined costs in T1D and T2D were estimated to be SEK 1,249 lower and SEK 1,181 higher over the short-term, and SEK 157,258 and SEK 2,114 lower over the long-term. Benefits were due to lower insulin doses in T1D, reduced rates of hypoglycemia, and lower incidences of diabetes-related complications. Insulin degludec was associated with an incremental cost-effectiveness ratio of SEK 64,298 per QALY gained for T2D over 1 year and considered dominant for T1D and T2D in all other comparisons.

Conclusions: Insulin degludec was projected to be cost-effective or dominant versus other basal insulins for the treatment of T1D and T2D in Sweden.

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Introduction

Diabetes represents a growing clinical and economic burden in Sweden, with prevalence of the disease expected to rise from 4.8% to 6.0% (with type 1 [T1D] and type 2 diabetes [T2D] estimated to account for 10% and 90% of cases, respectively), and diabetes-related expenditure projected to increase from approximately SEK 33 billion to SEK 35 billion (EUR 3.3 billion to EUR 3.5 billion, with SEK 1.00 approximately equal to EUR 0.10) between 2019 and 2045[1,2]. Healthcare systems are coming under ever-growing pressure with constrained budgets and increasing patient numbers, and payers often need to understand the benefits of investment in novel interventions, considering both the short- and long-term budgetary implications of reimbursement. Short-term cost-effectiveness analyses provide pertinent information for payers when considering annual budgets, while evaluations of interventions through long-term cost-effectiveness analyses are particularly crucial for diabetes as a large proportion of diabetes-related expenditure is associated with the treatment of long-term complications[3,4]. Landmark studies, such as the Diabetes Control and Complications Trial (DCCT) in T1D and the United Kingdom Prospective Diabetes Study (UKPDS) in T2D, have shown that reductions in glycated hemoglobin (HbA1c) result in fewer diabetes-related complications and improved patient outcomes in the long-term[5,6]. However, hypoglycemia is a common adverse event associated with insulin regimens that has pertinent clinical and economic impacts in the short-term[7,8]. Several studies

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have shown that hypoglycemic events not only have an impact on quality-of-life, but are also associated with substantial loss of workplace productivity and healthcare resource use – factors that are crucial in settings such as Sweden, where a societal perspective is often required for health economic evaluations[7–13].

Insulin regimens are essential for survival in T1D to replace lost insulin production, while insulin therapies maintain an important role for the treatment and control of progressive T2D. Based on guidelines published jointly by the European Association for the Study of Diabetes (EASD) and the American Diabetes Association (ADA), basal insulin therapies are indicated for the treatment of T2D as a third-line therapy in the majority of patients[14]. In patients with T2D with a compelling need to minimize the risk of hypoglycemia, avoid weight gain or promote weight loss, basal insulins are indicated as fourth-line therapy options[14].

Insulin degludec is a once-daily, long-acting basal insulin with a duration of action of more than 42 h, approved for the treatment of people with T1D and T2D[15]. Insulin degludec has been associated with lower rates of hypoglycemia versus other basal insulins in several clinical trials[16–18]. Recently, insulin degludec was assessed in a real-world setting in the prospective, observational, single-arm ReFLeCT study. ReFLeCT examined the impact of switching from non-degludec basal insulin therapy (with or without bolus insulin) to insulin degludec (with or without bolus insulin) in people with T1D and T2D[19]. This study showed that insulin degludec was associated with significantly fewer hypoglycemic events than previous insulin therapy, as well as significant reductions in HbA1c, in people with T1D and T2D, and lower insulin doses and slight increases in body weight in people with T1D.

The aim of the present analysis was to assess the impact of changes in hypoglycemic event rates on initiation of insulin degludec on short-term cost-effectiveness outcomes, and changes in HbA1c, body weight, and hypoglycemic events on long-term cost-effectiveness outcomes in patients with T1D and T2D in Sweden.

Methods

Modeling approach over 1 year

Short-term projections of cost-effectiveness were performed using a model built in Microsoft Excel 2016 (Microsoft Corporation, Redmond, WA), an older version of which was used in a previous short-term cost-effectiveness analysis of insulin degludec in Sweden (Supplementary Material, Figure S1)[20]. The model captured non-severe (sub-categorized into diurnal and nocturnal) and severe hypoglycemic event rates with insulin degludec and continuation of previous insulin therapy, as well as the costs of treating hypoglycemia, acquisition costs of included medications and consumables, and costs arising from loss of workplace productivity due to hypoglycemic events. Resource use captured basal and bolus insulin doses, routine needle use, self-monitoring of blood glucose (SMBG) tests, and additional blood glucose (BG) tests required following a hypoglycemic event. The model reported health outcomes of quality-adjusted life expectancy (expressed in quality-adjusted life years [QALYs]), direct and indirect costs, and, where applicable, incremental cost-effectiveness ratios (ICERs), which describe the cost per additional unit of effectiveness gained for the intervention versus the comparator. When an intervention is associated with improved clinical outcomes and cost savings, no ICER is calculated and it is instead considered dominant versus the comparator[21].

Clinical and cost outcomes were projected over a 1-year time horizon, with disease-specific and background mortality assumed to be zero in both treatment arms. Baseline quality-of-life and non-severe hypoglycemic event disutilities were taken from published sources, while severe hypoglycemic event disutilities were taken from an unpublished Sweden-specific subset of subsequently published data (Supplementary Material, Table S1)[22–24].

Long-term modeling approach

Long-term projections of cost-effectiveness were performed using the IQVIA CORE Diabetes Model (version 9.0; IQVIA, Durham, NC), an interactive, internet-based computer model developed to evaluate the long-term health outcomes and economic consequences of implementing interventions in the treatment of T1D and T2D (Supplementary Material, Figure S2)[25,26]. Previous publications have detailed the architecture, assumptions, features, and capabilities of the model, which have been validated both in 2004 and 2014[26,27]. Model outputs include time to onset and cumulative incidence of complications, life expectancy, quality-adjusted life expectancy (expressed in QALYs), direct and indirect costs, and, where required, ICERs.

Clinical and cost outcomes were projected over patient lifetimes, as per the guidelines for the assessment of cost-effectiveness for interventions for diabetes[28]. Background mortality was captured based on Sweden-specific life tables published by the World Health Organization (Supplementary Material, Table S2)[29]. Health-state utilities and event disutilities relating to quality-of-life were specific to T1D and T2D and were based on published sources (Supplementary Material, Table S3)[22,23,25,30–37].

Patients were assumed to switch to insulin degludec (maintaining any prior bolus insulin therapy) or continue previous insulin therapy for 5 years, before all patients in both treatment arms intensified to insulin degludec plus mealtime insulin aspart.

Clinical data

Baseline patient characteristics and treatment effects for insulin degludec were sourced from the ReFLeCT study (approved by the Institutional Review Board [IRB]), where available (Table 1 and Supplementary Material, Table S4)[19]. The ReFLeCT study enrolled 556 insulin-treated adults with T1D and 611 insulin-treated adults with T2D with treatment plans to initiate insulin degludec. No treatment effects were applied for the continuation of previous insulin therapy, with parameters for this treatment arm assumed to remain at

Table 1. Insulin doses and treatment effects from the ReFLeCT study applied in the cost-effectiveness analyses of insulin degludec in type 1 and type 2 diabetes in Sweden.

Parameter	Type 1 diabetes		Type 2 diabetes	
	Switching to insulin degludec	Continuation of previous insulin therapy	Switching to insulin degludec	Continuation of previous insulin therapy
Daily insulin doses (IU)				
Basal insulin	22.8	25.0	37.5	37.5
Bolus insulin	23.8	27.3	38.9	38.9
Physiological parameters applied in the first year of the long-term analysis				
HbA1c (%)	−0.15 (0.04)	0 (0)	−0.32 (0.05)	0 (0)
HbA1c (mmol/mol)	−1.6 (0.4)	0 (0)	−3.5 (0.5)	0 (0)
Body mass index (kg/m^2)	0.28 (0.07)	0 (0)	0 (0)*	0 (0)
Hypoglycemic events applied in the short- and long-term analyses				
Non-severe hypoglycemic events (per 100 patient-years)	6,530	7,896	764	1,402
Severe hypoglycemic events (per 100 patient-years)	22.7	81.0	2.00	2.00
Proportion of nocturnal non-severe hypoglycemic events	0.08	0.10	0.06	0.09
Proportion of nocturnal severe hypoglycemic events	0.00	0.00	0.00	0.00

Abbreviations. HbA1c, glycated hemoglobin; IU, international units.
Values are means (standard deviations).
*Difference reported in the ReFLeCT study did not reach statistical significance and was therefore not applied in the analysis.

baseline, as participants were receiving these medications prior to the study initiation. On initiation of insulin degludec, only treatment effects that reached statistical significance in the ReFLeCT study were applied. HbA1c was measured according to the National Glycohemoglobin Standardization Program (NGSP), based on the DCCT[38]. Change in HbA1c was not applied in the short-term analysis, as differences in glycemic control would not be expected to drive differences in complication rates over a 1-year time horizon.

Cost data and resource use

Costs were accounted from a Swedish societal perspective and expressed in 2018 Swedish krona (SEK). In the short-term analysis, direct costs captured costs of medications and consumables and costs of hypoglycemia, while indirect costs captured loss of workplace productivity arising from hypoglycemic events (Supplementary Material, Tables S5 and S6)[39,40]. In the long-term analysis, direct costs captured medication and consumables costs, costs of treating diabetes-related complications, and the costs of patient management (Supplementary Material, Tables S5 and S7–S11). Indirect costs in the long-term analysis captured loss of workplace productivity from annual days off work estimates estimated by Sørenson and Plough[41] and the most recent annual salaries available in Sweden (Supplementary Material, Table S12)[42]. Indirect costs in both the short- and long-term analyses were only accrued while simulated patients were below the set retirement age (65 years). Costs of included medications and consumables were based on published list prices (sourced in November 2019), while costs of complications were based on published sources and inflated to 2018 SEK where appropriate using the most recently available inflation rate for health published by Statistics Sweden (Supplementary Material, Table S11)[39,40,43–48].

The cost of basal insulin therapy in the continuation of a previous therapy arm was based on a weighted average of basal insulin use in the ReFLeCT study. In T1D, 63.8% of people were receiving insulin glargine U100, 22.7% were receiving insulin detemir, and 13.5% were receiving other or unclassified basal insulins. In T2D, 59.1% of people were receiving insulin glargine U100, 20.8% were receiving insulin detemir, and 20.1% were receiving other or unclassified basal insulins. People receiving other or unclassified basal insulins in both the T1D and T2D analyses were assumed to receive insulin NPH, the lowest priced basal insulin in Sweden, to ensure the analyses were conservative from the perspective of insulin degludec. The daily doses of basal insulin (22.8 and 25.0 international units [IU] for insulin degludec and comparator insulin, respectively, in T1D, and 37.5 IU in both arms for T2D) were based on data from the ReFLeCT study. The daily doses of insulin aspart in each treatment arm (23.8 and 27.3 IU for insulin degludec and comparator insulin, respectively, in T1D, and 38.9 IU in both arms for T2D) were weighted according to the proportion of patients receiving bolus insulin.

Sensitivity analyses

The projection of long-term outcomes from short-term data is associated with uncertainty. To evaluate the impact of alternative data inputs and assumptions on long-term cost-effectiveness outcomes, several sensitivity analyses were performed. These included:

- Shortening the time horizon of the analysis to 20 years, 10 years, and 1 year (for which it should be noted that not all patients had died, and therefore not all relevant clinical and cost outcomes were captured);
- Applying discount rates of 0% and 5% in separate analyses;
- Evaluating the key drivers of clinical benefits by applying the differences in HbA1c, body mass index (BMI), and hypoglycemia in turn in separate analyses;
- Application of the biosimilar insulin glargine (Abasaglar) price rather than the insulin glargine U100 (Lantus) price in the previous insulin therapy treatment arm (Supplementary Material, Table S5);

- Abolishing the dose differences between the two treatment arms; and
- Combining the application of the biosimilar insulin glargine price in the previous insulin therapy treatment arm with the abolition of the differences in dosing.

As the projection of short-term outcomes is associated with less uncertainty, only two sensitivity analyses were performed for the short-term approach. In one analysis, the price of biosimilar insulin glargine was applied in the place of insulin glargine U100 in the continuation of the previous insulin therapy arm, while, in the other, people in the T2D cohort were assumed to accrue indirect costs.

Results

Short-term base case analysis

Short-term projections of clinical and cost outcomes over a 1-year time horizon indicated that switching to insulin degludec resulted in improved quality-adjusted life expectancy of 0.04 QALYs in people with T1D and 0.02 QALYs in people with T2D compared with continuation of previous basal insulin therapy (Table 2). Clinical benefits were a result of fewer hypoglycemic events with insulin degludec versus continuation of previous insulin therapy.

Direct costs were estimated to be SEK 795 lower with insulin degludec in people with T1D over 1 year, with higher treatment costs entirely offset due to cost savings from avoidance of hypoglycemic events (SEK 1,191 per patient; Figure 1). Further indirect cost savings of SEK 453 were achieved through reduced loss of workplace productivity, leading to total combined cost savings of SEK 1,249 for insulin degludec in people with T1D. In people with T2D, insulin degludec was associated with direct cost increases of SEK 1,181 versus continuation of previous insulin therapy, with higher treatment costs partially offset by cost savings due to avoidance of hypoglycemia (SEK 440 per patient). Indirect costs were not accrued in the T2D analyses as patients were beyond the set retirement age (65 years) at baseline.

With improved clinical outcomes and cost savings, insulin degludec was considered dominant versus continuation of previous insulin therapy for people with T1D over a 1-year time horizon in Sweden (Table 2). For people with T2D, insulin degludec was associated with improved clinical outcomes and increased costs, and was therefore associated with an ICER of SEK 64,298 per QALY gained versus continuation of previous insulin therapy (Table 2). Based on a willingness-to-pay threshold of SEK 500,000 per QALY gained in Sweden, insulin degludec was considered a cost-effective treatment option in people with T2D versus continuation of previous insulin therapy over the short-term.

Long-term base case analysis

Long-term projections of clinical outcomes indicated that switching to insulin degludec resulted in improved life expectancy of 0.06 years and improved quality-adjusted life expectancy of 0.16 QALYs versus continuation of previous insulin therapy in people with T1D, and improved life expectancy and quality-adjusted life expectancy of 0.05 years and 0.08 QALYs, respectively, in people with T2D (Table 3). Clinical benefits were a result of reduced incidences of diabetes-related complications with insulin degludec in both comparisons, with the mean time to onset of any diabetes-related complication estimated to be 0.3 and 0.2 years longer in the T1D and T2D analyses, respectively.

Over patient lifetimes, direct costs were estimated to be SEK 7,559 and SEK 2,114 lower with insulin degludec in people with T1D and T2D, respectively, with higher treatment costs entirely offset by cost savings due to avoidance of diabetes-related complications (most notably renal complications in T1D, with mean cost savings of SEK 3,492 per patient, and diabetic foot ulcer, amputation, and neuropathy complications in T2D, with mean cost savings of SEK 5,469 per patient; Figure 2). Indirect cost savings were only accrued in the T1D analyses and totaled SEK 149,699. As per the short-term analysis, indirect costs were not accumulated in the long-term T2D analyses as patients were above the set retirement age (65 years) at baseline.

With improved clinical outcomes and cost savings, insulin degludec was considered dominant versus continuation of previous insulin therapy for people with T1D and T2D over a lifetime time horizon in Sweden (Table 3).

Sensitivity analyses

Type 1 diabetes

Sensitivity analyses showed that the results of the base case analyses were robust to changes in input parameters and assumptions (Table 4). In the long-term T1D analyses, application of shorter time horizons led to reduced quality-adjusted life expectancy for both treatment arms, and reduced incremental benefits with insulin degludec, demonstrating the importance of reductions in the incidence of long-term complications. However, switching to insulin degludec remained dominant versus previous insulin therapy. Lowering the discount rates to 0% led to increased clinical benefits and cost savings with insulin degludec, while increasing the discount rates to 5% had the converse effect, with clinical benefits and cost savings reduced.

Testing for the key drivers of clinical benefits by applying each of the HbA1c, BMI, and hypoglycemic event differences in turn showed that fewer hypoglycemic events with insulin degludec were the biggest driver of improved quality-adjusted life expectancy and cost savings, with benefits of 0.09 QALYs and cost savings of SEK 137,785 per patient when only this difference between the treatment arms was applied. The difference in HbA1c also made a substantial contribution, with improvements in quality-adjusted life expectancy of 0.04 QALYs when only this difference was applied. Differences in BMI made negligible contributions to the clinical benefits observed in the base case analysis.

Applying the cost of biosimilar insulin glargine in the previous insulin therapy arm of the long-term analysis led to slightly decreased cost savings, but no changes to the

Table 2. Short-term cost-effectiveness outcomes of insulin degludec versus continuation of previous insulin therapy in type 1 and type 2 diabetes in Sweden.

Health outcomes	Switching to insulin degludec	Continuation of previous insulin therapy	Difference
Type 1 diabetes			
Quality-of-life (QALYs)	0.74	0.70	+0.04
Direct costs (SEK)	11,778	12,573	−795
Combined costs (SEK)	12,582	13,830	−1 249
ICER based on direct costs	Insulin degludec dominant		
ICER based on combined costs	Insulin degludec dominant		
Type 2 diabetes			
Quality-of-life (QALYs)	0.74	0.72	+0.02
Direct costs (SEK)*	12,881	11,699	+1 181
ICER based on direct costs*	SEK 64,298 per QALY gained		

Abbreviations. ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; SEK, 2018 Swedish krona.
Values are means. Combined costs are a sum of direct and indirect costs.
*Only direct costs were accrued in the type 2 diabetes analysis, as the mean age of the population at baseline was greater than the defined retirement age.

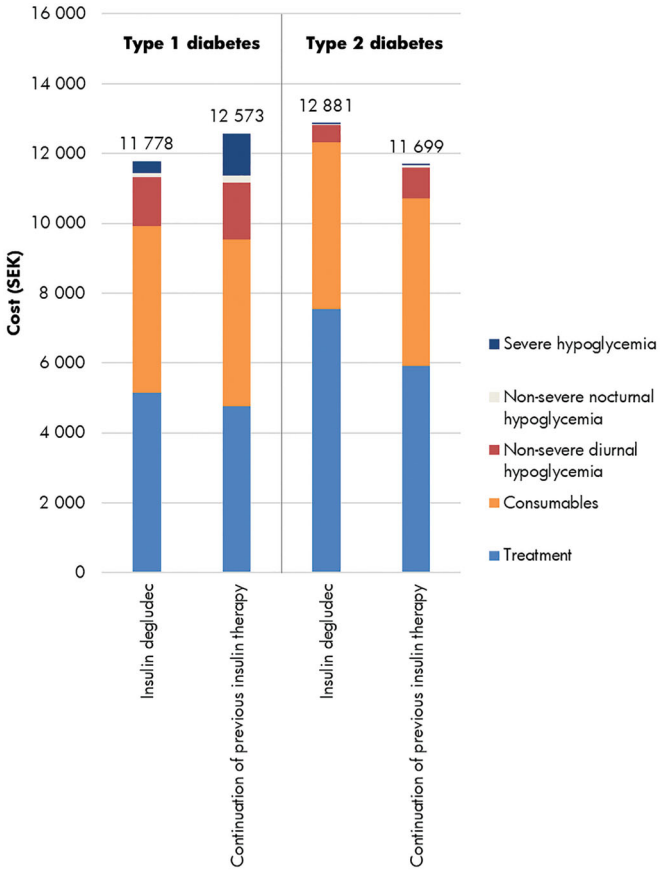

Figure 1. Short-term mean direct costs over 1 year in the cost-effectiveness analyses of insulin degludec in type 1 and type 2 diabetes in Sweden. SEK, 2018 Swedish krona.

conclusion that switching to insulin degludec was dominant. A similar outcome was observed in the short-term analysis with this price applied, with reduced cost savings, but insulin degludec remaining dominant versus previous insulin therapy. Abolishing the differences in doses of basal insulins between the treatment arms of the long-term analysis and combining this with the price of biosimilar insulin glargine in separate analyses led to only minor changes in cost outcomes and insulin degludec remained dominant versus continuation of previous insulin therapy.

Type 2 diabetes

Sensitivity analyses around the key inputs and assumptions of the T2D analyses also showed that the results of the base case analyses were robust to changes (Table 4). Application of shorter time horizons led to reduced clinical outcomes for both treatment arms – with a 1-year time horizon applied, insulin degludec was associated with an ICER of SEK 156,379 per QALY gained, while use of a 10-year time horizon yielded an ICER of SEK 24,890 per QALY gained. Application of a 20-year time horizon resulted in cost savings and switching to insulin degludec was considered dominant versus previous insulin therapy. Lowering the discount rates to 0% led to greater clinical benefits and cost savings with insulin degludec, while increasing the discount rates to 5% had the converse effect, but insulin degludec remained dominant.

Testing for the key drivers of clinical benefits by applying the HbA1c and hypoglycemic event differences in turn showed that the greater reduction in HbA1c with insulin degludec was the biggest driver of improved outcomes, with clinical benefits of 0.05 QALYs and cost savings of SEK 337 per patient when only these differences between the treatment arms were applied. The difference in hypoglycemic event rates also made a substantial contribution, with improvements in quality-adjusted life expectancy of 0.03 QALYs when only this difference was applied. There was no difference in changes in BMI between the treatment arms in the T2D analyses, as there was no statistically significant difference between the treatment arms for this parameter in people with T2D in the ReFLeCT study.

Applying the cost of biosimilar insulin glargine in the previous insulin therapy arm of the long-term analysis led to smaller cost savings with insulin degludec, but it remained dominant versus continuation of previous insulin therapy. In the short-term analysis, applying this price led to increased incremental costs, and an ICER of SEK 85,035 per QALY gained for insulin degludec versus previous insulin therapy. Assuming people in the T2D cohort accrued indirect costs led to reduced incremental costs with insulin degludec, and it was associated with an ICER of SEK 30,500 per QALY gained.

Table 3. Long-term cost-effectiveness outcomes of insulin degludec versus continuation of previous insulin therapy in type 1 and type 2 diabetes in Sweden.

Health outcomes	Switching to insulin degludec	Continuation of previous insulin therapy	Difference
Type 1 diabetes			
Undiscounted life expectancy (years)	29.36	29.23	+0.13
Discounted life expectancy (years)	18.21	18.15	+0.06
Discounted quality-adjusted life expectancy (QALYs)	12.78	12.62	+0.16
Discounted direct costs (SEK)	658,848	666,407	−7,559
Discounted combined costs (SEK)	3,900,725	4,057,983	−157,258
ICER based on direct costs	Insulin degludec dominant		
ICER based on combined costs	Insulin degludec dominant		
Type 2 diabetes			
Undiscounted life expectancy (years)	16.96	16.88	+0.08
Discounted life expectancy (years)	12.29	12.24	+0.05
Discounted quality-adjusted life expectancy (QALYs)	8.48	8.40	+0.08
Discounted direct costs (SEK)*	552,358	554,472	−2,114
ICER based on direct costs*	Insulin degludec dominant		

Abbreviations. ICER, incremental cost-effectiveness ratio; QALY, quality-adjusted life year; SEK, 2018 Swedish krona.
Values are means. Combined costs are a sum of direct and indirect costs.
*Only direct costs were accrued in the type 2 diabetes analysis, as the mean age of the population at baseline was greater than the defined retirement age.

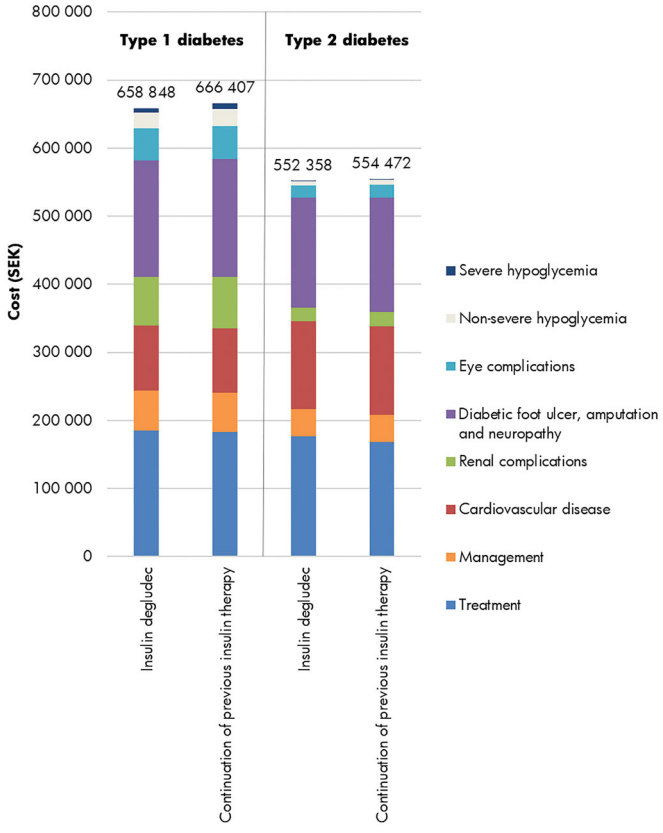

Figure 2. Long-term mean direct costs over patient lifetimes in the cost-effectiveness analyses of insulin degludec in type 1 and type 2 diabetes in Sweden. SEK, 2018 Swedish krona.

Discussion

The present analysis has shown that, based on both short- and long-term projections of outcomes from the real-world ReFLeCT study, switching to insulin degludec results in improved clinical outcomes versus continuation of previous insulin therapy in people with T1D and T2D in Sweden[19]. Over a 1-year time horizon, insulin degludec was associated with cost savings in people with T1D, but cost increases in people with T2D. Over patient lifetimes, cost savings were projected in both T1D and T2D with insulin degludec. Clinical benefits in the short-term analysis were a result of fewer hypoglycemic events. In the long-term analysis, clinical benefits were achieved through projected reduced incidences and delayed time to onset of diabetes-related complications with insulin degludec, due to the greater reductions in HbA1c. Reductions in the incidences of diabetes-related complications also yielded cost savings in both the T1D and T2D long-term analyses, with higher treatment costs entirely offset. Based on a willingness-to-pay threshold of SEK 500,000 per QALY gained in Sweden, insulin degludec was considered a dominant treatment option in people with T1D and a cost-effective treatment option in people with T2D versus continuation of previous insulin therapy over the short-term, and a dominant treatment option in both people with T1D and T2D versus continuation of previous insulin therapy over the long-term.

Insulin degludec has long been associated with comparable glycemic control but fewer hypoglycemic events versus other basal insulins in several clinical trials[16–18]. However, evidence suggests that the burden of hypoglycemic events are often underestimated in clinical trials compared with real-world practice[49]. Up to now, observational studies that examined insulin degludec with hypoglycemia events prospectively recorded were lacking, but the ReFLeCT study offers a novel source of evidence to fill this data gap[19]. Using data from the ReFLeCT study, the present analyses have shown that reductions in hypoglycemia are key drivers of improvements in quality-of-life for both people with T1D and T2D, while reducing costs for the healthcare payer over patient lifetimes. These clinical benefits were observed over both the short- and long-term, with results over a 1-year time horizon comparable across the two different models, and insulin degludec remained a cost-effective or dominant treatment option in both T1D and T2D. Additional significant benefits observed with insulin degludec in the ReFLeCT study, such as greater reductions in HbA1c, were also projected to lead to further long-term improvements in life expectancy and quality-adjusted life expectancy, while providing further cost savings from fewer diabetes-related complications[19].

The use of evidence from a real-world study might also represent a limitation of the present analysis, but these data provide robust evidence of how the included interventions

Table 4. Sensitivity analysis results of insulin degludec versus continuation of previous insulin therapy in type 1 and type 2 diabetes in Sweden.

Analysis	Type 1 diabetes			Type 2 diabetes		
	Δ discounted QALE (QALYs)	Δ discounted combined costs (SEK)	ICER (SEK per QALY gained)	Δ discounted QALE (QALYs)	Δ discounted combined costs (SEK)	ICER (SEK per QALY gained)
Short-term analysis						
Base case	+0.04	−1,249	Degludec dominant	+0.02	+1 181	64,298
Biosimilar insulin glargine (Abasaglar) cost applied for insulin glargine U100 in continuation of previous insulin therapy arm	+0.04	−982	Degludec dominant	+0.02	+1 562	85,035
People in the T2D cohort assumed to accrue indirect costs	-	-	-	+0.02	+560	30,500
Long-term analysis						
Base case	+0.16	−157,258	Degludec dominant	+0.08	−2,114	Degludec dominant
1-year time horizon	+0.03	−39,379	Degludec dominant	+0.01	+1,095	156,379
10-year time horizon	+0.11	−149,273	Degludec dominant	+0.05	+1,249	24,890
20-year time horizon	+0.12	−154,838	Degludec dominant	+0.08	−2,757	Degludec dominant
0% discount rates	+0.23	−177,901	Degludec dominant	+0.11	−3,226	Degludec dominant
5% discount rates	+0.13	−145,558	Degludec dominant	+0.07	−1,482	Degludec dominant
HbA1c difference only	+0.04	−5,998	Degludec dominant	+0.05	−337	Degludec dominant
Hypoglycemia rate difference only	+0.09	−137,785	Degludec dominant	+0.03	+5 447	173,467
BMI difference only	+0.00	+4,040	Degludec equally effective and more costly	Difference not statistically significant		
Biosimilar insulin glargine (Abasaglar) cost applied for insulin glargine U100 in continuation of previous insulin therapy arm	+0.16	−156,107	Degludec dominant	+0.08	−574	Degludec dominant
Dose difference abolished	+0.16	−154,622	Degludec dominant	Difference not statistically significant		
Biosimilar insulin glargine (Abasaglar) cost applied for insulin glargine U100 in continuation of previous insulin therapy arm and dose difference abolished	+0.16	−153,471	Degludec dominant	Difference not statistically significant		

Abbreviations. BMI, body mass index; HbA1c, glycated hemoglobin; ICER, incremental cost-effectiveness ratio; QALE, quality-adjusted life expectancy; QALY, quality-adjusted life year; SEK, 2018 Swedish krona. Combined costs are a sum of direct and indirect costs.

perform in real-world clinical practice and possibly include more accurate rates of hypoglycemia than those reported in clinical trials[49]. While confounding factors can often play a role in real-world studies, the present analysis aimed to mitigate some uncertainty by applying only statistically significant differences between the interventions. The results of the present health economic analysis are also in line with previous long-term cost-effectiveness analyses of insulin degludec versus insulin glargine based on real-world data, with insulin degludec representing a dominant treatment option in both T1D and T2D in Italy[50]. The use of data from a single-arm study might also be seen as a potential weakness, as treatment effects are inseparable from study effects. Changes in insulin doses, dose intervals, and add-on or removal of bolus insulin and other antihyperglycemic medications were at the discretion of the treating physician during the ReFLeCT study and this could have influenced outcomes. However, the proportion of patients using antidiabetic therapies during the 12-month follow-up period was similar to that of the baseline period. Moreover, results from both the present study and previous analyses based on real-world data match those in several other country settings based on clinical trial data, with the consistency between the two types of data sources lending credence to the conclusions of the present study[51–53].

The projection of long-term outcomes from short-term data represents a limitation of the long-term analysis. This is, however, an essential tenet of all long-term diabetes modeling, and arguably represents the most robust source of evidence in the absence of long-term clinical trial data. The inclusion of the short-term analysis, as well as the performed sensitivity analyses that test the inputs and assumptions of the present study, also mitigate some of the uncertainty around these long-term projections and represent a key strength, with insulin degludec remaining a cost-effective or dominant treatment option throughout.

Conclusions

Compared to previous basal insulin therapy (with insulin glargine U100 at both originator and biosimilar prices), switching to insulin degludec was projected to be dominant in people with T1D and cost-effective in people with T2D over 1 year, and dominant in both people with T1D and T2D over a lifetime time horizon from a Swedish societal perspective.

Transparency

Declaration of funding

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Declaration of financial/other interests

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Data availability statement

All data generated or analyzed during this study are included in this published article/as supplementary information files.

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